

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2022

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO

Commission File Number 001-39335

Repare Therapeutics Inc.

(Exact name of Registrant as specified in its Charter)

Québec
(State or other jurisdiction of
incorporation or organization)

7210 Frederick-Banting, Suite 100
St-Laurent, Québec, Canada
(Address of principal executive offices)

Not applicable
(I.R.S. Employer
Identification No.)

H4S 2A1
(Zip Code)

Registrant's telephone number, including area code: (857) 412-7018

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Shares, no par value	RPTX	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input type="checkbox"/>		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

The aggregate market value of the registrant's common shares held by non-affiliates was \$454,878,023 as of June 30, 2022, based on a total of 32,514,512 common shares held by non-affiliates and a closing price of \$13.99 as reported on The Nasdaq Stock Market on June 30, 2022.

The number of shares of registrant's common shares outstanding as of February 24, 2023 was 42,077,896.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for the registrant's 2023 annual meeting of shareholders, which is to be filed within 120 days after the end of the registrant's fiscal year ended December 31, 2022, are incorporated by reference into Part III of this Form 10-K, to the extent described in Part III.

Table of Contents

	<u>Page</u>
<u>SUMMARY RISK FACTORS</u>	1
<u>SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS</u>	3
<u>PART I</u>	5
Item 1. <u>Business</u>	5
Item 1A. <u>Risk Factors</u>	50
Item 1B. <u>Unresolved Staff Comments</u>	104
Item 2. <u>Properties</u>	104
Item 3. <u>Legal Proceedings</u>	104
Item 4. <u>Mine Safety Disclosures</u>	105
<u>PART II</u>	106
Item 5. <u>Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	106
Item 6. <u>[Reserved]</u>	106
Item 7. <u>Management’s Discussion and Analysis of Financial Condition and Results of Operations</u>	107
Item 7A. <u>Quantitative and Qualitative Disclosures About Market Risk</u>	124
Item 8. <u>Financial Statements and Supplementary Data</u>	125
Item 9. <u>Changes in and Disagreements With Accountants on Accounting and Financial Disclosure</u>	161
Item 9A. <u>Controls and Procedures</u>	161
Item 9B. <u>Other Information</u>	162
Item 9C. <u>Disclosure Regarding Foreign Jurisdictions that Prevent Inspections</u>	162
<u>PART III</u>	163
Item 10. <u>Directors, Executive Officers and Corporate Governance</u>	163
Item 11. <u>Executive Compensation</u>	163
Item 12. <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	163
Item 13. <u>Certain Relationships and Related Transactions, and Director Independence</u>	163
Item 14. <u>Principal Accounting Fees and Services</u>	163
<u>PART IV</u>	164
Item 15. <u>Exhibits, Financial Statement Schedules</u>	164
Item 16. <u>Form 10-K Summary</u>	168

SUMMARY RISK FACTORS

Investing in our common shares involves numerous risks, including the risks described in “Part I—Item 1A. Risk Factors” of this Annual Report on Form 10-K. Below are some of our principal risks, any one of which could materially adversely affect our business, financial condition, results of operations, and prospects:

- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We will require substantial additional funding to finance our operations. If we are unable to raise capital when needed, we could be forced to delay, reduce, or terminate certain of our product development programs or other operations.
- We are very early in our development efforts. If we are unable to advance our product candidates into and through clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Our business substantially depends upon the successful development of product candidates generated through the application of our SNIPRx platform, and in particular, our initial product candidates, camonsertib and RP-6306. If we or our collaborators, are unable to obtain regulatory approval for, and successfully commercialize, products developed through the application of our SNIPRx platform, our business may be materially harmed.
- The effects of health epidemics, including the ongoing COVID-19 pandemic, in regions where we, or the third parties on which we rely, have business operations could adversely impact our business, including our preclinical studies and clinical trials. The COVID-19 pandemic could materially affect our operations, including at our offices in Montréal and in the Boston Metro Area, and at our clinical trial sites, as well as the business or operations of our CROs or other third parties with whom we conduct business.
- The successful development of targeted therapeutics, including our portfolio of synthetic lethality small molecule inhibitors, as well as any related diagnostics, is highly uncertain.
- The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, on a timely basis or at all, our business will be substantially harmed.
- Synthetic lethality represents an emerging class of precision medicine targets, and negative perceptions of the efficacy, safety, or tolerability of this class of targets, including any that we develop, could adversely affect our ability to conduct our business, advance our product candidates or obtain regulatory approvals.
- We may not be successful in applying our SNIPRx platform to discover synthetic lethality targets with therapeutic and commercial potential or in the discovery and development of commercially viable product candidates for us or our collaborators.
- Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates. We may find it difficult to enroll patients in our ongoing and planned clinical trials with the genomic alterations that these trials are designed to target.
- We face substantial competition, which may result in others developing or commercializing drugs before or more successfully than us.
- If we fail to develop new products and product candidates or compete successfully with respect to acquisitions, joint ventures, licenses or other collaboration opportunities, our ability to continue to expand our product pipeline and our growth and development would be impaired.
- We rely on third parties to supply and manufacture our product candidates, and we expect to continue to rely on third parties to manufacture our products, if approved. The development of such product candidates and the commercialization of any products, if approved, could be stopped, delayed, or made less profitable if any such third party fails to provide us with sufficient quantities of product candidates or products or fails to do so at acceptable quality levels or prices or fails to maintain or achieve satisfactory regulatory compliance.

- Our success depends in part on our ability to obtain intellectual property rights for our proprietary technologies and product candidates, as well as our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- The trading price of our common shares has been and is likely to continue to be volatile and fluctuate substantially.

SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our strategy, future financial condition, future operations, research and development costs, plans and objectives of management, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “positioned,” “potential,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain.

The forward-looking statements in this Annual Report include, among other things, statements about:

- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and related preparatory work and the period during which the results of the trials will become available, as well as our research and development programs;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to obtain regulatory approval of RP-6306 and any of our other current and future product candidates that we develop;
- our ability to identify and develop additional product candidates using our SNIPRx platform;
- business disruptions affecting the initiation, patient enrollment, development and operation of our clinical trials, including a public health emergency or pandemic, such as the coronavirus disease, or COVID-19, pandemic;
- the evolving impact of the COVID-19 pandemic and any variants on our operations, the continuity of our business, including our preclinical studies and clinical trials, supply chains, general economic conditions and our ability to raise additional capital;
- our ability to enroll patients in clinical trials, to timely and successfully complete those trials and to receive necessary regulatory approvals;
- the timing of completion of enrollment and availability of data from our current preclinical studies and clinical trials, including our Phase 1 clinical trials of RP-6306;
- the expected timing of filings with regulatory authorities for any product candidates that we develop;
- our expectations regarding the potential market size and the rate and degree of market acceptance for any product candidates that we develop, including other current and future product candidates that we develop;
- our ability to receive any milestone or royalty payments under our collaboration and license agreements;
- the effects of competition with respect to RP-6306, camonsertib or any of our other current or future product candidates, as well as innovations by current and future competitors in our industry;
- our ability to fund our working capital requirements;
- our intellectual property position, including the scope of protection we are able to establish, maintain and enforce for intellectual property rights covering our product candidates;
- our financial performance and our ability to effectively manage our anticipated growth;
- our ability to obtain additional funding for our operations; and
- other risks and uncertainties, including those listed under the section titled “Risk Factors” in this Annual Report.

Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, and involve known and unknown risks, uncertainties and other factors including, without limitation, risks, uncertainties and assumptions regarding the impact of the COVID-19 pandemic on our business, operations, strategy, goals and anticipated timelines, our ongoing and planned preclinical activities, our ability to initiate, enroll, conduct or complete ongoing and planned clinical trials, our timelines for regulatory submissions and our financial position that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. You are urged to carefully review the disclosures we make concerning these risks and other factors that may affect our business and operating results in this Annual Report. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this document. Except as required by law, we do not intend, and undertake no obligation, to update any forward-looking information to reflect events or circumstances.

Item 1. Business.**Overview**

We are a leading clinical-stage precision oncology company enabled by our proprietary synthetic lethality approach to the discovery and development of novel therapeutics. Synthetic lethality, or SL, represents a clinically validated approach to drug development. We use our proprietary, genome-wide, CRISPR-enabled SNIPRx platform to systematically discover and develop highly targeted cancer therapies focused on genomic instability, including DNA damage repair. SL arises when a deficiency in either of two genes is tolerated in cells, but simultaneous deficiencies in both genes cause cell death. Cancer cells that contain a mutation in one gene of a SL pair are susceptible to therapeutic intervention targeting the other gene pair. Using our SNIPRx platform, we are developing our pipeline of SL product candidates, including our initial product candidate, camonsertib (RP-3500 or RG6526), a potent and selective oral small molecule inhibitor of ATR (Ataxia-Telangiectasia and Rad3-related protein kinase) for the treatment of solid tumors with specific DNA damage repair-related genomic alterations, including those in the ATM gene (ataxia telangiectasia mutated kinase). In July 2020, we began dosing patients in our Phase 1/2 TRESR (Treatment Enabled by SNIPRx) clinical trial of camonsertib in advanced solid tumors and, in August 2021, we began dosing patients in our Phase 1b/2 ATTACC clinical trial of camonsertib to evaluate the safety and efficacy of camonsertib in combination with approved poly (ADP-ribose) polymerase, or PARP, inhibitors, olaparib and niraparib, in patients with molecularly selected cancers. We signed a worldwide license and collaboration agreement with Roche for the development and commercialization of camonsertib in June 2022, which resulted in a \$125 million upfront payment and up to an additional \$1.172 billion in potential development, regulatory, commercial and sales milestones, plus royalties on global net product sales.

In April 2021, we initiated our Phase 1 MYTHIC clinical trial for RP-6306, our PKMYT1 (Protein Kinase Membrane-associated tyrosine- and threonine- specific cdc-2 inhibitory kinase) SL inhibitor, as a monotherapy for the treatment of molecularly selected advanced solid tumors, and anticipate early Phase 1 read-outs from the trial in the first half of 2023. We initiated Phase 1 combination studies of RP-6306 with gemcitabine (MAGNETIC) in December 2021, camonsertib (MYTHIC) in May 2022, and FOLFIRI (MINOTAUR) in August 2022, each for the treatment of molecularly selected advanced solid tumors, and anticipate providing an update on some of these combination studies in the fourth quarter of 2023. In the fourth quarter of 2022, we received fast track designation for RP-6306 in combination with gemcitabine for the treatment of adult patients with CCNE1 amplified, or FBXW7, or PPP2R1A mutated platinum resistant ovarian cancer. Based on promising preclinical data released at the 34th EORTC-NCI-AACR Symposium in October 2022, we are working with clinical investigators to initiate clinical testing, as part of an investigator-sponsored trial (IST), of a fourth new RP-6306 combination with carboplatin, with first patient dosing expected in the first half of 2023. In the fourth quarter of 2022, we entered into an agreement with Canadian Cancer Trials Group, or CCTG, for a planned, basket Phase 2 IST to evaluate RP-6306 in patients with selected, advanced cancers receiving standard agents. We plan to modify the trial to include a sub-study, which will evaluate RP-6306 in combination with gemcitabine in patients with CD4/6i-resistant ER+/HER2- metastatic breast cancer.

We continue to focus on the advancement of our preclinical programs into clinical development. We expect to initiate IND-enabling studies in the first half of 2023 for a small molecule against an undisclosed target with potential to enter the clinic in late 2023 or early 2024, which represents an acceleration from our prior expectations for this program. We are also pursuing development of an inhibitor of polymerase theta (Polθ) in collaboration with Ono, as Polθ is SL with multiple gene deficiencies found in tumors, including BRCA alterations. In 2022, we selected a proposed inhibitor, which we designated as RP-2119. In February 2023, based on our review of ongoing preclinical studies, we elected to prioritize other Polθ inhibiting compounds in our preclinical development portfolio, which we believe have a higher probability for clinical impact relative to RP-2119. We are now guiding toward clinical entry for a Polθ inhibitor in 2024.

We believe our powerful SL-based approach to the development of new precision oncology therapeutics has multiple potential benefits:

- **Ability to address previously untargetable tumor biology**, including, for example, loss-of-function mutations;
- **Enhanced benefit-risk profile**, by precisely targeting tumor cells with the defined mutation while sparing normal, non-cancerous cells;
- **Genetic stratification of patients**, potentially enabling higher response rates; and
- **Tumor-agnostic approach**, focusing on specific genetics and enabling the application to multiple tumor types.

A cornerstone of our company is our SNIPRx platform, which enables us to accurately identify SL gene pairs and the corresponding patients who are most likely to benefit from our therapies based on the genetic profile of their tumors. These differentiated patient selection insights have driven the development of our initial product candidate, camonsertib, which is designed as a selective inhibitor of the DNA repair protein ataxia telangiectasia and Rad3-related protein, or ATR, a kinase that is activated by DNA replication stress. Tumors containing alterations in genes encoding other DNA repair proteins, such as ataxia-telangiectasia mutated kinase, or ATM, are SL with ATR inhibition and were observed to be hypersensitive to camonsertib in our preclinical models. We believe that the preclinical selectivity and pharmacokinetic properties of camonsertib support the profile of a differentiated therapy with the potential to enhance anti-tumor activity as compared to third party ATR inhibitors currently in development. Based on our preclinical studies, we believe camonsertib has the potential to provide therapeutic benefit to identified patient populations both as a monotherapy and in combination with other therapies such as poly (ADP-ribose) polymerase, or PARP, inhibitors.

We are developing a portfolio of product candidates based on targets identified using our SNIPRx platform to treat cancers with a high unmet medical need. Our second designated program, RP-6306, is focused on a novel target we discovered to be SL with amplification of cyclin E1, or CCNE1, or deleterious alterations in FBXW7, or PPP2R1A in tumors such as gynecological, colorectal and upper gastrointestinal malignancies.

The core of our SNIPRx platform is the ability to identify both known and novel SL targets. Our SNIPRx platform begins with a genome-wide CRISPR-based screening approach that utilizes our proprietary isogenic cell lines, which are cell lines that are identical with the exception of a single genomic alteration, to identify SL gene pairs. Our systematic and comprehensive screening approach has been optimized to significantly reduce false negatives, providing the opportunity to identify a larger and more accurate set of SL interactions as compared to what others have reported with CRISPR-based screening technologies.









We have systematically analyzed genomic data from approximately 60,000 tumor samples and identified a set of clinically relevant tumor genomic alterations, which we refer to as tumor lesions, that are linked to genomic instability. The initial tumor lesions are present in approximately 30% of tumors. For each of these tumor lesions, we have completed a SNIPRx screen campaign to identify both previously reported and unreported targets that are SL with the tumor lesion of the campaign. The majority of our SNIPRx screen campaigns have identified multiple potential targets, which allows us to prioritize and select targets based on their potential to be amenable to small molecule inhibitors with drug-like properties. Once a SL product candidate is identified, we perform our proprietary SNIPRx Targeted Expansion of Patient Populations, or STEP², screens to identify additional genomic alterations that are SL to our product candidate. Using these screens, we are able to enrich the patient population in our clinical trials and expand the patient populations that may be addressable with our product candidates.

We are a leader in developing innovative SL therapies and have built our SNIPRx platform based on three primary pillars:

1. **Identify** novel SL targets using our proprietary, genome-wide, CRISPR-enabled screening technology against clinically relevant genomic alterations in tumors with high unmet medical need;
2. **Design and synthesize** potent and selective small molecule inhibitors of these targets; and
3. **Expand** beyond the initial target population based on the additional genomic alterations identified by our proprietary STEP² screens that are SL with our inhibitors.

Our Pipeline

We are leveraging our proprietary SNIPRx platform to discover, validate and build a robust pipeline of SL-based therapeutics. Our current pipeline is represented in the diagram below.

		SL Pair		Discovery	IND-Enabling	Phase 1/2	Pivotal	Anticipated Milestones	Rights						
	Lesion Network	Drug Target													
Clinical	Camonsertib (RP-3500 / RG6526)	ATM + 16 STEP ² lesions	ATR	Ph1/2 TRESR: Monotherapy				<ul style="list-style-type: none"> H1'23 initial PARP combination data Summer/Fall '23 initial gemcitabine combination data 	 						
				Ph1/2 TRESR: PARP (talazoparib) Combo						Ph1/2 ATTAC: PARP (olaparib/niraparib) Combo				Ph1/2 TRESR: Gemcitabine Combo	
Clinical	PKMYT1 inhibitor RP-6306	CCNE1, FBXW7, PPP2R1A	PKMYT1	Ph2 CCTG BASKET IST				<ul style="list-style-type: none"> 2023 Ph2 Basket IST start H1'23 Ph1 carboplatin combination study start H1'23 initial Ph1 monox data Q4'23 initial Ph1 combination data 							
				Ph1 MYTHIC: Monox + Camonsertib Combo						Ph1 MAGNETIC: Gemcitabine Combo			Ph1 MINOTAUR: FOLFIRI Combo		
Preclinical	Undisclosed	Undisclosed	Undisclosed					<ul style="list-style-type: none"> H1'23 IND-enabling studies Late '23/Early '24 Clinic 							
	Polθ inhibitor	BRCA1/2 + others	Polθ					<ul style="list-style-type: none"> 2024 Clinical entry 							
Discovery	SNIPRx [®] platform			Additional SL targets in advanced stages of development											
				Discovery and validation of new SL precision oncology targets					 						

Our Corporate History and Team

Our company was founded in 2016 by field-leading academics and Versant Ventures to systematically employ SL insights and platforms and develop new precision oncology medicines. Our co-founder, Daniel Durocher, Ph.D., a principal investigator at the Lunenfeld-Tanenbaum Research Institute, was an early pioneer of genome-wide, SL screening using CRISPR, which formed the framework for our SNIPRx platform. Our other co-founders, Agnel Sfeir, Ph.D. now at Memorial Sloan Kettering Cancer Center and Frank Sicheri, Ph.D. at the Lunenfeld-Tanenbaum Research Institute, also played a key role in the development of our company.

We have assembled a highly qualified management team with broad experience in drug discovery and development to execute on our mission to develop novel precision oncology therapies based on SL. Our scientific co-founders and members of our management team collectively have extensive experience in oncology drug discovery and development and are pioneers in the SL field. Our management team includes industry veterans with prior experience at companies such as Pfizer, AstraZeneca, GSK, Merck, Eli Lilly and Company, Bicycle Therapeutics, Y-mAbs Therapeutics, Santhera Pharmaceuticals and Clementia Pharmaceuticals. We have an experienced research and development team focused on leveraging our deep expertise and differentiated know-how across genomic target identification, target prioritization and selection, drug discovery chemistry and clinical development to develop highly potent and selective small molecule inhibitors based on SL for the treatment of cancer.

Our Strategy

Our goal is to be the leading biopharmaceutical company developing precision oncology, small molecule therapies based on SL. The key elements of our strategy are to:

- **Advance our initial product candidate, camonsertib, by completing ongoing clinical development and supporting collaboration partner Roche in driving broad global development and commercialization.** We designed camonsertib to have a highly selective and potent profile that may enable it to be a leading inhibitor of ATR, if approved, that is further leveraged by our differentiated STEP² patient selection approach. In July 2020, we began monotherapy dosing in our open-label Phase 1/2 clinical trial. In parallel with the monotherapy dose-escalation portion of the trial, in February 2021, we initiated patient recruitment of the combination therapy arm to evaluate the safety and efficacy of

camonsertib in combination with a PARP inhibitor, talazoparib in the same patient subgroups. In August 2021, we initiated patient recruitment in our open-label Phase 1b/2 ATTACC trial of camonsertib in combination with niraparib and olaparib, two additional PARP inhibitors. In October 2021, we presented initial Phase 1 monotherapy clinical data from our open-label Phase 1/2 TRESR trial of camonsertib in patients with solid tumors. We then presented comprehensive Phase 1 monotherapy clinical data from this trial in April 2022. In June 2022, we announced a worldwide license and collaboration agreement with Roche for the development and commercialization of camonsertib for the treatment of tumors with specific synthetic-lethal genomic alterations. Under the terms of collaboration, Roche assumes all subsequent development of camonsertib with the potential to expand development into additional tumor indications and multiple combination studies.

- **Advance RP-6306 through clinical development by leveraging our differentiated STEP² patient selection approach.** We designed RP-6306 to be a first-in-class, highly selective and potent small-molecule, oral inhibitor of PKMYT1, which is a novel target that we discovered to be synthetic lethal with CCNE1 amplification and other deleterious genetic alterations. In April 2021, we began dosing patients in our open-label Phase 1 MYTHIC trial of RP-6306 designed to evaluate the safety and tolerability of RP-6306 in advanced solid tumors that are characterized by genomic alterations predicted by our SNIPRx platform to be sensitive to RP-6306. In December 2021, we enrolled the first patient in our open-label Phase 1 MAGNETIC trial to evaluate the safety and tolerability of RP-6306 in combination with gemcitabine. In January 2022, we initiated patient recruitment in our open-label Phase 1 MINOTAUR trial to evaluate the safety and tolerability of RP-6306 in combination with FOLFIRI. In May 2022, we initiated patient recruitment in a new arm of the Phase 1 MYTHIC clinical trial, which is designed to evaluate the safety and tolerability of RP-6306 in combination with camonsertib in patients with advanced solid tumors. In the fourth quarter of 2022, we received fast track designation for RP-6306 in combination with gemcitabine for the treatment of adult patients with CCNE1 amplified, or FBXW7 or PPP2R1A mutated platinum resistant ovarian cancer. Based on promising preclinical data released at the 34th EORTC-NCI-AACR Symposium in October 2022, we are working with clinical investigators to initiate clinical testing of a new carboplatin combination with RP-6306 that is expected to dose the first patient in the first half of 2023. In the fourth quarter of 2022, we entered into an agreement with CCTG for a planned, basket Phase 2 IST to evaluate RP-6306 in patients with selected, advanced cancers receiving standard agents. A sub-study under the master protocol will evaluate RP-6306 in combination with gemcitabine in patients with CD4/Gi-resistant ER+/HER2- metastatic breast cancer. We plan to provide an initial Phase 1 clinical data readout for RP-6306 in the first half of 2023 for monotherapy, and anticipate providing an update on some of the combination studies in the fourth quarter of 2023.
- **Continue to advance our preclinical programs into clinical development.** In addition to camonsertib and RP-6306, we have several programs in preclinical development. We expect to initiate IND-enabling studies in the first half of 2023 for a small molecule against an undisclosed target with potential to enter the clinic in late 2023 or early 2024, which represents an acceleration from our prior expectations for this program. We are also pursuing development of an inhibitor of polymerase theta (Polθ) in collaboration with Ono, as Polθ is SL with multiple gene deficiencies found in tumors, including BRCA alterations. In 2022, we selected a proposed inhibitor, which we designated as RP-2119, and initiated IND-enabling studies. In January 2023, we amended our research services, license and collaboration agreement, or the Ono Agreement, with Ono Pharmaceutical Co., Ltd., or Ono, to extend the research term until July 31, 2023. In the first quarter of 2023, we received an approximate \$1.5 million (¥200 million) research service payment from Ono due to the achievement of a specified research trigger for our Polθ program, under the companies' 2019 agreement. In February 2023, based on our review of ongoing preclinical studies, we elected to prioritize other Polθ inhibiting compounds in our preclinical development portfolio, which we believe have a higher probability for clinical impact relative to RP-2119. We are now guiding toward clinical entry for a Polθ inhibitor in 2024.
- **Extend our leading position in SL drug discovery.** We have systematically analyzed genomic data from approximately 60,000 tumor samples and have identified a set of tumor lesions that are linked to genomic instability. This current set of tumor lesions provides us with the opportunity to be among the first to mine this substantial, largely non-overlapping genomic space for new SL gene pairs and develop a robust portfolio of novel targeted therapeutics. We intend to continue leveraging our leading position in the identification of novel oncology SL gene pairs and systematically applying our STEP² screens to expand

the addressable patient populations for each of our product candidates. We believe our approach will allow us to continue to build a sustainable and long-term pipeline of novel product candidates for the targeted treatment of cancers with high unmet medical need.

- **Opportunistically pursue strategic partnerships to maximize the full potential of our pipeline and SNIPRx platform.** The large number of pre-existing mutations affecting genomic stability in tumors combined with the high throughput of our SNIPRx platform has the potential to provide us with an abundance of novel targets. We believe this provides the opportunity to selectively enter into strategic partnerships and leverage our partners' complementary capabilities. We regularly evaluate the potential of partnerships and other collaborative efforts to maximize the long-term value of our portfolio. We believe our collaboration with Bristol Myers Squibb highlights the potential broad application of our platform in the search for the next generation of precision oncology medicines.

Background

Targeted Oncology Therapeutics

The first-generation of approved targeted therapies were predominately directed at driver mutations, which target specific types of receptor tyrosine kinases, such as, bcr-abl, EGFR and HER2, and have largely represented the focus of the targeted oncology sector for the last 20 years. A rapid evolution in the understanding of tumor biology coupled with an improved ability to segment subsets of tumors based on genomic alterations have led to the development of new generations of targeted cancer therapies for a variety of additional tumor-specific genomic abnormalities.

Targeting DNA repair genes and specifically loss of function alterations is an emerging area of research with PARP inhibitors pioneering the field. The growing number of compounds in development and multiple clinical studies have begun to reveal patterns of clinical benefit alone and in combination with several other agents. We expect both monotherapy and combination trials with these agents to emerge quickly and reshape the therapeutic landscape across many disease areas. Consistent with this trend and the specific cell cycle-related mechanisms of action for our lead assets, we have initiated comprehensive development plans for camonsertib and RP-6306 alone or in combination with multiple agents.

The speed at which the field has identified genetic changes associated with tumors has outpaced the discovery and development of precision medicines that can target those alterations. Oncology drug development has been primarily focused on genes with readily druggable alterations that confer new or enhanced protein activity, known as gain-of-function targets, such as EGFR. These include both gain-of-function alterations, such as CCNE1, as well as loss-of-function alterations, such as BRCA1. In June 2019, the New England Journal of Medicine referred to SL as a particularly attractive means to target the complex and gene-network oriented relationships associated with this previously undiscovered domain of oncology targets.

The more recent ability to identify a tumor's genetic vulnerabilities and networks of genes responsible for more complex gene functions underlying many cancers has been enabled through new and disruptive technical breakthroughs in the field including:

- **Clinically-relevant tumor genomic data:** the increasing adoption and regulatory acceptance of molecular tumor testing, enabling the accurate profiling of patient tumors;
- **Consolidated and annotated databases:** the availability of multiple new and publicly accessible databases that consolidate, analyze, and synthesize new genetic data on tens of thousands of tumors; and
- **Tools to apply emerging genetic knowledge:** the emergence of new tools and methodologies, including CRISPR/Cas9, enabling large-scale studies of genetic networks underlying cancer biology.

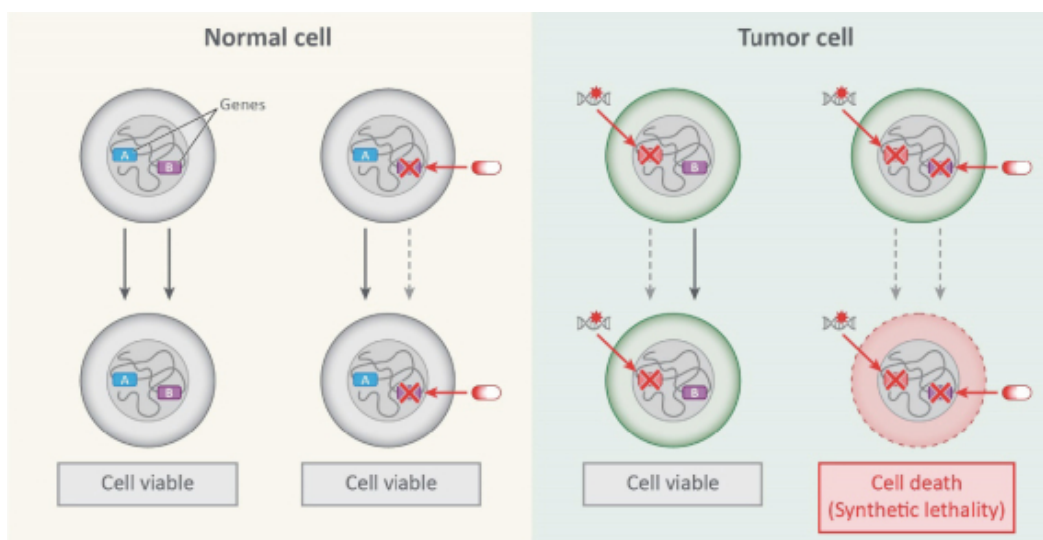
The Synthetic Lethality Opportunity and Challenge

Synthetic lethality is a powerful approach and opportunity in oncology drug development that combines two key principles in treating patients with cancer through precision oncology: (1) identifying and selecting patient

subgroups with specific genomic alterations in tumors that are most likely to benefit from these therapies and (2) improving tolerability and reducing toxicity by not affecting normal, non-cancerous cells.

SL arises when deficiencies in a pair of genes occur simultaneously to result in cell death, but if that deficiency exists in only one gene, the cell will survive. As depicted below, cancer cells that contain an alteration in one gene of a SL pair are susceptible to therapeutic intervention targeting the other gene pair, resulting in cell death, whereas normal cells are not affected by the inhibition of the targeted gene and remain viable.

Illustration of Synthetic Lethality Approach



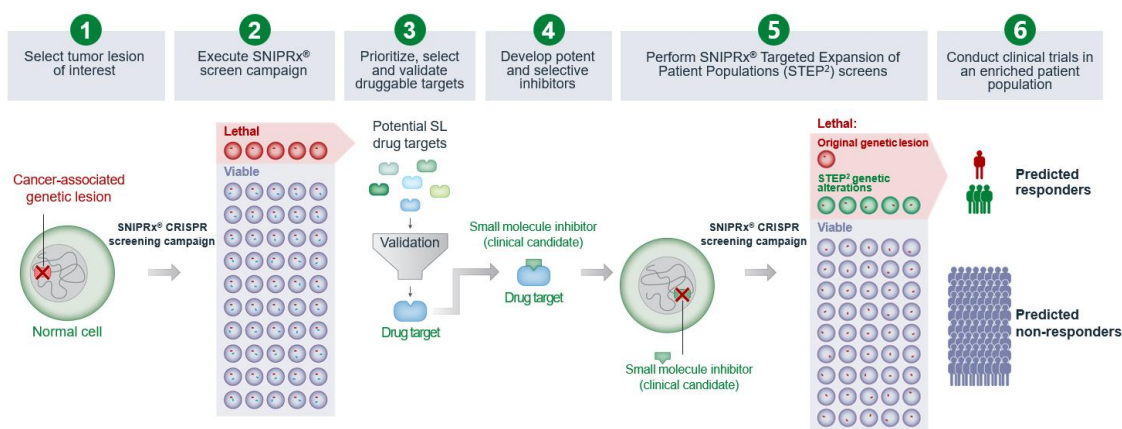
The first clinically-validated SL gene pair was PARP-BRCA1/2, and based on the efficacy of PARP inhibitors, the SL approach to treating cancer has achieved substantial commercial validation. PARP enzymes regulate critical DNA repair pathways that cancer cells rely on as they grow and divide. PARP inhibition blocks these pathways, preventing DNA repair in cancer cells with a BRCA1/2 alteration and resulting in cancer cell death while sparing normal cells. Multiple PARP inhibitors, including olaparib (AstraZeneca), niraparib (GlaxoSmithKline), talazoparib (Pfizer), rucaparib (Clovis) and pamiparib (Beigene), have been approved for the treatment of tumors with BRCA and other DNA damage repair alterations, including ovarian, breast, prostate and pancreatic cancers.

While SL offers a new route to uncover important gene targets for the treatment of cancers, identifying these SL gene pairs has been a challenge due to the lack of systematic, prospective, and large-scale methods to capture and exploit these gene-gene relationships for new drug discovery and development.

Our Approach: An Overview of Our Drug Discovery and Development Platform

Our SNIPRx platform integrates our deep expertise and differentiated know-how across genomic target identification, target prioritization and selection, drug discovery chemistry and clinical development. Our approach can be divided into six steps, as depicted in the graphic below.

Our Integrated Approach to Drug Discovery and Development



1. Select tumor lesion of interest.

Apply our deep understanding of tumor lesions with a bias for alterations associated with genomic instability and cancers with high unmet medical need.

Since 2016, we have systematically analyzed genomic data from approximately 60,000 tumor samples. We consult with leading oncology clinicians and key advisors to identify cancer types and subtypes where the current standard of care is not adequately improving patient survival. We then prioritize genetic lesions based on various criteria including mutation frequency and the feasibility of identifying lesion-positive patients. Of those, we focus on lesions that are known to directly or indirectly impact processes involved in genomic instability, such as DNA repair and cell cycle regulation.

2. Execute SNIPRx screen campaign.

Utilize our SNIPRx screening technology to identify target gene candidates that induce SL in the context of our set of tumor lesions.

For each of the tumor lesions we identified, each of which we refer to as an original tumor lesion, we have completed a screen campaign utilizing CRISPR technology and other tools to create proprietary isogenic cell lines, which are pairs of cell lines that are identical with the exception of a single genomic alteration. This allows us to identify, on a genome-wide basis, both known and novel targets that are SL with each original tumor lesion. Our SNIPRx platform has been optimized to both sensitivity and reproducibility, resulting in a significant decrease in false negatives compared to what has been reported with other CRISPR-based screening technologies.

3. Prioritize, select, and validate druggable targets.

Evaluate the multiple SL targets identified for each original tumor lesion.

Our screen campaigns result in the identification of multiple SL targets for each original tumor lesion. We prioritize and select targets to advance into drug discovery based on a systematic and proprietary set of criteria, which include thresholds for biological validation, cellular function, known and likely toxicity, druggability with small molecules, patentability, and the potential for clinical impact versus alternative therapies. Our processes include extensive *in vitro*, genetic, and *in vivo* animal validation of targets and comprehensive development of tool compounds for initial pharmacological corroboration.

4. Develop potent and selective inhibitors.

Develop small molecule product candidates that are highly potent and selective and advance them from lead discovery through the identification of a clinical candidate.

We have assembled an internal research team that has extensive experience in small molecule drug discovery with a proven track record of identifying development candidates and delivering them into and through the clinic. Our team has deep in-house capabilities in cell biology, molecular biology, biochemistry, enzymology, medicinal chemistry, computational chemistry, and molecular modeling. We also have proven capabilities in drug metabolism, pharmacokinetic/pharmacodynamics, and absorption, distribution, metabolism, and excretion evaluation, as well as pharmacology, including dedicated *in vivo* animal facilities to internally drive translational studies for human clinical trials. We believe these capabilities were demonstrated in the discovery and development of camonsertib and RP-6306.

5. Perform SNIPRx Targeted Expansion of Patient Populations (STEP²) screens.

Expand our potential patient populations beyond those identified by the original SL pair.

Once we have identified a clinical candidate, our STEP² screens utilize a set of cell lines that, when treated with our clinical candidate, elucidate genes that, when knocked down, cause sensitivity to our selected inhibitor. These screens not only confirm the SL relationship with the original tumor lesion, but also identify additional genomic alterations that confer a response to our product candidates and are mutually exclusive from the original tumor lesion. We believe the identification of these new SL pairs allows us to rationally expand our targeted patient populations by enabling us to potentially treat patients with tumors across multiple genomic alterations with the same product candidate.

6. Conduct clinical trials in an enriched patient population.

Design our clinical trials for efficient clinical development.

For our clinical trials, we plan to enroll patients with tumors that contain either the original tumor lesion or any one of the genomic alterations identified by our STEP² screens. We believe this strategy will allow us to enroll only those patients who are most likely to achieve clinical benefit from our product candidates. In addition, we are prioritizing tumor types for which there are no effective therapies currently available. We plan to evaluate multiple cohorts of patients based on specific genomic alterations, which may enable us to pursue an accelerated regulatory approval pathway for certain targeted patient populations.

Our SNIPRx Platform

The core of our SNIPRx platform is the ability to identify both known and novel SL targets. We believe that our platform and approach provide many key advantages as highlighted below.

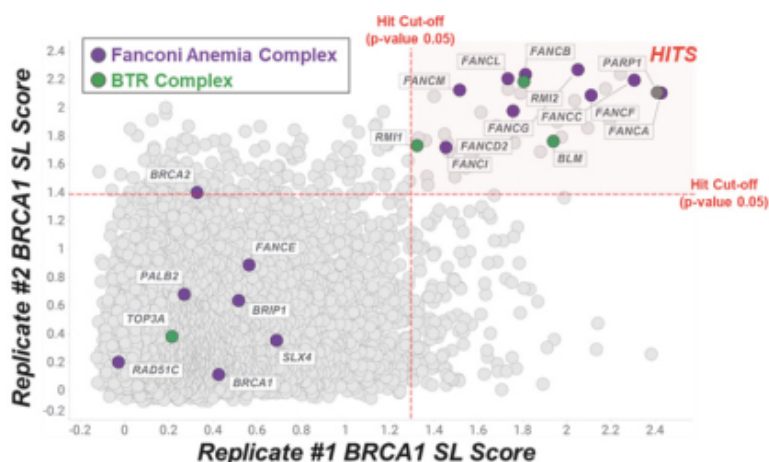
- **Designed to Address Previously Untargetable Tumor Biology.** Oncology drug development has been primarily focused on genes with readily druggable alterations that confer new or enhanced protein activity, known as gain-of-function targets, such as EGFR. The remaining targets have historically been considered undruggable. These include both gain-of-function alterations, such as CCNE1, as well as loss-of-function alterations, such as BRCA1. Our SNIPRx platform has demonstrated an ability to identify novel SL relationships, including those that address previously untargetable tumor biology.
- **Applies Our Proprietary Genome-wide Library.** Genome-scale screens often identify many genes coding for the same protein complex or cellular pathway, thereby increasing confidence in those hits. These screens allow us to screen the entire genome to determine the top hits across all genes, as compared to the more limited druggable gene libraries. In addition, because the definition of what is druggable is continuously evolving, by using genome-scale screens, we are able to mine the results of our existing screens as new therapeutic modalities emerge. Our genome-wide libraries, together with our industrialized and optimized screening approach and technology, result in a significant reduction in false negative hits.

- **Utilizes Isogenic Cell Lines.** We believe a key differentiator of our SNIPRx platform is the utilization of thoroughly characterized proprietary isogenic cell lines for our CRISPR-based genome-wide SL screen campaigns. We use normal, non-cancerous cell lines to engineer our isogenic cell models, which enable us to mine for SL interactions between two genes in models with clean genetic backgrounds that have minimal mutations and normal chromosome numbers. We have also developed a proprietary computational algorithm that is specifically designed to identify SL interactions from our isogenic screens. We believe using isogenic cell lines gives us a significant competitive advantage since most SL screening approaches used by others are based on cancer cell line panels, which we believe are less accurate due to their propensity to result in variable data.
- **Focuses on Niche of Genomic Instability.** Based on the well-established network of SL interactions in DNA synthesis and repair across model organisms, we have found and believe we will continue to find clear and reproducible SL interactions through our SNIPRx platform. Genomic instability is an early event that underlies all cancer, and many of the genes we screen represent early hits in cancer that may have less heterogeneity in later stage tumors. The genomic instability space is enriched with genes encoding enzymatic activity, which provides us with ample opportunity to identify novel druggable genes for development into small molecule precision oncology therapies. We believe developing product candidates that target genomic instability may lead to durable responses with resulting clinical benefits for patients.

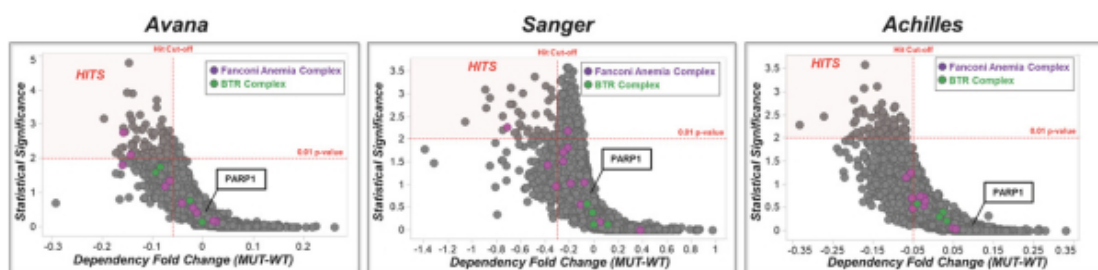
One example that illustrates the power of our SNIPRx platform is a SL screen campaign that we conducted in an isogenic pair of cell lines in which one cell line had a BRCA1 mutation and the other cell line was normal for BRCA1. The results of this screen campaign are graphically depicted below. The top-right quadrant of Graphic A highlights the SL hits resulting from our screen and shows that we were able to identify PARP1 as a SL hit with BRCA1. In addition, two additional sets of genes were identified to be SL with BRCA1: (1) the genes encoding the Fanconi Anemia pathway, which are depicted in purple, and (2) the genes coding for the BLM-RMI1-RMI2 complex, which are depicted in green. The independent identification by our SNIPRx screen campaign of multiple genes within a pathway or complex greatly increases confidence that those are true SL hits. In contrast, external cell panel screens that look for SL hits by comparing a panel of cancer cell lines that have either BRCA1-mutant or normal BRCA1 cell lines do not identify these validated BRCA1 SL genes. As shown in Graphic B below, multiple cancer cell line panel screens utilizing CRISPR or shRNA all failed to identify PARP1 as a SL hit with BRCA1.

SNIPRx Screen Campaign Identifies Both Known and Novel SL Pairs Undetected by Cancer Cell Line Panels

A. SNIPRx BRCA1 Isogenic SL Screen



B. External BRCA1 Cell Panel SL Screens



Our Clinical Stage Product Candidates

Camonsertib, Also Known as RP-3500 or RG6526, an Oral ATR Inhibitor

Overview

Our initial clinical-stage product candidate, camonsertib, is a potent and selective oral small molecule inhibitor of ATR that we are developing for the treatment of tumors with mutations in ATM, which is a SL pair with ATR. ATR is a critical DNA damage response, or DDR, protein that acts as both the master regulator of the response to DNA replication stress, as well as a central effector of the DNA damage checkpoint. Based on the previously published SL relationship between ATR and ATM, ATR has been the target of prior drug discovery efforts, and ATR inhibitors in development have demonstrated promising, durable clinical responses in a small number of patients in early clinical trials. Through our STEP² screens, we believe that we have more precisely identified and expanded the patient populations that would benefit from camonsertib, which allows us to differentiate and enrich our clinical development strategy as well as address multiple types of solid tumors.

Camonsertib has demonstrated an optimized anti-tumor effect, selectivity, and pharmacokinetics profile in preclinical studies that we believe supports the potential for it to be a leading ATR inhibitor, if approved. We also conducted multiple STEP² screens in which we confirmed the SL relationship between ATR and ATM and identified an additional 19 genes that are also SL with ATR, potentially expanding the patient populations that may benefit from our product candidate. In July 2020, we began dosing in our open-label Phase 1/2 clinical trial of camonsertib in patients with advanced tumors that have alterations in the ATM gene or a subset of 16 additional genetic alterations identified through our STEP² screens. We believe the design of our trial allows us to enrich the patient population in our trials with those who are most likely to respond to camonsertib. In parallel with the monotherapy dose-escalation portion of the trial, in February 2021 we initiated patient recruitment of the combination therapy arm to evaluate the safety and efficacy of camonsertib in combination with a PARP inhibitor, talazoparib in the same patient subgroups. In August 2021, we initiated patient recruitment in our open-label Phase 1b/2 ATTACC trial of camonsertib in combination with niraparib and olaparib, two additional PARP inhibitors. In October 2021, we presented initial Phase 1 monotherapy clinical data from our open-label Phase 1/2 TRESR trial in patients with solid tumors at the AACRA-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. The presentation included the recommended Phase 2 dose and schedule choice and confirmed camonsertib activity in tumors with alterations hypothesized by our SNIPRx platform.

In April 2022, we presented comprehensive Phase 1 monotherapy clinical data from the TRESR Phase 1/2 trial, reflecting analysis of 120 patients, of which 99 patients were evaluable for efficacy as of the data cutoff date of February 14, 2022 (excluding one patient evaluated as of March 22, 2022). The study included 95 patients who received therapeutically active doses or at the recommended Phase 2 dose schedule of 3 days on / 4 days off, and reflecting the data cutoff of mid-February 2022. Monotherapy with camonsertib continued to appear safe and well tolerated. Anemia was the most common treatment-related adverse event and easily manageable. Only 24.2% of all patients in the 3 days on / 4 days off schedule experienced Grade 3 anemia, and none experienced Grade 4 anemia. Camonsertib monotherapy resulted in durable clinical benefit across tumor types and genomic alterations, with

enriched benefit demonstrated in specific patient subsets. These updated monotherapy results showed a 43% clinical benefit rate, or CBR, which was defined as response or treatment duration of at least 16 weeks without progression, an overall response rate of 14%, and a median progression free survival, or mPFS, of 15 weeks in solid tumors across genotypes, with potential best-in-class safety and tolerability. The overall CBR in patients after PARP inhibitor failure was 47%. We observed camonsertib demonstrated robust activity in patients with ovarian cancer (n=20), demonstrating 75% CBR after dosing with camonsertib, an overall response rate of 25%, and a mPFS of 35 weeks. The ovarian cancer patient population was heavily pretreated and comprised a hard to treat population: of which 90% had previous treatment with PARP inhibitors and 85% were platinum resistant. The responders included one complete response, three partial responses as determined by RECIST 1.1 criteria, and one durable and ongoing CA-125 response in a patient with stable disease. The TRESR study comprises the largest set of tumors with detailed genomic analysis evaluated with ATR inhibitor, or ATRi, monotherapy. Genomic subsets of tumors beyond ATM included tumors harboring alterations in ATR-sensitizing genes, with responses observed in tumors harboring BRCA1/2, SETD2 and RAD51C alterations. In patients with BRCA1/2 mutated tumors (n = 37), response rate was 14% and included two patients with ovarian cancer, and one each with breast cancer, head and neck squamous cell carcinoma, and melanoma. In patients with tumors carrying BRCA1 mutations, the CBR was 48%. In patients with tumors with ATM loss-of-function, or LOF (n = 34), response rate was 9% including one RECIST 1.1 confirmed/unconfirmed response, and two prostate specific antigen responses. An additional patient with pancreatic cancer and ATM LOF had a late response, just after the data cutoff after 54 weeks of treatment. The CBR in the patients with ATM LOF was 44% and mPFS was 17 weeks. Sequencing data demonstrated biallelic gene LOF, an emerging biomarker for synthetic lethal therapies, could potentially be leveraged to further enrich for patients most likely to benefit from camonsertib. CBR in patients with biallelic LOF was significantly higher (47%) compared to the CBR in patients with non-biallelic tumors (15%).

In June 2022, we announced a worldwide license and collaboration agreement with Roche for the development and commercialization of camonsertib for the treatment of tumors with specific synthetic-lethal genomic alterations. Under the terms of the collaboration, Roche assumes all subsequent development of camonsertib with the potential to expand development into additional tumor indications and multiple combination studies. Under the terms of the agreement, we received a \$125 million upfront payment in July 2022, and are eligible to receive up to \$1.2 billion in potential clinical, regulatory, commercial and sales milestones, including up to \$55 million in potential near-term payments, and royalties on global net sales ranging from high-single-digits to high-teens. The collaboration also provides our company with the ability to opt-in to a 50/50 U.S. co-development and profit share arrangement, including participation in U.S. co-promotion if U.S. regulatory approval is received. If we choose to exercise the co-development and profit share option, we will continue to be eligible to receive certain clinical, regulatory, commercial and sales milestone payments, in addition to full ex-U.S. royalties.

Mechanism of Action

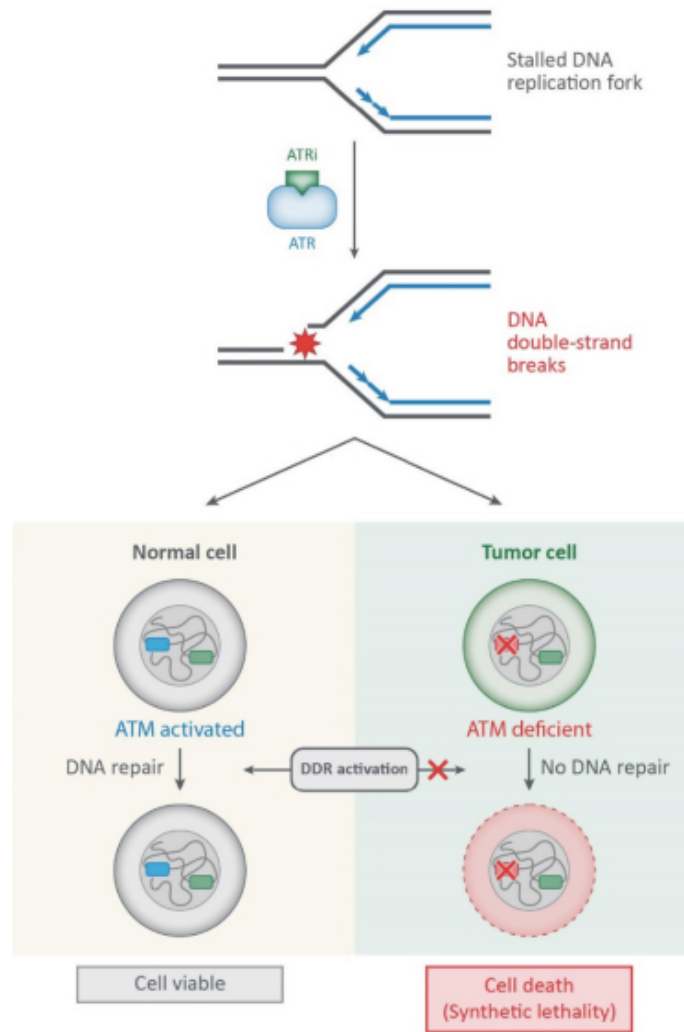
ATR is a protein kinase that acts at multiple levels of the DDR network. It is activated when problems with ongoing DNA replication are identified, a phenomenon known as DNA replication stress. It uses its kinase activity to stabilize the DNA replication machinery locally and to suppress the initiation of DNA replication globally. As a consequence, ATR prevents the formation of DNA damage when DNA replication is stressed. In addition to these roles, ATR also restrains cell cycle progression when it is activated, a phenomenon known as the DNA damage checkpoint. ATR is one member of an extensive network of proteins that serve to recognize early stages of DNA damage, prevent replication from proceeding through these damaged sites and repair the damage. Cancer cells with alterations in genes encoding this network of DDR proteins are highly dependent on ATR for survival. ATR's central role in the regulation of replication stress has led to the development of multiple ATR inhibitors that have demonstrated durable responses in early clinical trials.

The ATR Partner Genes and Proposed Synthetic Lethality Pairs

ATM is a DDR protein related to ATR that is responsible for sensing and signaling DNA double-strand breaks. Our ATR inhibitor STEP² screen campaigns confirmed that ATM-deficient cells rely on ATR activity for survival. ATM orchestrates the response to double-strand break repair and thus, ATM-deficient tumors have an impaired response to DNA breaks. SL screens conducted in our laboratories have identified that at least 16 additional genes are SL with ATR inhibition, making cancer cells that are deficient in those genes highly sensitive to killing by ATR

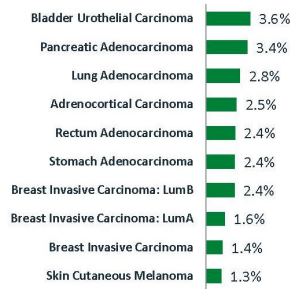
inhibitors. An overview of the ATM-ATR SL relationship, as one of the examples of the sensitivity genes, is illustrated below.

Mechanism of ATM-ATR Synthetic Lethality

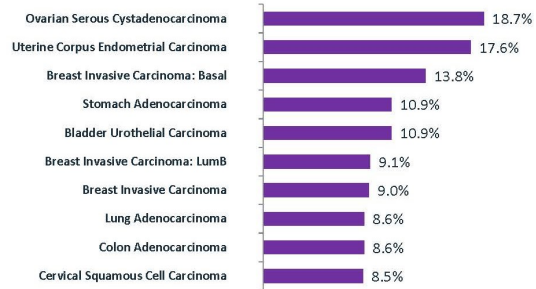


The gene encoding for ATM is frequently mutated in cancer. An analysis of sequence data collected as part of The Cancer Genome Atlas, or TCGA, found that between 1% and 4% of solid tumors, such as breast, bladder, pancreatic and lung cancers, have deficiencies in ATM, as depicted in the graphs below. Beyond ATM, 16 of 19 additional, mutually exclusive genomic alterations identified as SL with camonsertib, with average prevalence of approximately 10% across multiple tumors, were eligible for recruitment into clinical trials.

Top 10 tumor types with highest prevalence of ATM deficiency



Top 10 tumor types with highest prevalence of ATM deficiency or STEP² genomic alterations



Clinical Validation of ATR Inhibitors in ATM-Deficient Tumors and in Other Genetic Backgrounds Hypothesized to Sensitize Tumors to ATRi

Early phase studies evaluating third party ATR inhibitors as a monotherapy support the rationale for prospective patient selection for tumors carrying genomic alterations hypothesized to sensitize tumors ATR inhibition. A Phase 1 of Bayer's ATR inhibitor suggested antitumor activity in solid tumors with certain DDR defects, including ATM loss (Yap, Cancer Discovery 2020). The subsequent dose expansion cohort enrolled an additional 143 patients, prospectively selected for presence of DDR gene defects. While the overall response rate was low (4%), durable responses were observed in tumors with ATM or BRCA mutations (Yap, AACR 2022). In addition, out of a cohort of 17 patients receiving EMD's ATR inhibitor, the single responder was a patient with metastatic colorectal cancer with loss of ATM (Yap, JCO 2020).

The Phase 1/2 TRESR study prospectively selected for patients with tumors carrying DNA damage repair loss-of-function mutations predicted to sensitize to camonsertib. Following our first clinical data release at the AACR-ASCO-NCI meeting in October 2021, we presented comprehensive Phase 1 monotherapy data from this study at the AACR annual conference in April 2022. Camonsertib monotherapy resulted in durable responses across tumor types and genomic alterations, including ATM, BRCA1, BRCA2, RAD51C, CDK12, and SETD2. Antitumor activity was validated by molecular responses in 41% of evaluable patients.

In June 2022, we announced a worldwide license and collaboration agreement with Roche for the development and commercialization of camonsertib, which provided further validation of our clinical program through the addition of a strategic partner with a leading global footprint and unique expertise in precision oncology.

Our Solution, Camonsertib

We identified ATR as one of the SL targets through our SNIPRx screen campaign of ATM and selected ATR as a target for our initial product candidate, camonsertib, based on:

- (i) existing third party clinical and preclinical support for the potential of ATR inhibition as a precision oncology therapy;
- (ii) our ability to design an ATR inhibitor with enhanced chemical properties, such as potency and selectivity; and
- (iii) the results of our STEP² screens, which identified 19 additional genomic alterations beyond ATM deficiency to be SL with ATR, facilitating the expansion of the addressable patient populations.

We designed camonsertib as an oral small molecule ATR inhibitor with increased potency and a similar or improved selectivity profile compared to other known ATR inhibitors. Camonsertib has demonstrated a favorable

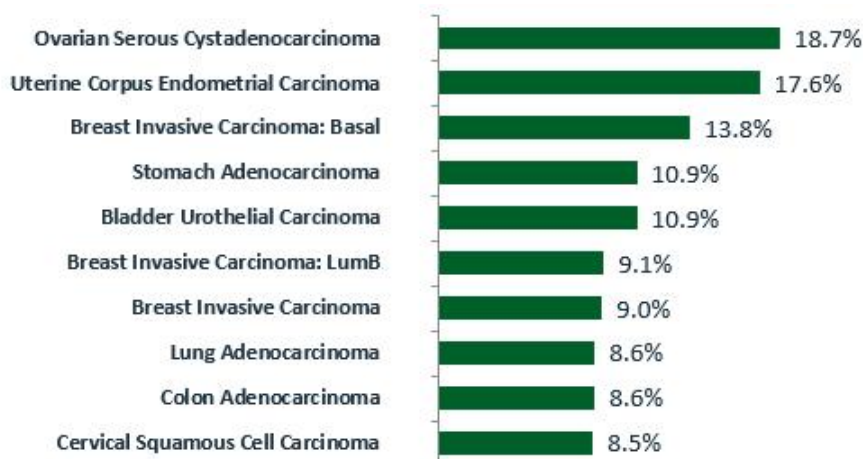
pharmacokinetic profile in multiple preclinical models, including rodent and canine, and a distribution, metabolism and excretion profile that suggests a low potential for drug-drug interactions in the clinic. The clinical trial of camonsertib in patients with recurrent cancers is ongoing.

Our STEP² screens have generated proprietary patient selection insights that we believe provide the rationale to expand the potential patient populations addressable by camonsertib beyond patients with tumors carrying ATM genetic defects. We have identified 19 genomic alterations, in addition to ATM deficiency, that confer sensitivity to camonsertib. This 19 gene set, which we refer to as our STEP²-identified genes, includes several novel genes that have not been previously reported as rendering sensitivity to ATR inhibitors. In addition, many of the genes we have selected do not overlap with previously identified genes in the homologous recombination defect panel, which is utilized to identify patients for treatment with PARP inhibitors and is currently used by others to test for sensitivity to ATR inhibitors. Furthermore, our STEP² screens demonstrated that two genes previously reported by others to be sensitive to ATR inhibition were not sensitive and hence, those genes were excluded from our set of STEP²-identified genes.

The sensitivity and accuracy of our STEP² screens enable the identification of several novel gene alterations, including certain genes that are not yet included in commercially available Next Generation Sequencing cancer panels or Clinical Laboratory Improvement Amendments, or CLIA, validated panels used in large academic centers. For our Phase 1/2 clinical trial, we identified and partnered with multiple large, leading clinical centers globally where tumor sequencing is a component of standard of care. These centers' panels are validated and sufficiently large to accommodate screening for alterations in ATM or our STEP²-identified genes. These panels include the majority, and in the case of whole genome or whole exome sequencing, all of these genes. For genes that are not available on certain panels at a particular clinical site, we identified surrogate genes that are co-deleted with the STEP² genes and have an approximate 30% to 80% probability of concomitant loss, which we believe has and will provide sufficient enrichment for our clinical trial. By working in collaboration with our clinical partners to access their existing patient databases, we believe that we will be able to efficiently identify existing and new patients who may be eligible for our clinical trial.

Based on the prevalence of ATM deficiencies and our STEP²-identified genomic alterations across various solid tumors, as shown in the graph below, we believe that camonsertib has the potential to benefit a significant number of patients representing a large unmet medical need.

**Top 10 Tumor Types with Highest Prevalence of ATM Deficiency
or 16 STEP² Genomic Alterations**



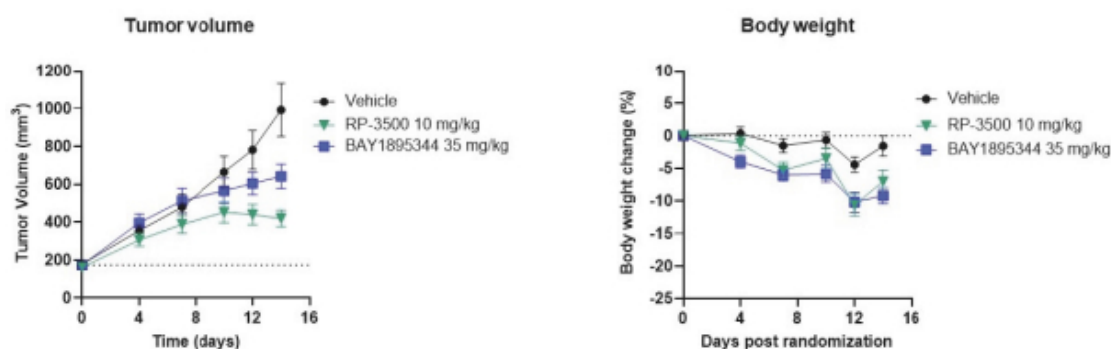
As part of our development strategy for camonsertib, we are evaluating the potential anti-tumor activity of camonsertib in combination with an approved PARP inhibitor based on the synergies we have observed in our

preclinical studies. PARP inhibitors lead to the stabilization of PARP-DNA complexes that block the progression of replication forks. ATR activity stabilizes the DNA replication forks that are destabilized by PARP inhibition and inhibition of ATR causes stalled replication forks to collapse and form cytotoxic DNA double-strand breaks. As a consequence, ATR inhibition can potentiate the cytotoxic effects of PARP inhibitors. We note that this phenomenon is particularly prominent under conditions where some cancer-relevant DDR genes, such as those identified through our STEP² screens, are inactivated, thereby creating a potential therapeutic window.

Preclinical Data: Monotherapy

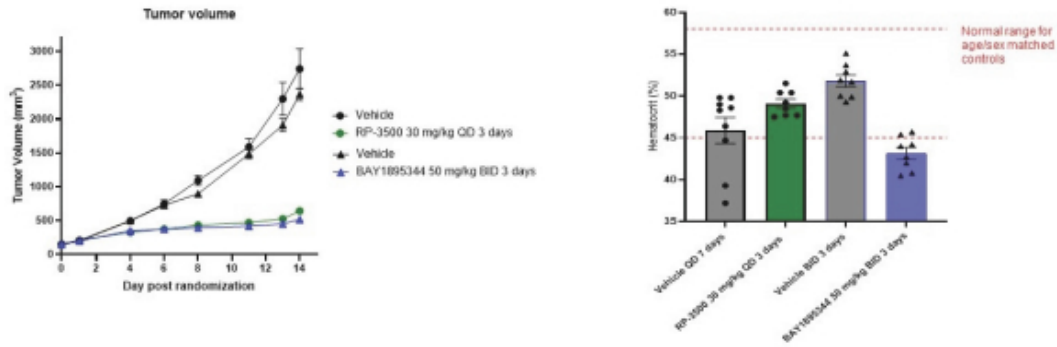
We observed camonsertib to have a favorable tolerability and pharmacokinetics profile across multiple preclinical studies and animal models, which we believe supports advancing the product candidate into clinical trials. In a preclinical study, we evaluated continuous daily dosing of camonsertib in a colon cancer xenograft model with CW-2 cancer cells, which contain an inactivating mutation in ATM that confers sensitivity to ATR inhibition. In this study, we injected mice with tumor cells and waited for tumor growth to approximately 200 mm³ before initiating daily dosing over a period of 14 days with vehicle, camonsertib at its maximum tolerated dose, or MTD, of 10 mg/kg/day, or Bayer's ATR inhibitor product candidate, BAY1895344, at what we determined to be its MTD of 35 mg/kg/day (n=10 mice per group). Both camonsertib and BAY1895344 demonstrated statistically significant suppression of tumor growth as compared to vehicle. Importantly, we observed statistically significant higher suppression of tumor growth with camonsertib as compared to BAY1895344 (p=0.018). Body weight loss as a measurement of tolerability was similar for both compounds in this study.

Statistically Significant Tumor Growth Suppression in Colon Cancer Model



In another preclinical study using an intermittent dosing schedule, we evaluated camonsertib in comparison to BAY1895344 in a Granta-519 mantle cell lymphoma xenograft model. Similar to CW-2 cancer cells, Granta-519 cancer cells also contain an inactivating mutation in ATM that confers sensitivity to ATR inhibition. In this study, we injected mice with tumor cells and waited for tumor growth to approximately 150 mm³ before initiating intermittent dosing with vehicle or either treatment (n=9 mice per group). We observed that both camonsertib and BAY1895344 exhibited tolerability at higher doses when administered on a three days per week schedule than their respective MTDs from the daily dosing CW-2 colon cancer study. The MTDs utilizing this intermittent dosing schedule were determined to be 30 mg/kg daily for camonsertib and 50 mg/kg twice-daily for BAY1895344. Both agents demonstrated similar and significant suppression of tumor growth in this model without body weight loss. However, significant anemia, or hematocrit reduction, was observed in mice treated with BAY1895344 (p=0.0002), whereas we did not observe these tolerability issues with camonsertib, which we believe supports our hypothesis of a favorable tolerability profile for camonsertib.

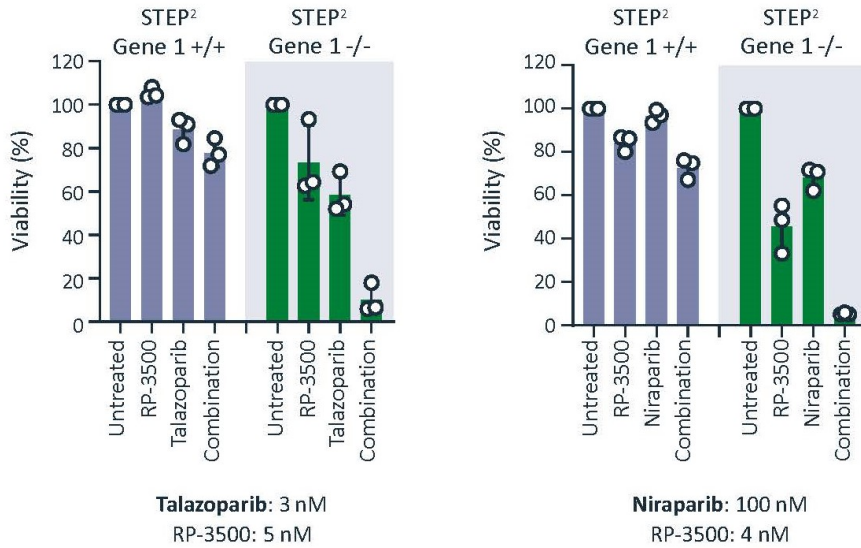
Camonsertib Exhibits Tumor Growth Suppression Without Significant Anemia Measured as Hematocrit in Mantle Cell Lymphoma Model



Preclinical Data: Combination Therapy with PARP

Of our 19 STEP²-identified genes for camonsertib as a monotherapy, we have identified a subset of genes that are particularly sensitive to the combination of camonsertib and PARP inhibitors. The graphs below illustrate two examples of this subset of genes where synergy was demonstrated between camonsertib and PARP inhibitors.

Significant Synergy Demonstrated by Combination of Camonsertib and PARP Inhibitors



+/+ : Wild Type
-/- : Genomically altered

We observed *in vitro* killing of cells carrying this subset of genomic alterations at low concentrations of both compounds, whereas only a minimal effect was seen on control wild-type cells. Based on this finding, we believe that the combination of camonsertib with lower doses of PARP inhibitors could lead to efficient anti-tumor activity while

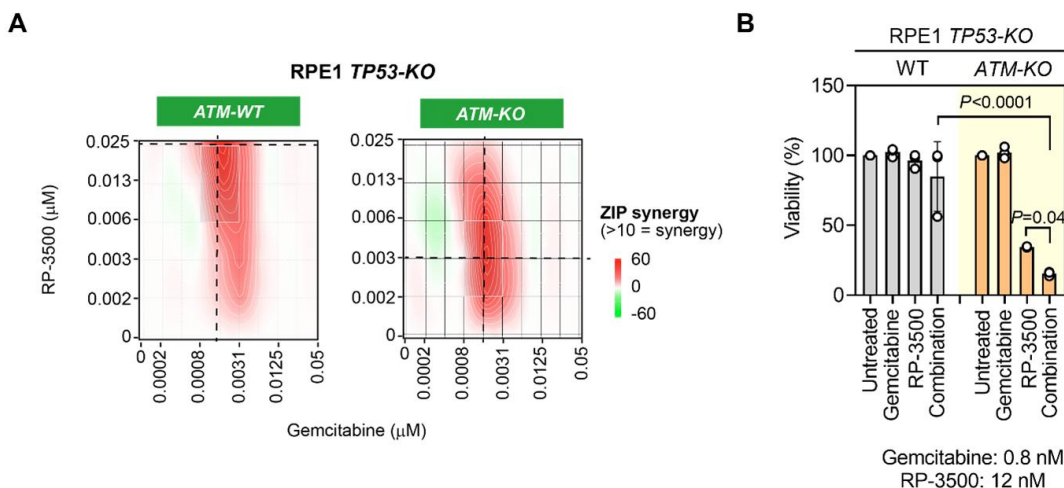
potentially addressing the tolerability issues observed with PARP inhibitors, where a majority of patients in clinical trials of niraparib and talazoparib required a dose reduction or interruption in dosing. We are currently exploring the ATR-PARP inhibitor synergy in additional ongoing studies in xenograft models.

Preclinical Data: Combination Therapy with Gemcitabine

Gemcitabine is an antimetabolite chemotherapeutic agent that is commonly used in various solid tumors such as pancreatic, breast, ovarian, and non-small cell lung cancer. Gemcitabine is metabolized by the tumor cells and incorporated in their DNA, resulting in blockage of DNA polymerases and replication fork stalling. This gemcitabine-induced replication stress increases the tumor cells' dependency on the ATR pathway and gemcitabine is therefore known to strongly enhance the cytotoxic effects of ATR inhibitors.

Our preclinical data demonstrate that gemcitabine shows strong synergy with camonsertib in ATM-deficient (ATM-KO) cells, whereas much higher doses are required to achieve the same degree of synergy in ATM-proficient (ATM-WT) cells (Figure A below). Consequently, camonsertib combined with gemcitabine kills ATM-KO cells at low concentrations that show little effect in WT cells (Figure B below). We therefore believe that the combination with gemcitabine may enhance the anti-tumor activity of camonsertib in ATM-deficient cancers at tolerated doses. We are currently evaluating this combination in tumor cells carrying additional STEP² alterations as well as in animal models.

Sensitivity of ATM-deficient cells to the combination of camonsertib and gemcitabine

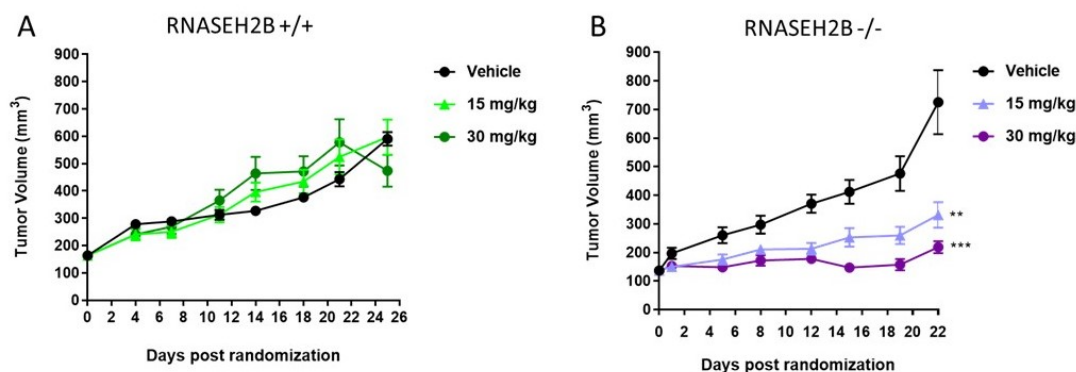


Preclinical Validation of STEP² Screens

Through our STEP² screens of ATR inhibitors, we confirmed the SL relationship between ATR and ATM and identified an additional 19 genomic alterations that confer sensitivity to camonsertib. In follow-up studies with cancer cell line pairs, in which the only difference is the inactivation of the target genes, we are confirming the sensitivity of these genomic alterations to camonsertib, and this extensive validation effort is still being expanded. We are also creating xenograft models using both the parent cell lines and the inactivated cell line. In such a model using one of

the STEP²-identified genes, camonsertib led to statistically significant suppression of tumor growth, whereas it had no anti-tumor effect in tumors created with wild-type parent cells, as shown in the model below.

Tumor Growth Suppression in a *RNASEH2B*^{-/-} 5637 Bladder Isogenic Xenograft Model



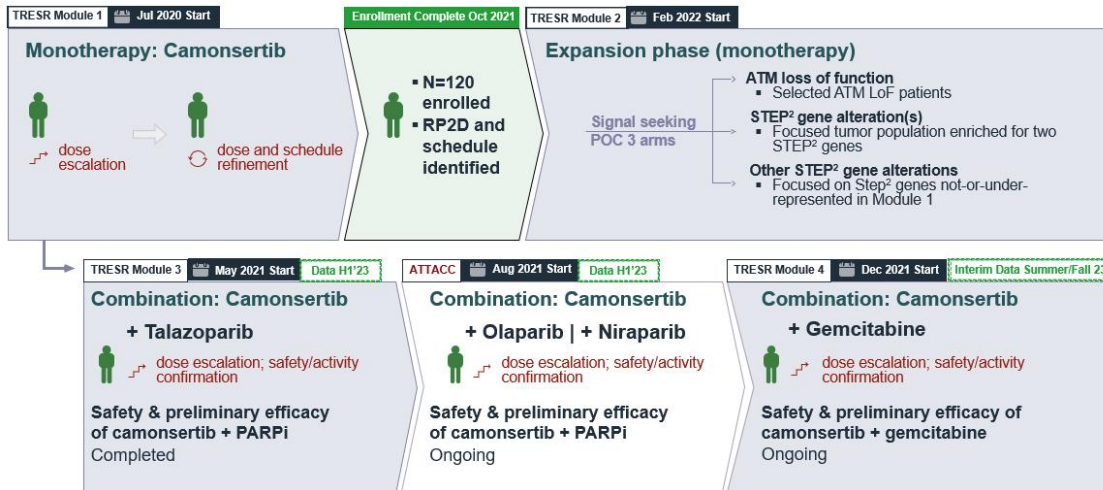
Camonsertib Clinical Trial Program

Design of Trials:

In July 2020, we initiated our open-label Phase 1/2 clinical trial of camonsertib as both a monotherapy and in combination with talazoparib, an approved PARP inhibitor. The trial is designed to evaluate the oral administration of camonsertib in patients with advanced recurrent tumors of different histologies with ATM loss-of-function or a subset comprised of 16 of the 19 STEP²-identified genomic alterations, for which recent in-vitro studies suggested a higher confidence of success.

In the ongoing monotherapy dose escalation phase of our trial, we are evaluating the dosing regimen and safety of camonsertib to establish the recommended dose for the expansion phase of the trial. In three expansion cohorts, each of which has been designed to enroll patients based on ATM loss-of-function or different STEP²-identified genomic alterations, we will assess the preliminary efficacy of camonsertib at the recommended dose and schedule. In parallel with the monotherapy dose escalation phase, the trial is designed to enroll a separate arm to evaluate camonsertib in combination with talazoparib, an approved PARP inhibitor. An efficacy evaluation is performed every six weeks for the first five months and every nine weeks thereafter. As of the date of this Annual Report, we have activated twelve clinical trial sites in North America and Europe, all of which are actively enrolling patients. We observed initial signs of biological and clinical activity as monotherapy and evaluated multiple doses and schedules. We established the recommended Phase 2 dose as 160 mg once daily 3 days on / 4 days off, given continuously every week with a tolerability and safety profile that is favorable and the dominant on-target toxicity is anemia. Grade 3 anemia was reported at 15% with no grade 4 anemia and other grade 3 or 4 toxicities were at maximum 5%. Clinical responders were seen across multiple genomic alterations and tumor types. Clinical benefit rate reported at the AACR-ASCP-NCI meeting in October 2021 was 49%. In February 2021, we initiated recruitment of patients for the talazoparib combination arm of the trial. In December 2021 we entered the Phase 2 part of the trial with expansion into specific tumor and genotype cohorts. We reported complete safety and efficacy data for the monotherapy dose escalation phase of the trial at AACR in April 2022.

The design of our Phase 1/2 clinical trial for camonsertib, now partnered with Roche, is summarized in the diagram below.



Full Dataset from the TRESR Phase 1/2 Trial Presented at AACR 2022:

In April 2022, we presented comprehensive Phase 1 monotherapy clinical data from the TRESR Phase 1/2 trial, reflecting analysis of 120 patients, of which 99 patients were evaluable for efficacy as of the data cutoff date of February 14, 2022 (excluding one patient evaluated as of March 22, 2022). The study included 95 patients who received therapeutically active doses or at the recommended Phase 2 dose schedule of 3 days on / 4 days off, and reflecting the data cutoff of mid-February 2022. Monotherapy with camonsertib continued to appear safe and well tolerated. Anemia was the most common treatment-related adverse event and easily manageable. Only 24.2% of all patients in the 3 days on / 4 days off schedule experienced Grade 3 anemia, and none experienced Grade 4 anemia. Camonsertib monotherapy resulted in durable clinical benefit across tumor types and genomic alterations, with enriched benefit demonstrated in specific patient subsets. These updated monotherapy results showed a 43% CBR, which was defined as response or treatment duration of at least 16 weeks without progression, an overall response rate of 14%, and a mPFS of 15 weeks in solid tumors across genotypes, with potential best-in-class safety and tolerability. The overall CBR in patients after PARP inhibitor failure was 47%.

We observed camonsertib demonstrated robust activity in patients with ovarian cancer (n=20), demonstrating 75% CBR after dosing with camonsertib, an overall response rate of 25%, and a mPFS of 35 weeks. The ovarian cancer patient population was heavily pretreated and comprised a hard to treat population: of which 90% had previous treatment with PARP inhibitors and 85% were platinum resistant. The responders included one complete response, three partial responses as determined by RECIST 1.1 criteria, and one durable and ongoing CA-125 response in a patient with stable disease.

The TRESR study comprises the largest set of tumors with detailed genomic analysis evaluated with ATRi monotherapy. Genomic subsets of tumors beyond ATM included tumors harboring alterations in ATR-sensitizing genes, with responses observed in tumors harboring BRCA1/2, SETD2 and RAD51C alterations. In patients with BRCA1/2 mutated tumors (n = 37), response rate was 14% and included two patients with ovarian cancer, and one each with breast cancer, head and neck squamous cell carcinoma, and melanoma. In patients with tumors carrying BRCA1 mutations, the CBR was 48%. In patients with tumors with ATM loss-of-function, or LOF, (n = 34), response rate was 9% including one RECIST 1.1 confirmed/unconfirmed response, and two prostate specific antigen responses. An additional patient with pancreatic cancer and ATM LOF had a late response, just after the data cutoff after 54 weeks of treatment. The CBR in the patients with ATM LOF was 44% and mPFS was 17 weeks. Sequencing data demonstrated biallelic gene LOF, an emerging biomarker for synthetic lethal therapies, could potentially be leveraged to further enrich for patients most likely to benefit from camonsertib. CBR in patients with biallelic LOF was significantly higher (47%) compared to the CBR in patients with non-biallelic tumors (15%).

RP-6306, Our Novel, First-in-Class PKMYT1 Inhibitor Program

Overview

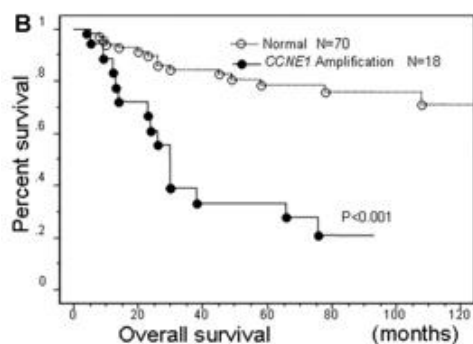
Using our proprietary, CRISPR-based SNIPRx discovery platform, we identified PKMYT1 as a strong hit in a CCNE1-overexpression SL screen. PKMYT1 is a kinase that phosphorylates CDK1, thereby holding the cyclin B-CDK1 complex in an inactive state until the cell is ready to enter mitosis. RP-6306 is being developed as a highly potent and selective PKMYT1 inhibitor that preferentially kills tumor cells overexpressing CCNE1 and was shown to inhibit the growth of a broad range of CCNE1-amplified tumors in xenograft/PDX preclinical models, both as a single agent and in combination therapy settings. RP-6306 has a favorable preclinical PK profile as well as low potential for drug-drug interactions. Application of our STEP² genome-wide chemical screen has identified other gene alterations beyond CCNE1 amplification that are uniquely targetable by RP-6306, including tumors that have loss of FBXW7 function, a cell-cycle regulator that has been implicated as a key genetic driver in a broad range of cancers, and represent further areas of unmet medical need. We initiated patient recruitment in our open-label Phase 1 MYTHIC trial, as a monotherapy, for this program in April 2021. Our Phase 1 trial is enrolling patients suffering from recurrent tumors characterized by CCNE1 amplification and other genomic alterations which our STEP² preclinical studies predicted to be sensitive to RP-6306. We are evaluating more than one schedule, if necessary, at which the capsules are given in this dose escalation trial. The primary objective is to establish the recommended Phase 2 dose and schedule for RP-6306 for further studies as monotherapy and assess preliminary safety, tolerability, PK, and PD in patients. In December 2021, we enrolled the first patient in our open-label Phase 1 MAGNETIC trial to evaluate the safety and tolerability of RP-6306 in combination with gemcitabine. In January 2022, we initiated patient recruitment in our open-label Phase 1 MINOTAUR trial to evaluate the safety and tolerability of RP-6306 in combination with FOLFIRI. In May 2022, we initiated patient recruitment in a new arm of the Phase 1 MYTHIC clinical trial, which is designed to evaluate the safety and tolerability of RP-6306 in combination with camonsertib in patients with advanced solid tumors. In the fourth quarter of 2022, we received fast track designation for RP-6306 in combination with gemcitabine for the treatment of adult patients with CCNE1 amplified, or FBXW7 or PPP2R1A mutated platinum resistant ovarian cancer. Based on promising preclinical data released at the 34th EORTC-NCI-AACR Symposium in October 2022, we are working with clinical investigators to initiate clinical testing, as part of an investigator-sponsored trial (IST), of a fourth new RP-6306 combination with carboplatin, with first patient dosing expected in the first half of 2023. In the fourth quarter of 2022, we entered into an agreement with CCTG for a planned, basket Phase 2 IST to evaluate RP-6306 in patients with selected, advanced cancers receiving standard agents. We have planned a sub-study under this trial, which will allow us to evaluate RP-6306 in combination with gemcitabine in patients with CD4/6i-resistant ER+/HER2- metastatic breast cancer. We plan to provide an initial Phase 1 clinical data readout for RP-6306 in the first half of 2023 for monotherapy, and anticipate providing an update on some of the combination studies in the fourth quarter of 2023.

Mechanism of Action

PKMYT1, the gene targeted by RP-6306 has not previously been published as a SL gene pair with CCNE1 amplification, and we are not aware of any advanced drug discovery efforts against this target. In preclinical studies, we observed that the deletion of this gene was well tolerated in wild-type cells, but it caused lethality in isogenic cancer cells that overexpressed CCNE1.

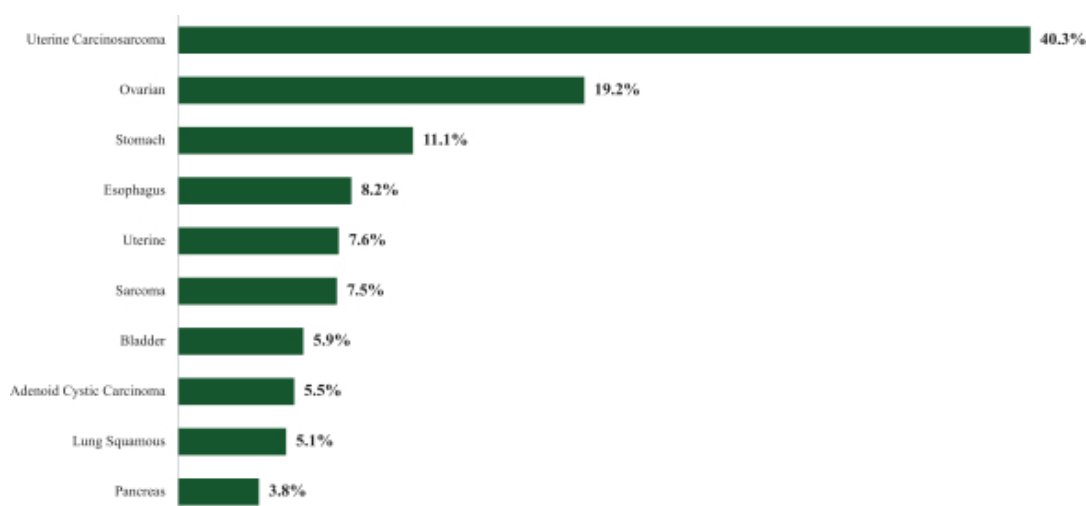
High levels of CCNE1 protein, an activating subunit of cyclin dependent kinase 2, or CDK2, are often observed in patients across multiple tumor types. Deregulation of cell cycle control is thought to be a prerequisite for tumor development, and several studies have demonstrated accelerated entry of cells into the S phase, or DNA synthesis phase, of the cell cycle, due to constitutive, or “always-on,” expression of CCNE1. Such an accelerated entry of cells into the S phase is a common sign of unregulated, cancerous growth. CCNE1 amplification can induce chromosome instability, another sign of cancer, by contributing to inappropriate initiation of DNA replication. Several studies have demonstrated that CCNE1 amplification or constitutive expression is associated with disease progression in various malignancies as well as poor clinical prognosis in patients across multiple cancers, including ovarian, breast, bladder, and colorectal cancer. For example, clinical data from patients with ovarian cancer indicate that those with CCNE1-amplified tumors have significantly shorter overall survival than those with tumors without CCNE1 amplification, as shown below.

CCNE1 Amplification is Associated with Significantly Shorter Overall Survival in Patients with Ovarian Cancer



CCNE1 amplification is found in 4% of tumors in the pan-cancer TCGA studies. Over 40% of uterine carcinosarcoma cancers and 10% to 20% of ovarian and stomach cancers harbor CCNE1 amplification. Together, these cancers lead to over 40,000 deaths each year in the United States. Additional cancer types also harbor CCNE1 amplification at a lower frequency, including up to 3% to 8% of esophagus, bladder, lung, and pancreatic cancers, as shown below.

Top 10 Tumor Types with Highest Frequency of CCNE1 Amplification



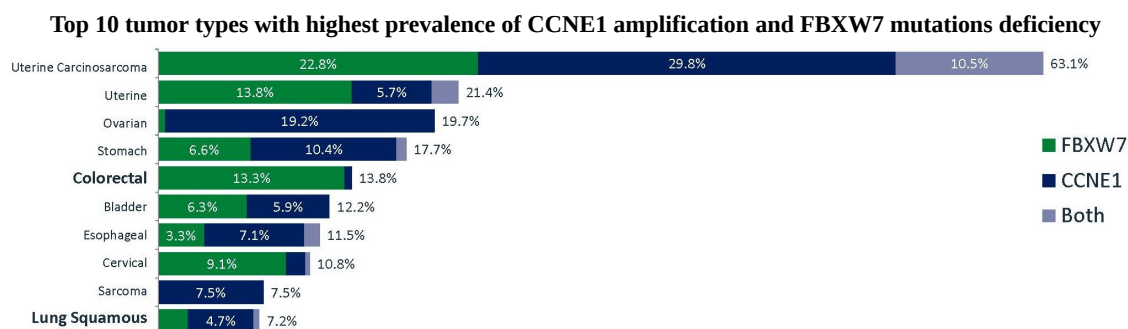
Our Solution, RP-6306

We identified PKMYT1 as a critical SL target for patients with CCNE1 amplification through our SNIPRx screening campaign and selected PKMYT1 as a target for our lead product candidate, RP-6306, based on:

- i. the target validation for PKMYT1;
- ii. our ability to design potent and selective PKMYT1 inhibitors; and
- iii. the results of our STEP² screens, which identified at least two additional genomic alterations beyond CCNE1 amplification to be SL with PKMYT1 inhibitor facilitating the expansion of the addressable patient populations.

We designed RP-6306 as an oral small molecule PKMYT1 inhibitor with significant potency and an encouraging selectivity profile as a first in class compound. RP-6306 has demonstrated a favorable pharmacokinetic profile in multiple preclinical models, including rodent and canine, and a distribution, metabolism and excretion profile that suggests a low potential for drug-drug interactions in the clinic. The clinical trial of RP-6306 in patients with recurrent cancers is ongoing.

Our STEP² screens have generated proprietary patient selection insights that we believe provide the rationale to expand the potential patient populations addressable by RP-6306 beyond patients with tumors carrying CCNE1 amplification. We have specifically identified FBXW7 and PPP2R1A genomic alterations, in addition to CCNE1 amplification, that confer sensitivity to RP-6306. This set of genes offers extended patient populations such as about 13% of colorectal cancer and other high unmet need tumors as presented in the graph below.



The proposed alterations specific to RP-6306 tumors are easily identifiable in commercially available Next Generation Sequencing cancer panels or CLIA-validated panels used in large academic centers. For our Phase 1/2 clinical trial, we identified and partnered with multiple large, leading clinical centers globally where tumor sequencing is a component of standard of care. These centers' panels are validated and sufficiently large to accommodate screening for alterations in FBXW7 and CCNE1 or our other STEP²-identified genes. By working in collaboration with our clinical partners to access their existing patient databases, we are able to efficiently identify patients who may be eligible for our clinical trial.

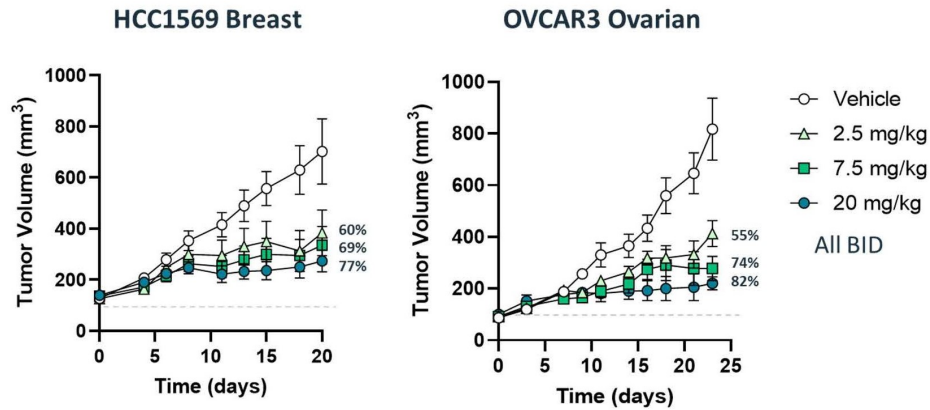
Based on the prevalence of RP-6306 relevant genomic alterations across various solid tumors, as shown in the graph above, we believe that RP-6306 has the potential to benefit a significant number of patients representing a large unmet medical need.

Preclinical data: Monotherapy

We observed that RP-6306 has a favorable tolerability and PK profile preclinically which we believe supported advancement of the product candidate into clinical trials. We tested RP-6306 as a single agent in two preclinical cell line derived models of cancer selected to represent our target patient populations by having amplification of CCNE1. The HCC1569 breast cancer model and the OVCAR3 ovarian cancer model with CCNE1 copy numbers of 34-fold and 14-fold above ploidy, respectively. In the HCC1569 breast cancer xenograft model, RP-6306 was orally administered at doses of 2.5, 7.5 or 20 mg/kg twice daily (BID) for 28 days. RP-6306 produced a dose-dependent reduction in tumor growth reaching a statistically significant difference at all doses and a maximum effect of 77%. In the 20 mg/kg group, mice exhibited body weight loss of 3.2% at the end of study. In the OVCAR3 ovarian cancer xenograft model, RP-6306 was orally administered at doses of 2.5, 7.5 or 20 mg/kg twice daily (BID) for 28 days. RP-6306 produced a dose-dependent reduction in tumor growth reaching a statistically significant difference at all doses and a maximum effect of 82%. In the 20 mg/kg group, mice exhibited body weight loss of 6.9% at the end of study.

In preclinical studies, RP-6306 demonstrated *in vivo* anti-tumor activity in two cell line derived xenograft models with CCNE1 amplification. In both models, we observed statistically significant dose-dependent tumor growth suppression across a range of doses from 2.5 to 20 mg/kg BID (twice-daily administration for RP-6306).

RP-6306 Demonstrates Tumor Growth Suppression in CCNE1-Amplified Cell Line Derived Xenograft Models



Preclinical Data: Combination Therapies with RP-6306

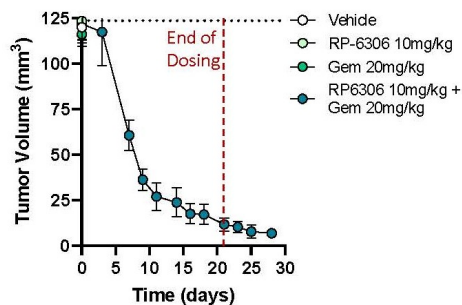
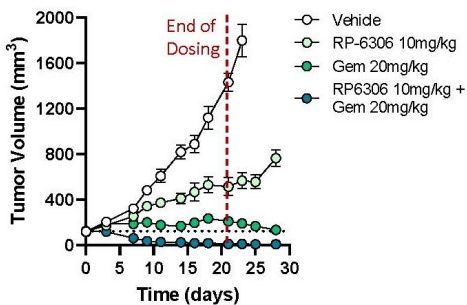
Chemotherapeutic drugs have diverse mechanisms of action, and some target DNA replication and induce DNA replication stress. During the S-phase of the cell cycle, DNA is replicated to create DNA for two daughter cells following cell division. S-phase disrupting drugs increase dependence on cell cycle checkpoints. Combining this S-phase vulnerability with RP-6306, which forces S-phase replicating cells into premature mitosis, is expected to be catastrophic to tumor cells.

Gemcitabine prolongs the S-phase by both interfering with DNA polymerase and disrupting the supply of nucleotides. Clinically, gemcitabine has been used as a single agent or in combination with carboplatin, cisplatin, or paclitaxel for the treatment of pancreatic, ovarian, breast, bladder, testicular, and non-small cell lung cancer. Recent studies have tested gemcitabine in combination with DNA damage repair inhibitors (PARP and ATR inhibitors), as well as cell cycle inhibitors (WEE1, CDK4/6, and Chk1 inhibitors) across a spectrum of relapsed or refractory advanced solid tumors. Attempts to combine gemcitabine with inhibitors of these checkpoints have struggled with toxicity, impacting proliferating tumor and normal tissue with similar effect. In a setting of CCNE1, FBXW7, PPP2R1A, and potentially other RP-6306 STEP² genetic alterations, however, it is expected that gemcitabine will exacerbate the replication stress environment where PKMYT1 is essential for survival and provide synthetic lethal synergy with enhanced benefit and therapeutic index.

The rationale behind combining RP-6306 and FOLFIRI in CCNE1-amplified or FBXW7-mutated tumors is similar to that of gemcitabine. The two main agents found in FOLFIRI are irinotecan (metabolized in tissues to SN-38) and fluorouracil, both of which act specifically in S-phase. SN-38 acts on the topoisomerase I-DNA complex and prevents re-ligation of the DNA strand, resulting in double-strand DNA breaks and cell death. Fluorouracil acts as a thymidylate synthase inhibitor which blocks synthesis of the pyrimidine thymidine, required for DNA replication. Combining this chemotherapy-induced S-phase vulnerability with RP-6306, which forces S-phase replicating cells into premature mitosis, is expected to be catastrophic to tumor cells.

The combination of RP-6306 and gemcitabine was evaluated in CCNE1 amplified model of ovarian cancer (OVCAR3) on a continuous BID dosing of RP-6306 at 10mg/kg and gemcitabine at 20mg/kg once weekly. The combination resulted in complete tumor regression that was significantly better than either agent alone with minimal impact on body weight loss (6.8% for the combination at the end of dosing).

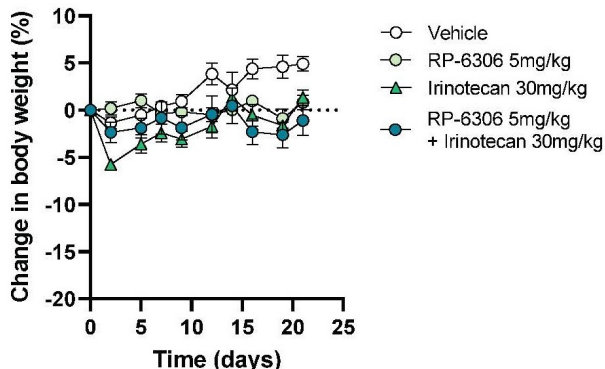
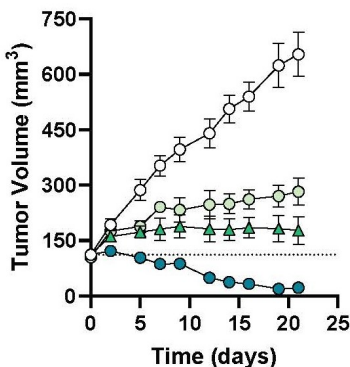
RP-6306 + Gemcitabine Drives Regression and No Serious Toxicity in CCNE1-Amplified Cell Line Derived Xenograft
OVCAR3; CCNE1 CN = 14 **Robust regression**



Gemcitabine dosed once a week and RP-6306 dosed twice daily

The combination of RP-6306 and irinotecan was evaluated in CCNE1-amplified model of breast cancer (HCC1569) on a continuous BID dosing of RP-6306 at 5 mg/kg and irinotecan at 30 mg/kg three times a week. The combination resulted in tumor regression that was significantly better than either agent alone with minimal impact on weight loss (1.5% for the combination at the end of dosing).

RP-6306 + Irinotecan Drives Regression and is Well Tolerated in CCNE1-Amplified Cell Line Derived Xenograft
HCC1569; CCNE1 CN = 34 **Tolerability**

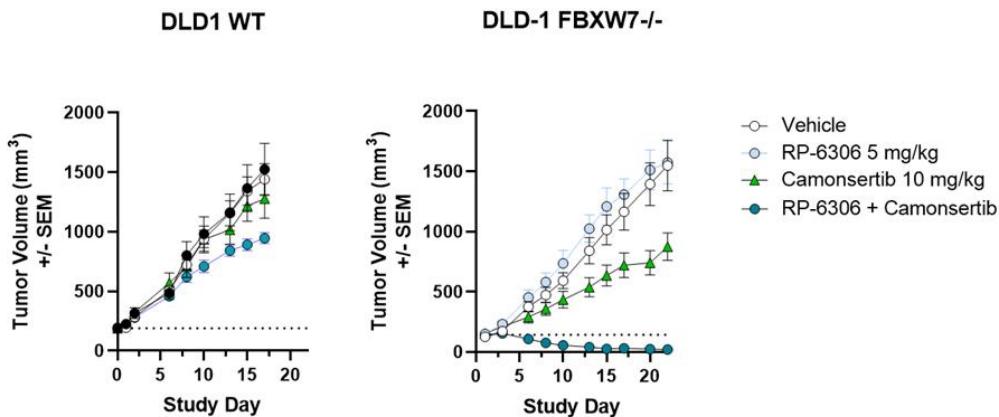


Irinotecan dosed three times a week and RP-6306 dosed twice daily

The combination of low dose RP-6306 and camonsertib was evaluated in a pair of isogenic models of colorectal cancer having normal FBXW7 or FBXW7 loss-of-function. RP-6306 was administered at 5mg/kg BID and camonsertib was administered at 10mg/kg QD three times a week. Neither compound alone nor the combination substantially impacted tumor growth of FBXW7-normal tumors. In contrast, a low dose of RP-6306 in combination

with camonsertib resulted in profound regression of FBXW7 loss-of-function tumors with 3 of 8 mice tumor free on day 22. The combination was well tolerated with a < 8% maximal mean body weight loss.

RP-6306 + Camonsertib Selectively Drives Regression and is Well Tolerated in a FBXW7 Loss-of-Function Cell Line Derived Xenograft

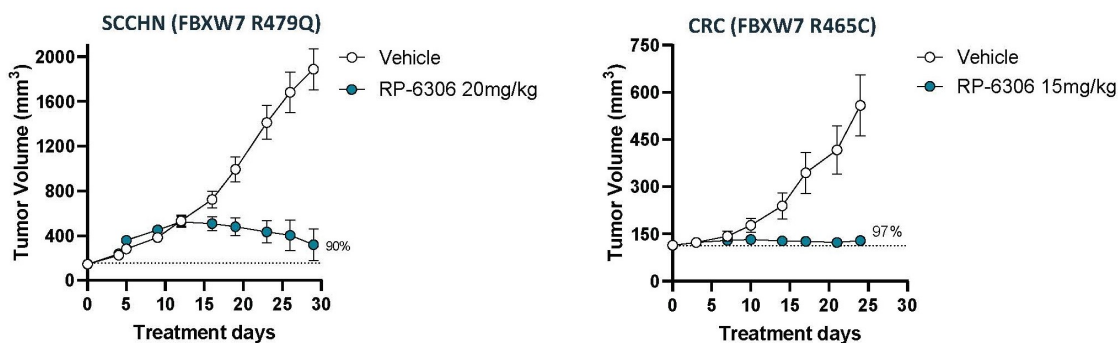


Preclinical Validation of STEP² Screens

To identify additional genetic lesions which might have a synthetic lethal relationship with PKMYT1, several STEP² screens were conducted. These genome wide CRISPR screens were conducted with sub-cytotoxic concentrations of PKMYT1 inhibitor and identified FBXW7 and several additional genetic alterations. FBXW7 is known to be mutated in colorectal cancers and NSCLC, among others. FBXW7 is an E3-ubiquitin ligase that targets Cyclin E1 (as well as other oncogenes) for degradation by the proteasome and has been shown to be a tumor suppressor gene. Therefore, there exists a strong mechanistic rationale for synthetic lethality with PKMYT1, and they represent a significant opportunity to expand the clinical utility of RP-6306.

In preclinical studies, RP-6306 demonstrated in vivo anti-tumor activity in two patient derived xenograft models with FBXW7 inactivating mutations. In both models, we observed statistically significant tumor growth suppression with twice daily administration for RP-6306.

RP-6306 Demonstrates Tumor Growth Suppression of FBXW7-Mutated Patient Derived Xenograft Models

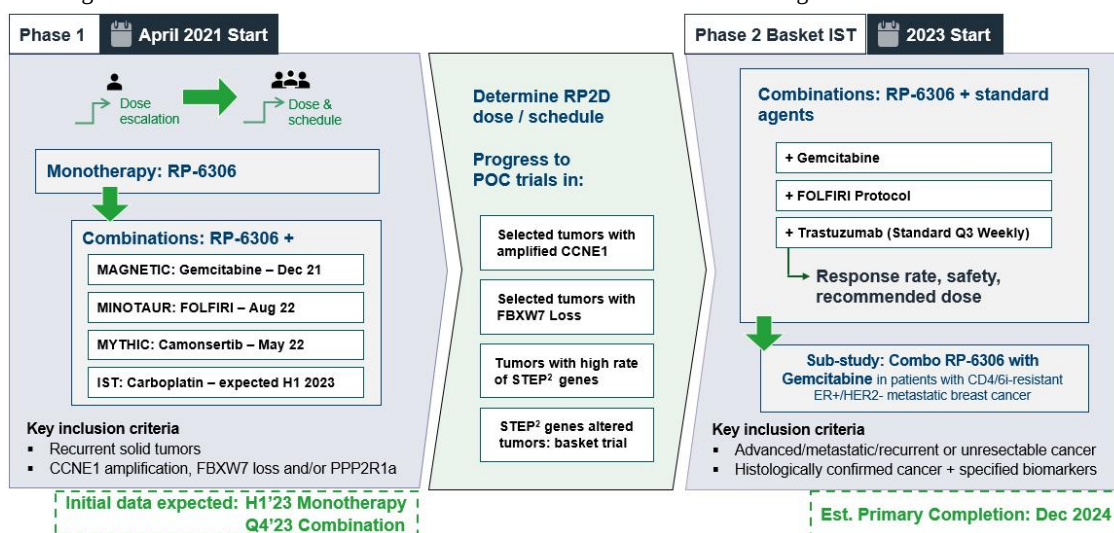


Design of Trials

In April 2021, we initiated our open-label Phase 1 MYTHIC clinical trial of RP-6306 as a monotherapy. The trial is designed to evaluate the oral administration of RP-6306 in patients with advanced recurrent tumors of different histologies in tumors with detected CCNE1 amplification, deleterious alterations in FBXW7, PPP2R1A and other STEP² genes, for which recent in-vitro studies suggested a higher confidence of success.

In the ongoing monotherapy dose escalation phase of our MYTHIC trial, we are evaluating the dosing regimen and safety of RP-6306. The MYTHIC trial is enrolling patients suffering from recurrent tumors characterized by CCNE1 amplification and other genomic alterations, which our STEP² preclinical studies predicted to be sensitive to RP-6306. We are evaluating more than one schedule at which the capsules are given, as necessary, in this dose escalation trial. The primary objective is to establish dose and schedule for RP-6306 for further studies as monotherapy and assess preliminary safety and tolerability in patients. The clinical plan beyond the dose escalation and initial explorations of dose and safety is presented below. In parallel with the monotherapy dose escalation phase, two other trials were initiated in February 2022 and December 2021, which we refer to as the MINOTAUR and MAGNETIC trials, to evaluate RP-6306 in combination with FOLFIRI and gemcitabine, respectively. In May 2022, we initiated patient recruitment in a new arm of the Phase 1 MYTHIC clinical trial, which is designed to evaluate the safety and tolerability of RP-6306 in combination with camonsertib in patients with advanced solid tumors. In the fourth quarter of 2022, we received fast track designation for RP-6306 in combination with gemcitabine for the treatment of adult patients with CCNE1 amplified, or FBXW7 or PPP2R1A mutated platinum resistant ovarian cancer. Based on promising preclinical data released at the 34th EORTC-NCI-AACR Symposium in October 2022, we are working with clinical investigators to initiate clinical testing, as part of an investigator-sponsored trial (IST), of a fourth new RP-6306 combination with carboplatin, with first patient dosing expected in the first half of 2023. In the fourth quarter of 2022, we entered into an agreement with CCTG for a planned, basket Phase 2 IST to evaluate RP-6306 in patients with selected, advanced cancers receiving standard agents. We plan to initiate a sub-study, which will allow us to evaluate RP-6306 in combination with gemcitabine in patients with CD4/6i-resistant ER+/HER2- metastatic breast cancer. We plan to provide an initial Phase 1 clinical data readout for RP-6306 in the first half of 2023 for monotherapy, and anticipate providing an update on some of the combination studies in the fourth quarter of 2023.

The designs of our Phase 1 clinical trial and Phase 2 IST are summarized in the diagram below.



Our Polymerase Theta (Polθ) Preclinical Program

We are developing a small molecule inhibitor of Polθ, a SL target associated with BRCA mutations as well as other genomic alterations, in collaboration with Ono. This program was initially added to our portfolio through a

collaboration with our co-founder, Dr. Agnel Sfeir, now at Memorial Sloan Kettering Cancer Center, who initially published her observations on the SL between BRCA and Pol θ in *Nature* in 2016.

Polymerase theta enzyme, or POLQ, is a DNA polymerase enzyme that participates in the repair of double-strand breaks in DNA. Mutations in genes such as BRCA1 and BRCA2 increase the frequency of these breaks, resulting in SL with Pol θ . Preclinical studies have shown that inactivation of Pol θ both on its own and in combination with PARP inhibitors reduces survival in BRCA-mutated cells, but not in BRCA wild-type cells. BRCA1 and BRCA2 mutations are routinely identified in multiple genetic profiling tests and observed in approximately 1% to 7% of patients with breast and ovarian cancer. However, the frequency of mutations in one of these BRCA genes increases in women with a family history of disease and in certain subpopulations. For example, up to 37% of patients with breast cancer with low estrogen and progesterone receptor expression have BRCA mutations.

BRCA1 and BRCA2 mutations have also been shown in clinical trials to be SL with PARP inhibitors in multiple tumors, such as breast and ovarian cancer. While PARP inhibitors have proven effective in BRCA-mutant tumors, no statistically significant survival benefit has been reported in breast or pancreatic cancer to date, highlighting the potential for other SL targets, such as Pol θ , to demonstrate meaningful efficacy as a monotherapy or in combination with PARP inhibitors. In 2022, we selected a proposed inhibitor, which we designated as RP-2119, and initiated IND-enabling studies. In February 2023, based on our review of ongoing preclinical studies, we elected to prioritize other Pol θ inhibiting compounds in our preclinical development portfolio, which we believe have a higher probability for clinical impact relative to RP-2119. We are now guiding toward clinical entry for a Pol θ inhibitor in 2024.

Intellectual Property

We strive to protect and enhance the proprietary technologies, inventions, and improvements that we believe are important to our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms, and our product candidates that are important to the development and implementation of our business.

As of December 31, 2022, our patent portfolio relating to our product candidates included seven pending U.S. provisional patent applications, consisting of; two applications covering uses of ATR inhibitors; two applications covering CCNE1-SL inhibitors and their use; one application covering the manufacture of RP-6306; and two applications covering PolQ inhibitors and their use. In addition, our patent portfolio included six pending international applications under the Patent Cooperation Treaty of 1970, or the PCT, three covering camonsertib and/or its uses and three covering RP-6306 and its uses. Our portfolio also included five pending U.S. non-provisional patent applications, three covering camonsertib and its use and two covering RP-6306 derivatives.

As of December 31, 2022, three of our four PCT applications have composition of matter or method of treatment and use claims covering camonsertib. Any application, if issued, claiming priority to any of these PCT applications is expected to expire in 2040, not including any patent term adjustment. One of our four solely owned PCT applications has composition of matter claims covering RP-6306. Any application, if issued, claiming priority to this PCT application is expected to expire in 2041, not including any patent term adjustment. Any patent issuing in our solely owned, pending U.S. non-provisional patent application having composition of matter and method of treatment and use claims covering camonsertib and its use is expected to expire in 2039, not including any patent term adjustment. Any patent issuing in our solely owned, pending U.S. non-provisional patent application having method of treatment and use claims covering certain uses of camonsertib is expected to expire in 2040, not including any patent term adjustment. Any U.S. patent, if issued, claiming priority to any one of the U.S. provisional patent applications covering uses of camonsertib is expected to expire in 2043. Any U.S. patent, if issued, claiming priority to any one of the U.S. provisional patent applications covering CCNE1-SL inhibitors and their use, is expected to expire in 2042. Any U.S. patent, if issued, claiming priority to either of the U.S. provisional patent applications covering CCNE1-SL inhibitors, including RP-6306 and its use, is expected to expire in 2043. Any U.S. patent, if issued, claiming priority to the U.S. provisional patent applications covering uses of CCNE1-SL inhibitors, including RP-6306, is expected to expire in 2043. Any U.S. patent, if issued, claiming priority to the U.S. provisional patent applications covering PolQ inhibitors and their use, is expected to expire in 2043.

As of December 31, 2022, our patent portfolio also included two co-owned, pending international applications under the Patent Cooperation Treaty of 1970, or the PCT. The PCT applications cover uses of CCNE1-SL inhibitors, including RP-6306. Any U.S. patent, if issued, claiming priority to the PCT applications is expected to expire in 2041 or 2042, respectively.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The PCT is an international patent law treaty that provides a unified procedure for filing patent applications to protect inventions in each of its contracting states. Thus, a single PCT application can be converted into a patent application in any of the PCT-contracting states, and is considered a simple, cost-effective means for seeking patent protection in numerous regions or countries. This nationalization (converting into an application in any of the contracting states) typically occurs 18 months after the PCT application filing date. An applicant must undertake prosecution within the allotted time in each of the contracting states or on a regional basis if it determines to undertake patent issuance in protection in such country or territory. Pursuant to its PCT application, the Company expects to pursue patent protection in the United States.

In addition, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our collaborators and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees, and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidates or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future product candidates may have an adverse impact on us. For more information, please see “Risk Factors—Risks Related to Intellectual Property.”

Collaborations and License Agreements

Collaboration and Worldwide License Agreement with Roche

In June 2022, we announced a worldwide license and collaboration agreement with Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd (collectively, Roche), or the Roche Agreement for the development and commercialization of camonsertib and specified other ATR inhibitors for the treatment of tumors with specific synthetic-lethal genomic alterations. Under the Roche Agreement, Roche assumes all subsequent development of camonsertib with the potential to expand development into additional tumor indications and multiple combination studies.

Under the terms of the Roche Agreement, we received a \$125 million upfront payment in July 2022, and are eligible to receive up to \$1.172 billion in potential clinical, regulatory, commercial and sales milestones, including up to \$55 million in potential near-term payments, and royalties on global net sales ranging from high-single-digits to high-teens. We received \$5.6 million in October 2022 for the transfer of clinical trial material on hand to Roche, as agreed to pursuant to the Roche Agreement. In December 2022 we received an additional payment of \$4.0 million negotiated with Roche for revisions to the clinical development plan under the Roche Agreement as agreed to by the parties on July 13, 2022. The Roche Agreement also provides our company with the ability to opt-in to a 50/50 U.S. co-development and profit share arrangement, including participation in U.S. co-promotion if U.S. regulatory approval is received, that is exercisable prior to the commencement of the first pivotal clinical trial of camonsertib. If we choose to exercise the co-development and profit share option, we will continue to be eligible to receive certain clinical, regulatory, commercial and sales milestone payments, in addition to full ex-U.S. royalties. Royalties are payable by Roche on a product by product and country by country basis until the later of 12 years following the first commercial sale of a licensed product in such country or the expiration of certain exclusivity rights.

We have agreed to complete the specified ongoing clinical trials, TRESR and ATTACC, at our expense. We have also retained the right to conduct specified clinical trials of camonsertib in combination with our PKMYT1 compound, RP-6306.

The Roche Agreement was subsequently amended in October 2022 to extend the timeline to negotiate in good faith the parties' rights and obligations with respect to certain clinical trials and to clarify indications included in the development plan that are subject to milestones.

Collaboration and License Agreement with Bristol-Myers Squibb Company

In May 2020, we entered into a collaboration and license agreement, or the BMS Agreement, with Bristol-Myers Squibb Company, or Bristol Myers Squibb, pursuant to which we and Bristol Myers Squibb have agreed to collaborate in the research and development of potential new product candidates for the treatment of cancer.

We are providing Bristol Myers Squibb access to a selected number of our existing early SNIPRx screening campaigns and novel campaigns. We are responsible for carrying out early-stage research activities directed to identifying and validating potential targets for licensing by Bristol Myers Squibb, in accordance with a mutually agreed upon research plan. The collaboration consists of programs directed to both druggable targets and to targets commonly considered undruggable by traditional small molecule approaches. In the event that Bristol Myers Squibb elects to obtain an exclusive license on for the subsequent development, manufacture and commercialization of a program, Bristol Myers Squibb will then be solely responsible for all such worldwide activities. The research collaboration will be overseen by a joint steering committee through completion of all research activities.

The BMS Agreement has been subsequently amended in July, September and November 2020 to expand our collaboration with Bristol Myers Squibb. We amended the BMS Agreement to, among other things: (i) include additional campaigns to the list of Existing Repare Campaigns (as such term is defined in the BMS Agreement) from which Bristol Myers Squibb may select campaigns under the BMS agreement, and (ii) enable unblinding of a Bristol Myers Squibb alliance manager in order to streamline the collaboration and selection process.

Under the terms of the BMS Agreement, Bristol Myers Squibb paid us an initial upfront fee payment of \$50.0 million. In connection with entering into the BMS Agreement, we also entered into a warrant agreement with an affiliate of Bristol Myers Squibb pursuant to which we issued a warrant for total proceeds of \$15.0 million, which was automatically exercised into 750,000 common shares upon closing of our IPO at which time the warrants were cancelled.

For each of the targets in the collaboration, we are entitled to receive, on a program-by-program basis, option exercise fees ranging in the low six figures depending on the nature of the applicable program. Bristol Myers Squibb has the right to retain rights to certain back-up programs in exchange for a one-time payment in the low eight figures per program. Additionally, we are entitled to receive additional fees ranging in the low to mid seven figures upon the selection of certain programs beyond a specified limit.

In October 2021, we received notification from Bristol Myers Squibb of their option exercise for two druggable targets directed at a single synthetic lethal lesion, pursuant to the terms of the BMS Agreement.

Under the BMS Agreement, we are entitled to receive up to \$3.0 billion in total milestones across all potential programs. Such milestones consist of \$301.0 million in total milestones per program, including \$176.0 million in the aggregate for certain specified research, development, and regulatory milestones and \$125.0 million in the aggregate for certain specified commercial milestones. We are also entitled to a tiered percentage royalty on annual net sales ranging from high-single digits to low-double digits, subject to certain specified reductions. Royalties are payable by Bristol Myers Squibb on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last valid claim covering the licensed product in such country, expiration of all applicable regulatory exclusivities in such country for such licensed product and the tenth anniversary of the first commercial sale of such licensed product in such country.

On a program-by-program basis, prior to the earlier of such program ceasing to be included under the BMS Agreement and expiration of the last to expire royalty term for such program, we, alone and with third parties, are prohibited from researching, developing, manufacturing and commercializing products that are directed to the applicable target for such program.

We also have provided Bristol Myers Squibb with certain, limited rights to first negotiate with us if we determine to divest, license, or collaborate with others regarding certain existing programs, including in the event that we received an unsolicited offer to do so. The right to first negotiation expressly excludes any potential Change of Control transaction (as such term is contractually defined in the BMS Agreement).

The BMS Agreement will expire on a licensed product-by-licensed product and country-by-country basis on expiration of the applicable royalty term and in its entirety upon expiration of the last royalty term. Either party may terminate the BMS Agreement earlier upon an uncured material breach of the agreement by the other party, or the insolvency of the other party. Additionally, Bristol Myers Squibb may terminate the BMS Agreement for any or no reason on a program-by-program basis upon specified written notice.

Research Services, License and Collaboration Agreement with Ono Pharmaceutical Co.

All payments by Ono to us are presented in U.S. dollars. Future payments as disclosed in this summary have been converted to U.S. dollars at the December 31, 2022 exchange rate of \$1.00 = [131.12] Japanese yen.

In January 2019, we entered into a research services, license and collaboration agreement, or the Ono Agreement, with Ono Pharmaceutical Co., Ltd., or Ono, pursuant to which we and Ono have agreed to collaborate in the research of potential product candidates targeting Polθ and the development of our small molecule Polθ inhibitor program. We are primarily responsible for carrying out research activities to identify a product candidate for the program, to be licensed to Ono, in accordance with a mutually agreed upon research plan until the first submission of an IND in the United States or Japan. In the event that Ono elects to collaborate on the subsequent development and commercialization of a proposed product candidate, Ono will then be responsible for such activities in Japan, South Korea, Taiwan, Hong Kong, Macau and certain other Southeast Asian countries, and we will be responsible for such activities in the rest of the world. The collaboration will be overseen by a joint research committee through development candidate selection and a joint steering committee thereafter. Except as set forth below, each party will bear its own expenses in connection with research, development, and commercialization activities under the Ono Agreement.

In October 2021, we entered into an amendment to the Ono Agreement whereby the Research Term, as defined in the Ono Agreement, was extended by one year at no additional cost to us. In January 2023, we and Ono entered into a second amendment to the Ono Agreement whereby the Research Term was extended until July 31, 2023.

Under the terms of the Ono Agreement, Ono paid us an initial upfront fee payment of ¥110 million (approximately \$1.0 million). Additionally, in connection with the research activities to be conducted by us pursuant to the Ono Agreement, Ono paid us an initial upfront research service payment of ¥790 million (approximately \$7.1 million) and has agreed to make research service payments up to an aggregate of ¥750 million (approximately \$5.7 million) upon (i) certain specified research triggers and (ii) the election by Ono to collaborate on the development and

commercialization of a proposed product candidate. In October 2021 and December 2022, the Company achieved specified research triggers amounting to ¥100 million (\$0.9 million) and ¥200 million (\$1.5 million), respectively, as research service payments provided for in the Ono Agreement. The ¥200 million (\$1.5 million) is included in the collaboration revenue receivable at December 31, 2022 and was subsequently received in January 2023. Upon election by Ono to collaborate on a proposed product candidate, Ono shall be responsible for a specified percentage of research and development costs for the IND-enabling studies of the selected product candidate. As of December 31, 2022 there was \$10.5 million classified as current deferred revenue related to the Ono Agreement.

Under the Ono Agreement, we are also entitled to receive up to ¥5.11 billion (approximately \$39.0 million) in the aggregate for certain specified development and regulatory milestones, ¥12.1 billion (approximately \$92.3 million) in the aggregate for certain specified commercial milestones and a tiered percentage royalty on annual net sales in Ono's territory ranging from high-single digits to low teens, subject to certain specified reductions. Royalties are payable by Ono on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last valid claim covering the licensed product in such country and the tenth anniversary of the first commercial sale of such licensed product in such country.

During the term of the Ono Agreement, we, alone and with third parties, are prohibited from researching, developing, manufacturing and commercializing products that inhibit or modulate Polθ as a mechanism of action in Ono's territory (as such term is defined in the Ono Agreement). During the term of the Ono Agreement, Ono, alone and with third parties, is prohibited from researching, developing, manufacturing and commercializing products, other than licensed products, that inhibit or modulate Polθ as a mechanism of action in Ono's territory.

The collaboration and research obligations of the Ono Agreement may be terminated upon the mutual written consent of both parties on or before the two-year anniversary of the Ono Agreement. The Ono Agreement expires on the date of expiration of all royalty obligations. Either party may terminate the Ono Agreement earlier upon an uncured material breach of the agreement by the other party, the insolvency of the other party, or the initiation of an action challenging the validity or enforceability of a party's patents. Additionally, Ono may terminate the Ono Agreement for any or no reason on a product-by-product and country-by-country basis upon specified written notice, as well as on a product-by-product basis for safety or efficacy reasons upon abbreviated written notice. Moreover, in the event that we are acquired by a third party and after any such acquisition the acquirer initiates a competing program in Ono's territory, Ono will have the right to treat such initiation as a material breach.

License Agreement with New York University

In December 2016, we entered into a license agreement with New York University pursuant to which we obtained a worldwide, royalty-bearing, exclusive license under certain current and/or future patents and know-how of New York University to research, develop and commercialize products that are covered by such licensed patents or otherwise modulate Polθ. Upon initial entry into the license agreement, we issued New York University 60,211 common shares in December 2016 as consideration for the license.

In July 2018, we subsequently amended and restated our license agreement with NYU, which we refer to, as amended and restated, as the NYU Agreement. Pursuant to the terms of the NYU Agreement, we are obligated to use reasonable diligence in connection with the research, development, and commercialization of the licensed products (as such term is defined in the NYU Agreement), including specified minimum annual spends on research and development.

Under the terms of the NYU Agreement, we are obligated to pay New York University annual license maintenance fees in the low five figures that are creditable against any milestone payments payable in such year. Additionally, in connection with development, regulatory and commercial activities, we have agreed to make milestone payments of (i) \$2.6 million in the aggregate for a product covered by a licensed patent that achieves specified development and sales milestones for the first indication, (ii) \$1.3 million in the aggregate for a product covered by a licensed patent that achieves specified development and sales milestones for a second indication, (iii) \$575,000 in the aggregate for a product covered by a licensed patent that achieves specified development and sales milestones for each of a third and fourth indication, (iv) \$1.3 million in the aggregate for a product that is not covered by a licensed patent that achieves specified development and sales milestones for the first indication, (v) \$650,000 in the aggregate for a product that is not covered by a licensed patent that achieves specified development and sales

milestones for a second indication, (vi) \$287,500 in the aggregate for a product that is not covered by a licensed patent that achieves specified development and sales milestones for each of a third and fourth indication. We have the right to reduce these milestone payments by a specified amount of any milestones payable to a third party for a license required for the commercialization of a product candidate.

We are also obligated to pay New York University a low single digit royalty on net sales of any product covered by a licensed patent and a lower single digit royalty on net sales of any product that is not covered by a licensed patent, in each case subject to reduction by a specified amount of any royalties payable to a third party for a license to unblocking intellectual property. Moreover, we are obligated to pay New York University a percentage of any non-royalty consideration received by us from a sublicensee ranging in the low double digits.

Ono is considered a sublicensee under the terms of the NYU Agreement. Accordingly, we have paid New York University a specified percentage of the approximately \$1.0 million initial upfront fee payment we received from Ono and we will be required to pay New York University a percentage between the high teens and low twenties of any future payments received under the Ono Agreement from Ono for development, regulatory and commercial milestones, as well as low single digit royalties on annual net sales in Ono's territory.

Payments in respect of net sales or sublicense in a country shall remain in force on a product-by-product, country-by-country basis, with respect to (i) products that are not covered by a licensed patent, for ten years from the date of first commercial sale in such country and (ii) products that are covered by a licensed patent, until the expiration date of the last to expire of the licensed patents covering such product or its manufacture or use in the applicable country.

The NYU Agreement expires on the date of expiration of all royalty obligations. Either party may terminate the NYU Agreement earlier upon an uncured material breach of NYU Agreement by the other party or the insolvency of the other party.

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. We have established a wholly-owned U.S. subsidiary, Repare Therapeutics USA Inc., a Delaware corporation with operations in Cambridge, Massachusetts, to support our clinical development program and our potential commercialization efforts in the United States.

Manufacturing

We currently rely, and expect to continue to rely for the foreseeable future, on third-party contract manufacturing organizations, or CMOs, to produce our product candidates for preclinical and clinical testing, as well as for future commercial manufacture of any products that we may commercialize.

We require all of our CMOs to conduct manufacturing activities in compliance with current good manufacturing practice, or cGMP, requirements. We have assembled a team of experienced employees and consultants to provide the necessary technical, quality, and regulatory oversight over our CMOs. Currently, we have manufacturing and supply agreements with our CMOs for the manufacture of RP-6306 and our preclinical candidates, including the synthesis of the active pharmaceutical ingredient, or API, as well as drug product. Roche will manufacture and supply camonsertib for ongoing and future trials, in compliance with cGMP requirements.

All of our product candidates are small molecules and are manufactured in synthetic processes from available starting materials. The chemistry underlying our product candidates appears amenable to scale up and does not currently require unusual equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

We plan to continue to rely on third-party manufacturers for any future trials and commercialization of RP-6306, and any future product candidates, if approved, and will rely on Roche to manufacture and supply camonsertib for any future trials and commercialization, if approved. We anticipate that Roche and these CMOs will have capacity

to support commercial scale production, but we do not have any formal agreements in place at this time given our early stages of development. If needed, we believe we can identify and establish additional CMOs to provide API and finished drug product without significant disruption to our business or clinical development timelines.

Competition

The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, intense competition, and a strong emphasis on intellectual property. We believe that our approach, strategy, scientific capabilities, know-how and experience provide us with competitive advantages. However, we expect substantial competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions and governmental agencies and public and private research institutions worldwide. Many of our competitors, either alone or with their collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license, or commercialize products before or more successfully than we do.

We face competition from segments of the pharmaceutical, biotechnology and other related markets that pursue the development of precision oncology therapies for patients with genetically-defined cancers. Several biopharmaceutical companies, including Loxo Oncology, Inc. (acquired by Eli Lilly and Company), Blueprint Medicines Corporation, SpringWorks Therapeutics, Inc., Black Diamond Therapeutics, Inc., Deciphera Pharmaceuticals, Inc., Tango Therapeutics, Inc., Zentalis Pharmaceuticals, Inc., Turning Point Therapeutics, Inc. (acquired by Bristol Myers Squibb), and Exelixis, Inc. are developing precision oncology medicines. In addition, we may face competition from companies developing product candidates that are based on SL, including AstraZeneca, GlaxoSmithKline, Pfizer, Bayer, Merck Serono, Schrodinger, Inc., Exelixis, Inc., Artios Pharma Ltd., IDEAYA Biosciences, Inc, Impact Therapeutics, Aprea Therapeutics, Acrivon Therapeutics, Treadwell Therapeutics, Debiopharm Group, Varsity Pharma, Breakpoint Therapeutics, and Rhizen Pharmaceuticals AG.

Furthermore, we also face competition more broadly across the oncology market for cost-effective and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, biologic therapy, such as monoclonal and bispecific antibodies, immunotherapy, cell-based therapy and targeted therapy, or a combination of any such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market may pose challenges. In addition, many companies are developing new oncology therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

With respect to our initial product candidate, camonsertib (now partnered with Roche), several companies are developing ATR inhibitors with multiple monotherapy and/or combination trials ongoing, including AstraZeneca (AZD6738), Bayer (BAY1895344), Merck Serono (M4344, M6620, M1774) and most recently, Artios Pharma (ATR0380), Aprea Therapeutics/Atrin Pharmaceuticals (ATRN-119), and Impact Therapeutics (IMP9064). The intensity of trials with ATR inhibitors as monotherapy and in combination with immune-oncology compounds, chemotherapy and radiation, as well as other DDR inhibitors significantly increased over the last several months.

With respect to our PKMYT1 inhibitor product candidate, RP-6306, Exelixis, Inc. and Acrivon Therapeutics have disclosed PKMYT1 inhibitor programs in early preclinical development.

For our preclinical Polθ inhibitor program, Artios Pharma (ART-4215), IDEAYA Biosciences (in collaboration with GlaxoSmithKline plc), Varsity Pharma, Breakpoint Therapeutics, and Rhizen Pharmaceuticals AG have Polθ programs in various stages of clinical and preclinical development.

We could see a reduction or elimination in our commercial opportunity if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient to administer, are less expensive or with a more favorable label than our product candidates. Our competitors also may compete for available patient pool, slowing our accrual in trials, obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Government Regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture, and marketing of pharmaceutical products. These agencies and other federal, state, and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, packaging, recordkeeping, tracking, approval, import, export, distribution, advertising, and promotion of our products.

U.S. Government Regulation of Drug Products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve a pending New Drug Application, or NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- nonclinical laboratory and animal tests that must be conducted in accordance with good laboratory practices, or GLPs;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical trials may begin;
- approval by an independent institutional review board, or IRB, for each clinical site or centrally before each trial may be initiated;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed product candidate for its intended use, performed in accordance with good clinical practices, or GCPs;
- submission to the FDA of an NDA and payment of user fees;
- satisfactory completion of an FDA advisory committee review, if applicable;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with cGMP and good clinical practices, or GCPs;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;

- FDA review and approval of an NDA to permit commercial marketing for particular indications for use; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

The testing and approval process requires substantial time, effort, and financial resources.

Preclinical Studies

Preclinical studies include laboratory evaluation of drug substance chemistry, pharmacology, toxicity, and drug product formulation, as well as animal studies to assess potential safety and efficacy. Prior to commencing the first clinical trial with a product candidate, a sponsor must submit the results of the preclinical tests and preclinical literature, together with manufacturing information, analytical data and any available clinical data or literature, among other required information, to the FDA as part of an IND. Some preclinical studies may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the conduct of the clinical trial and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in FDA authorization to commence a clinical trial.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, as well as amendments to previously submitted clinical trials. Further, an independent IRB for each institution participating in the clinical trial must review and approve the plan for any clinical trial, its informed consent form, and other communications to study subjects before the clinical trial commences at that site. The IRB must continue to oversee the clinical trial while it is being conducted, including any changes to the study plans.

Regulatory authorities, an IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or the IRB's requirements, or if the drug has been associated with unexpected serious harm to subjects. Some studies also include a data safety monitoring board, which receives special access to unblinded data during the clinical trial and may advise the sponsor to halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy.

In general, for purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1—Studies are initially conducted to test the product candidate for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution and excretion in healthy volunteers or subjects with the target disease or condition. If possible, Phase 1 clinical trials may also be used to gain an initial indication of product effectiveness.
- Phase 2—Controlled studies are conducted with groups of subjects with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expansive Phase 3 clinical trials.
- Phase 3—These clinical trials are generally undertaken in larger subject populations to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded subject population at multiple clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. These clinical trials may be done at trial sites outside the United States as long as the global sites are also representative of the U.S. population and the conduct of the study at global sites comports with FDA regulations and guidance, such as compliance with GCPs.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information.

Clinical trials must be conducted under the supervision of qualified investigators in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial, and the review and approval of the study by an IRB. Investigators must also provide information to the clinical trial sponsors to allow the sponsors to make specified financial disclosures to the FDA. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated and a statistical analysis plan. Information about some clinical trials, including a description of the trial and trial results, must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and active pharmaceutical ingredients imported into the United States are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and the IRB and more frequently if serious adverse effects occur.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval, and priority review, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Under the fast track program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the drug candidate. To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

In addition, a sponsor can request breakthrough therapy designation for a drug if it is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

Drugs designated as breakthrough therapies are eligible for intensive guidance from the FDA on an efficient drug development program, organizational commitment to the development and review of the product including involvement of senior managers, and, like fast track products, are also eligible for rolling review of the NDA. Both fast track and breakthrough therapy products may be eligible for accelerated approval and/or priority review, if relevant criteria are met.

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. A drug candidate approved on this basis is subject to rigorous post marketing compliance requirements, including the completion of Phase 4 or post approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post approval studies and regularly update FDA on their progress, or confirm a clinical benefit during post marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated approval regulations are subject to prior review by the FDA.

Once an NDA is submitted for a product intended to treat a serious condition, the FDA may assign a priority review designation if FDA determines that the product, if approved, would provide a significant improvement in safety or effectiveness. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under the Prescription Drug User Fee Act, or PDUFA, guidelines. Under the current PDUFA performance goals, these six and ten month review periods are measured from the 60-day filing date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review from the date of submission.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. In addition, the manufacturer of an investigational drug for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on responding to requests for expanded access. Furthermore, fast track designation, breakthrough therapy designation, accelerated approval and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

NDA Submission and Review by the FDA

Assuming successful completion of the required clinical and preclinical testing, among other items, the results of product development, including chemistry, manufacture and controls, nonclinical studies and clinical trials are submitted to the FDA, along with proposed labeling, as part of an NDA. The submission of an NDA requires payment of a substantial user fee to the FDA. These user fees must be filed at the time of the first submission of the application, even if the application is being submitted on a rolling basis. Fee waivers or reductions are available in some circumstances.

In addition, under the Pediatric Research Equity Act, an NDA or supplement to an NDA for a new active ingredient, indication, dosage form, dosage regimen or route of administration must contain data that are adequate to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA must refer applications for drugs that contain active ingredients, including any ester or salt of the active ingredients, that have not previously been approved by the FDA to an advisory committee or provide in an action letter a summary of the reasons for not referring it to an advisory committee. The FDA may also refer drugs which present difficult questions of safety, purity, or potency to an advisory committee. An advisory committee is typically a panel that includes clinicians and other experts who review, evaluate, and make a recommendation as to

whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities, including contract manufacturers and subcontracts, are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs.

Once the FDA receives an application, it has 60 days to review the NDA to determine if it is substantially complete to permit a substantive review, before it accepts the application for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has set the review goal of 10 months from the 60-day filing date to complete its initial review of a standard NDA for a new molecular entity, or NME, and make a decision on the application. For priority review applications, the FDA has set the review goal of reviewing NME NDAs within six months of the 60-day filing date. Such deadlines are referred to as the PDUFA date. The PDUFA date is only a goal and the FDA does not always meet its PDUFA dates. The review process and the PDUFA date may also be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding the submission during the review period that amends the original application.

Once the FDA's review of the application is complete, the FDA will issue either a Complete Response Letter, or CRL, or approval letter. A CRL indicates that the review cycle of the application is complete, and the application is not ready for approval. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing, or other information or analyses in order for the FDA to reconsider the application in the future. Even with the submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product, or impose other conditions, including distribution restrictions or other risk management mechanisms. For example, the FDA may require a REMS as a condition of approval or following approval to mitigate any identified or suspected serious risks and ensure safe use of the drug. The FDA may prevent or limit further marketing of a product, or impose additional post-marketing requirements, based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements, FDA notification and FDA review and approval. Further, should new safety information arise, additional testing, product labeling or FDA notification may be required.

If regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed or may include contraindications, warnings, or precautions in the product labeling, which has resulted in a boxed warning. A boxed warning is the strictest warning put in the labeling of prescription drugs or drug products by the FDA when there is reasonable evidence of an association of a serious hazard with the drug. The FDA also may not approve the inclusion of all labeling claims sought by an applicant. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require Phase 4 post-marketing studies to monitor the effect of approved products and may limit further marketing of the product based on the results of these post-marketing studies.

U.S. Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including periodic reporting, product sampling and distribution, advertising, promotion, drug shortage reporting, compliance with any post-approval requirements imposed as a conditional of approval such as Phase 4 clinical trials, REMS and surveillance, recordkeeping and reporting requirements, including adverse experiences.

After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual program fee requirements for approved products, as well as new application fees for supplemental applications with clinical data. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and to list their drug products and are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMPs and other requirements, which impose procedural and documentation requirements.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented, or FDA notification. FDA regulations also require investigation and correction of any deviations from cGMPs and specifications and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in withdrawal of marketing approval, mandatory revisions to the approved labeling to add new safety information or other limitations, imposition of post-market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS program, among other consequences.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are consistent with the FDA approved labeling. Physicians, in their independent professional medical judgement, may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. However, manufacturers and third parties acting on their behalf are prohibited from marketing or promoting drugs in a manner inconsistent with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Failure to comply with any of the FDA's requirements could result in significant adverse enforcement actions. These include a variety of administrative or judicial sanctions, such as refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, modification of promotional materials or labeling, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, debarment, injunctions, fines, consent decrees, corporate integrity agreements, refusals of government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement or civil or criminal penalties, including fines and imprisonment. It is also possible that failure to comply with the FDA's requirements relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws. Any of these sanctions could result in adverse publicity, among other adverse consequences.

U.S. Marketing Exclusivity

The FDA provides periods of non-patent regulatory exclusivity, which provides the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug for a period of three or five years following the FDA's approval of the NDA. Five years of exclusivity are available to new chemical entities, or NCEs. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt, including a salt with hydrogen or coordination bonds, or other noncovalent, or not

involving the sharing of electron pairs between atoms, derivatives, such as a complex (i.e., formed by the chemical interaction of two compounds), chelate (i.e., a chemical compound), or clathrate (i.e., a polymer framework that traps molecules), of the molecule, responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review or approve an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. An ANDA or 505(b)(2) application, however, may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed.

Regulation outside the United States

We will be subject to similar foreign laws and regulations concerning the development of our product candidates outside of the United States.

Other Healthcare Laws and Regulations

Our business activities, including but not limited to, research, sales, promotion, distribution, medical education and other activities are subject to regulation by numerous regulatory and law enforcement authorities in the United States in addition to the FDA, including the Department of Justice, the Department of Health and Human Services, or HHS, and its various divisions, including Centers for Medicare & Medicaid Services, or CMS, and the Health Resources and Services Administration, the Department of Veterans Affairs, the Department of Defense and state and local governments. Our business activities must comply with numerous healthcare laws and regulations, including those described below.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for, or purchasing, leasing, ordering, or arranging for the purchase, lease or order of, any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other hand. The term remuneration has been interpreted broadly to include anything of value. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing, or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, amended the intent requirement of the federal Anti-Kickback Statute, and other healthcare criminal fraud statutes, so that a person or entity no longer needs to have actual knowledge of the federal Anti-Kickback Statute, or the specific intent to violate it, to have violated the statute. The ACA also provided that a violation of the federal Anti-Kickback Statute is grounds for the government or a whistleblower to assert that a claim for payment of items or services resulting from such violation constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act, or FCA.

The federal civil and criminal false claims laws, including the FCA, and civil monetary penalties laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the U.S. federal government, including the Medicare and Medicaid programs, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties. Government enforcement agencies and private whistleblowers have investigated pharmaceutical companies

for or asserted liability under the FCA for a variety of alleged promotional and marketing activities, such as providing free products to customers with the expectation that the customers would bill federal programs for the products; providing consulting fees and other benefits to physicians to induce them to prescribe products; engaging in promotion for “off-label” uses; and submitting inflated best price information to the Medicaid Rebate Program.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick, scheme or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Additionally, the ACA amended the intent requirement of some of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

Additionally, the federal Open Payments program pursuant to the Physician Payments Sunshine Act, created under Section 6002 of the ACA and its implementing regulations, requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with specified exceptions) to report annually information related to specified payments or other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physicians assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually specified ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, impose requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates and covered subcontractors. Among other things, HITECH makes HIPAA’s security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions.

Many states have also adopted laws similar to each of the above federal laws, which may be broader in scope and apply to items or services reimbursed by any third-party payor, including commercial insurers. We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and/or state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Ensuring that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, possible exclusion from government funded

healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could substantially disrupt our operations. If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Coverage and Reimbursement

Our ability to commercialize any products successfully will also depend in part on the extent to which coverage and adequate reimbursement for the procedures utilizing our product candidates, performed by health care providers, once approved, will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, determine which procedures, and the products utilized in such procedures, they will cover and establish reimbursement levels. Assuming coverage is obtained for procedures utilizing a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who undergo procedures for the treatment of their conditions, and their treating physicians, generally rely on third-party payors to reimburse all or part of the costs associated with the procedures which utilize our products. Treating physicians are unlikely to use and order our products unless coverage is provided and the reimbursement is adequate to cover all or a significant portion of the cost of the procedures which utilize our products. Therefore, coverage and adequate reimbursement for procedures which utilize new products is critical to the acceptance of such new products. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Government authorities and other third-party payors are developing increasingly sophisticated methods of cost containment, such as including price controls, restrictions on coverage and reimbursement and requirements for substitution of less expensive products and procedures. Government and other third-party payors are increasingly challenging the prices charged for health care products and procedures, examining the cost effectiveness of procedures, and the products used in such procedures, in addition to their safety and efficacy, and limiting or attempting to limit both coverage and the level of reimbursement. Further, no uniform policy requirement for coverage and reimbursement exists among third-party payors in the United States, which causes significant uncertainty related to the insurance coverage and reimbursement of newly approved products, and the procedures which may utilize such newly approved products. Therefore, coverage and reimbursement can differ significantly from payor to payor and health care provider to health care provider. As a result, the coverage determination process is often a time-consuming and costly process that requires the provision of scientific and clinical support for the use of new products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may be significant delays in obtaining coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA. Moreover, eligibility for coverage and reimbursement does not imply that a product, or the procedures which utilize such product, will be paid for in all cases or at a rate which the health care providers who purchase those products will find cost effective. Additionally, we expect pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes.

We cannot be sure that coverage and reimbursement will be available for any product that we commercialize, or the procedures which utilize such product, and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

Healthcare Reform Measures

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals designed to change the healthcare system. Among policy-makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, the pharmaceutical industry in the United States has been affected by the passage of ACA, which, among other things: imposed new fees on entities that manufacture or import certain branded prescription drugs; expanded pharmaceutical manufacturer obligations to provide discounts and rebates to certain government programs; implemented a licensure framework for follow-on biologic products; expanded health care fraud and abuse laws; revised the methodology by which rebates owed by manufacturers to the state and federal government under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics, including products that are inhaled, infused, instilled, implanted or injected; imposed an additional rebate similar to an inflation penalty on new formulations of drugs; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; expanded the 340B program which caps the price at which manufacturers can sell covered outpatient pharmaceuticals to specified hospitals, clinics and community health centers; and provided incentives to programs that increase the federal government's comparative effectiveness research.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and additional healthcare reform measures of the Biden administration will impact the ACA.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2.0% per fiscal year, which went into effect in April 2013, and due to subsequent legislative amendments will remain in effect through 2031, unless additional U.S. Congressional action is taken. These Medicare sequester reductions will be suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In addition, in January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several categories of healthcare providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, ended the use of the statutory formula for clinician payment and established a quality payment incentive program, also referred to as the Quality Payment Program. This program provides clinicians with two ways to participate, including through the Advanced Alternative Payment Models, or APMs, and the Merit-based Incentive Payment System, or MIPS. In November 2019, CMS issued a final rule finalizing the changes to the Quality Payment Program. At this time, it is unclear how the introduction of the Quality Payment Program will impact overall physician reimbursement under the Medicare program. Any

reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

In addition, there has been particular and increasing legislative and enforcement interest in the United States with respect to drug pricing practices in recent years, particularly with respect to drugs that have been subject to relatively large price increases over relatively short time periods. Specifically, there have been several recent U.S. Congressional inquiries, Presidential executive orders and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of prescription drugs under Medicare and reform government program reimbursement methodologies for pharmaceutical products. At the federal level, in July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at prescription drugs. In response to Biden’s executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within ninety (90) days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. In addition, individual states in the United States have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In the future, there will likely continue to be proposals relating to the reform of the U.S. healthcare system, some of which could further limit coverage and reimbursement of products.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the companies to maintain books and records that accurately and fairly reflect all transactions of the companies, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Employees and Human Capital Resources

As of February 24, 2023, we had 180 full-time employees, including 63 who hold an M.D. or Ph.D. degree. Of these full-time employees, 148 were primarily engaged in research and development activities and 32 were primarily engaged in management or general and administrative activities. None of our employees is represented by a labor union and we consider our employee relations to be good.

Corporate Information

We were incorporated under the Canada Business Corporations Act on September 6, 2016. Immediately prior to completion of our initial public offering on June 23, 2020, we were continued as a corporation under the Business Corporations Act (Québec), or the QBCA. Our principal executive offices are located at 7210 Frederick-Banting, Suite 100, St-Laurent, Quebec, H4S 2A1 and our telephone number is 857-412-7018. In June 2017, we incorporated our wholly-owned subsidiary, Repare Therapeutics USA Inc., a Delaware corporation, which is located at 101 Main Street, Suite 1650, Cambridge, Massachusetts 02142.

Available Information

We maintain an internet website at www.reparerx.com and make available free of charge through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act of 1934 (the "Exchange Act"). We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission (the "SEC"). You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at <http://www.sec.gov> and on SEDAR at <http://www.sedar.com>. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, specifically the sections title "Investors & Media" as a source of information about us.

The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be part of this Annual Report on Form 10-K. Our website address is included in this Annual Report on Form 10-K as an inactive technical reference only.

Item 1A. Risk Factors.

Investing in our common shares involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our consolidated financial statements and the related notes and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” before deciding whether to invest in our common shares. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. In such an event, the market price of our common shares could decline and you may lose all or part of your investment.

Risks Related to Our Financial Position and Capital Needs

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage biopharmaceutical company founded in 2016, and our operations to date have focused primarily on raising capital, organizing and staffing our company, conducting discovery and research activities, identifying potential synthetic lethal, or SL, gene pairs, establishing and protecting our intellectual property portfolio including for our proprietary SNIPRx platform, developing and progressing our product candidates through preclinical studies and clinical development, including continuing our open-label Phase 1/2 clinical trials of camonsertib and our ongoing Phase 1 clinical trials of RP-6306, and establishing arrangements with third parties for the manufacture of initial quantities of our product candidates and component materials. We do not have any product candidates approved for sale and have not generated any revenue from product sales. Additionally, as an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. In time, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Additionally, we expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any product revenue to date, and we are devoting substantially all of our financial resources and efforts to research and development of our product candidates including camonsertib and RP-6306, as well as to enhancing our SNIPRx platform. To date, we have primarily funded our operations through sales of equity securities, including our IPO in June 2020 and our follow-on offering in November 2021, as well as upfront payments from collaboration and research agreements.

We have incurred significant operating losses since our inception in 2016. Our net loss was \$29.0 million, and \$106.9 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of \$239.3 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. It could be several years, if ever, before we have a commercialized drug. We anticipate that our expenses will increase substantially if, and as, we:

- continue our ongoing and planned development of our product candidates, including our ongoing Phase 1 clinical trials of RP-6306;

- initiate preclinical studies and clinical trials for any additional product candidates that we may pursue in the future, including our earlier-stage programs;
- seek to identify novel SL targets, develop small molecule inhibitors of these targets, nominate and develop additional product candidates and further expand our clinical product pipeline;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- build a portfolio of product candidates through the discovery, development, or acquisition or in-license of drugs, product candidates or technologies;
- establish a sales, marketing, manufacturing and distribution capability to commercialize any product candidate for which we may obtain marketing approval;
- maintain, protect and expand our intellectual property portfolio;
- acquire or in-license other product candidates and technologies;
- hire additional clinical, regulatory and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses associated with operating as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials of any product candidates that we may pursue, obtaining regulatory approval, procuring commercial-scale manufacturing, marketing, and selling any products for which we may obtain regulatory approval, as well as discovering or acquiring and then developing additional product candidates. We are only in the preliminary stages of some of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. Our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform studies in addition to those we currently expect, or if there are any delays in the initiation and completion of our clinical trials or the development of RP-6306 or any future product candidates.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our common shares and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations. A decline in the value of our common shares could also cause you to lose all or part of your investment.

We will require substantial additional funding to finance our operations. If we are unable to raise capital when needed, we could be forced to delay, reduce, or terminate certain of our product development programs or other operations.

To date, we have primarily funded our operations through sales of equity securities, including our IPO in June 2020 and our follow-on offering in November 2021, as well as upfront payments from collaboration and research agreements. We expect to spend substantial amounts to advance our product candidates into clinical development and to complete the clinical development of, seek regulatory approvals for and commercialize our product candidates, if approved. We will require additional capital, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, milestone and royalty payments under our current or future strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of our product candidates. Furthermore, we have incurred and will continue to incur additional costs associated with operating as a public company. Adequate additional financing may not be available to us on acceptable terms, or at all. Weakness and volatility in the capital markets and the economy in general could limit our

access to capital markets and increase our costs of borrowing. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce, or eliminate certain of our research and development programs.

As of December 31, 2022, our cash and cash equivalents and marketable securities on hand was \$343.9 million. We believe that our existing cash on hand, will enable us to fund our operating expenses and capital expenditure requirements into 2026. However, we will need to obtain substantial additional funding in connection with our continuing operations and planned activities. Our future capital requirements will depend on many factors, including:

- the continuation of our ongoing and planned development of our product candidates, including our ongoing Phase 1 clinical trials of RP-6306;
- the timing, costs, progress and results of our ongoing clinical trials of RP-6306;
- the progress of preclinical development and possible clinical trials of our current earlier-stage programs;
- the scope, progress, results and costs of our research programs and preclinical development of other product candidates that we may pursue;
- the development requirements of other product candidates that we may pursue;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the timing and amount of milestone and royalty payments that we are required to make or eligible to receive under our current or future collaboration agreements, including the Roche Agreement;
- our election to opt-in to the co-development and profit share arrangement of camonsertib pursuant to the Roche Agreement;
- the cost of establishing a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA and other regulatory authorities;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the cost of expanding, maintaining and enforcing our intellectual property portfolio, including filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or any of our product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the extent to which we partner our programs, acquire or in-license other product candidates and technologies or enter into additional strategic collaborations;
- the revenue, if any, received from commercial sales of camonsertib, RP-6306 and any future product candidates for which we or our collaborators receive marketing approval;
- the addition of equipment and physical infrastructure to support our research and development; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, camonsertib, RP-6306

and any future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce, or altogether terminate our research and development programs or future commercialization efforts.

Raising additional capital will cause dilution to our shareholders, restrict our operations, or require us to relinquish rights to our product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through public or private equity or debt financings, third-party funding, marketing, and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt and equity financings, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, incurring additional debt, making capital expenditures, declaring dividends or placing limitations on our ability to acquire, sell or license intellectual property rights.

If we raise additional capital through future collaborations, strategic alliances, or third-party licensing arrangements, we may have to relinquish certain valuable rights to our intellectual property, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital when needed, we may be required to delay, limit, reduce or terminate our clinical development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise develop and market ourselves.

Risks Related to the Development of Our Product Candidates

We are very early in our development efforts. If we are unable to advance our product candidates into and through clinical development, obtain regulatory approval and ultimately commercialize any of our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We have no products approved for sale and our initial clinical product candidates, camonsertib and RP-6306, are still in the early stages of clinical development and will require additional clinical development, regulatory review and approval in each jurisdiction in which we intend to market it, access to sufficient commercial manufacturing capacity, and significant sales and marketing efforts before we can generate any revenue from product sales. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization, by us or our collaborators of camonsertib, RP-6306 and one or more of our other product candidates. The success of our product candidates will depend on several factors, including the following:

- successful completion of preclinical studies, including the identification of clinical candidates for each of our preclinical programs;
- approval of investigational new drug, or IND, applications for our planned or future clinical trials;
- acceptance by the FDA, EMA or foreign regulatory authority of our development strategy;
- successful initiation of clinical trials;
- successful patient enrollment in and completion of clinical trials;
- safety, tolerability and efficacy profiles for our product candidates that are satisfactory to the FDA, EMA or any foreign regulatory authority for marketing approval;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;

- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates, if any product candidates are approved;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other cancer therapies;
- obtaining and maintaining third-party coverage and adequate reimbursement and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement; and
- maintaining a continued acceptable safety profile of products following approval.

There is no guarantee that the results obtained in current preclinical studies, our ongoing open-label Phase 1/2 clinical trials of camonsertib, our ongoing Phase 1 clinical trials of RP-6306 or any future clinical trials of any product candidate will be sufficient to obtain regulatory approval or marketing authorization for such product candidate.

Many of these risks are beyond our control, including the risks related to clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, and sales efforts of any future collaborator. If we are unable to develop, receive regulatory approval for, or successfully commercialize our current or future product candidates, or if we experience delays as a result of any of these risks or otherwise, our business could be materially harmed.

Our business substantially depends upon the successful development of product candidates generated through the application of our SNIPRx platform, and in particular, our initial product candidates, camonsertib and RP-6306. If we or our collaborators are unable to obtain regulatory approval for, and successfully commercialize, products developed through the application of our SNIPRx platform, our business may be materially harmed.

Our initial clinical product candidates, camonsertib and RP-6306, were developed through the application of our SNIPRx platform. All of our product candidates to date were derived based on the same principle of SL. As such, negative results in the development of camonsertib or RP-6306 may also impact our ability to obtain regulatory approval for our other product candidates, either at all or within anticipated timeframes because, although other product candidates may target different indications, the underlying technology platform, manufacturing process and development process is the same for all of our product candidates. Accordingly, a failure in any one program may decrease trust in our technology and affect the ability to obtain regulatory approval to continue or conduct clinical programs for other product candidates. If camonsertib or RP-6306 shows unexpected adverse events or a lack of efficacy in the indications they are intended to treat, or if we or our collaborators experience other regulatory or developmental issues, our development plans and business could be significantly harmed.

We have limited experience as a company in conducting clinical trials.

We have limited experience as a company in conducting clinical trials. We began our first clinical trial of camonsertib in July 2020 and our first clinical trial of RP-6306 in April 2021. In part because of this lack of experience, we cannot be certain that our clinical trials will begin or be completed on time, if at all. Large-scale clinical trials would require significant additional financial and management resources and reliance on third-party clinical investigators, contract research organizations, or CROs, and consultants. Relying on third-party clinical investigators, CROs and consultants may force us to encounter delays that are outside of our control. We may be unable to identify and contract with sufficient investigators, CROs and consultants on a timely basis or at all. There can be no assurance that we will be able to negotiate and enter into any master services agreement with CROs, as necessary, on terms that are acceptable to us on a timely basis or at all.

We may not be able to file INDs or IND amendments to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

We have filed INDs for camonsertib and RP-6306, but we may not be able to file INDs for our other product candidates on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing further clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND. Any failure to file INDs on the timelines we expect or to obtain regulatory approvals for our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

The effects of health epidemics, including the ongoing COVID-19 pandemic, in regions where we, or the third parties on which we rely, have business operations could adversely impact our business, including our preclinical studies and clinical trials.

Our business could be adversely affected by health epidemics in regions where we have concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of third party manufacturers and CROs upon whom we rely. The COVID-19 pandemic had a modest impact on our business operations. For example, we are aware that several clinical trial sites involved in our clinical trials have in the past temporarily stopped or delayed enrolling new patients, with exemptions if appropriate, and it is possible that these or other clinical sites may be similarly affected in the future. We and the third-party clinical investigators and CROs with whom we work have also experienced staffing shortages at clinical trial sites, which could adversely affect the timing of our current and ongoing clinical trials. While it is not possible at this time to predict the duration and extent of the impact that COVID-19 will continue to have on worldwide economic activity and our business in particular, COVID-19 could adversely impact our business and ongoing and planning clinical trials, including as a result of delays or difficulties in clinical site initiation, difficulties in recruiting and retaining clinical site investigators and clinical site staff and interruption of our clinical supply chain or key clinical trial activities, such as clinical trial site monitoring, and supply chain interruptions caused by ongoing restrictions for the supply of materials for product candidates or other materials necessary to manufacture product to conduct preclinical tests.

The extent to which the COVID-19 coronavirus or any future outbreaks of contagious disease may impact our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, the results of vaccination efforts, resurgences of the virus, travel restrictions and social distancing in the United States, Canada and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States, Canada and other countries to contain and treat the disease.

The successful development of targeted therapeutics, including our portfolio of SL small molecule inhibitors, as well as any related diagnostics, is highly uncertain.

Successful development of targeted therapeutics, such as our portfolio of SL small molecule inhibitors, as well as any related diagnostics, is highly uncertain and is dependent on numerous factors, many of which are beyond our control. Our SNIPRx platform is based on new technologies and methods relating to precision target and biomarker identification, screening, and validation. While we believe our clinical development approach will eventually provide validation of our SNIPRx platform, we have not, to date, sought regulatory approval for any therapeutics developed through our platform. As such, it is difficult to accurately predict the developmental challenges we may incur for our current and future product candidates as we proceed through product discovery, identification, preclinical studies, and clinical trials.

Our SNIPRx platform is novel and may not be effective at identifying SL targets for product candidates. We therefore cannot provide any assurance that we will be able to successfully identify additional novel targets or product candidates, advance any of these additional product candidates or diagnostics for their associated biomarkers through the development process. Most of our proposed targets are unproven in clinical trials and there is no guarantee that the preclinical data will translate into a clinical relevance of such novel biomarkers and targets.

Targeted therapeutics that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- research or preclinical studies may show our targeted small molecule inhibitors or antagonists to be less effective than desired or to have harmful or problematic side effects or toxicities;
- failure to accurately identify, validate or develop clinically relevant biomarkers for our targeted therapeutic product candidates;
- trial results may show our targeted therapeutic small molecule inhibitors to be less effective than expected based on preclinical studies (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- the failure to receive the necessary regulatory approvals or a delay in receiving such approvals. Among other things, such delays may be caused by slow enrollment in clinical trials, patients dropping out of trials, length of time to achieve trial endpoints, additional time requirements for data analysis, preparation of IND applications, discussions with the FDA, an FDA request for additional preclinical or clinical data, or unexpected safety or manufacturing issues;
- manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that may make our targeted therapeutic small molecule inhibitors uneconomical;
- the size of the patient population that have disease with the appropriate biomarkers for which we are developing our product candidates may not be large enough to support commercial viability of our product candidates, if approved;
- proprietary rights of others and their competing products and technologies that may prevent our targeted therapeutic small molecule inhibitors, or the diagnostics for biomarkers associated with such small molecule inhibitors, from being commercialized;
- the development of alternative treatments or evolution in the standard of care for our targets may make our drugs less attractive; and
- our approach of using any of our product candidates in combination with other agents, including standard of care agents, may not materialize due to overlapping toxicity, high cost or an inability to replicate preclinical results in clinical trials.

As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our SNIPRx platform will result in the identification, development, and regulatory approval of any products.

We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We may not commercialize, market, promote or sell any product candidate without obtaining marketing approval from the FDA, EMA, or other comparable regulatory authority, and we may never receive such approvals. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. Competing clinical trials for the same populations targeted as ours may limit our enrollment, or the results of competitors with similar technologies and products may falsely undermine the potential of our SNIPRx platform. A failure of one or more clinical trials can occur at any stage of testing. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We or our collaborators may experience numerous unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize camonsertib, RP-6306 and any future product candidates, including:

- delays in reaching a consensus with regulatory authorities on design or implementation of our clinical trials;
- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, patients may drop out of these clinical trials at a higher rate than we anticipate or fail to return for post-treatment follow-up or we may fail to recruit suitable patients to participate in a trial;
- delays in our combination trials due to lack of access to the drugs with which we are testing our product candidates;
- clinical trials of our product candidates may produce negative or inconclusive results;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations, trial sites or manufacturing facilities;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- external business disruptions affecting the initiation, patient enrollment, development and operation of our clinical trials, including a public health emergency, such as the COVID-19 pandemic;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from future drug sales or other sources. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional testing to bridge our modified product candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring competing drugs to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;

- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our product development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all.

Clinical trials are very expensive, time consuming and difficult to design and implement.

Our product candidates will require clinical testing before we are prepared to submit a new drug application, or NDA, or equivalent application required in another jurisdiction for regulatory approval. We cannot predict with any certainty if or when we might submit an NDA or equivalent application required in another jurisdiction for regulatory approval for any of our product candidates or whether any such application will be approved by the FDA or other comparable regulatory authority, as applicable. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. For instance, the FDA or other comparable regulatory authority may not agree with our proposed endpoints for any future clinical trial of our product candidates, which may delay the commencement of our clinical trials. In addition, we may not succeed in developing and validating disease-relevant clinical endpoints based on insights regarding biological pathways for the diseases we are studying. The clinical trial process is also time consuming. We estimate that the successful completion of clinical trials for camonsertib, RP-6306 and any future product candidates will take several years to complete. Furthermore, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical trials.

Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials and we cannot assure you that any ongoing, planned or future clinical trials will lead to results sufficient for the necessary regulatory approvals.

We initiated our first clinical trial, an open-label Phase 1/2 clinical trial of camonsertib, in the third quarter of 2020 and initiated a Phase 1 clinical trial of RP-6306 in the second quarter of 2021. Success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical studies and earlier clinical trials does not ensure that later efficacy trials will be successful, nor does it predict final results. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events.

In addition, differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. The early trials will be single arm and not comparing the results with existing (or new) standard of care. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products or had to withdraw the product after comparator or later stage trials delivered results. The changing regulatory landscape may require larger and randomized trials that will take a longer time to perform.

Additionally, some of our trials may be open-label studies, where both the patient and investigator know whether the patient is receiving the investigational product candidate or an existing approved drug, introducing bias in early interpretation of the results. Most typically, open-label clinical trials test only the investigational product candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Therefore, it is possible that positive results observed in open-label trials will not be replicated in later placebo-controlled trials. Further, as our trials are in patients who encountered multiple therapy failures previously, interpretation of results may be biased both towards lesser activity and at the same time towards a population that is able to tolerate and possibly benefit from novel therapies. Hence interpretation of any results from this population may not directly translate to our eventual pivotal trial population that will likely be more homogenous and less pretreated.

Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. Moreover, as the development of the SL pair, ATM-ATR, is still early, any clinical validation of the SL approach to treating cancer may or may not validate our approach. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

Interim, “top-line” and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim, “top-line” or preliminary data from our ongoing and planned clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or “top-line” data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common shares to fluctuate significantly.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, on a timely basis or at all, our business will be substantially harmed.

The length of time necessary to complete clinical trials and to submit an application for marketing approval for a decision by a regulatory authority may be difficult to predict for targeted therapeutic small molecule inhibitors, in large part because of the limited regulatory history associated with them. The clinical trial requirements of the FDA and other comparable foreign regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. There is a limited history of multi-tumor indications, and any regulatory approvals may be conditioned upon confirmatory trials with clinical endpoints such as survival. Such trials are not only more expensive to conduct but take several years to complete. Increasing pressure from reimbursement bodies may result in poor (or no) acceptance of early trials for reimbursement. Except for certain PARP inhibitors, no products based on SL have been approved to date by regulators. As a result, the regulatory approval process for product candidates such as ours is uncertain and may be more expensive and take longer than the approval process for product candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or other comparable regions of the world or how long it will take to commercialize our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market would adversely affect our business, financial condition, results of operations and prospects.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA to the FDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Prior to obtaining approval to commercialize a product candidate in the United States or elsewhere, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA or comparable foreign regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other studies required by the FDA or comparable foreign regulatory authorities, approval of any regulatory approval applications that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

Of the large number of potential products in development, only a small percentage successfully complete the FDA or comparable foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a post-marketing risk management strategy such as a REMS or the equivalent in another jurisdiction. Regulatory authorities may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Synthetic lethality represents an emerging class of precision medicine targets, and negative perceptions of the efficacy, safety, or tolerability of this class of targets, including any that we develop, could adversely affect our ability to conduct our business, advance our product candidates or obtain regulatory approvals.

Aside from PARP inhibitors, such as Lynparza, Rubraca, Zejula and Talzenna, no small molecule inhibitor therapeutics for SL in DNA damage have been approved to date by the FDA or other comparable regulators. Adverse events in future clinical trials of our product candidates or in clinical trials of others developing similar products and

the resulting publicity, as well as any other adverse events in the field of SL, or other products that are perceived to be similar to SL, such as those related to gene therapy or gene editing, could result in a decrease in the perceived benefit of one or more of our programs, increased regulatory scrutiny, decreased confidence by patients and CROs in our product candidates, and less demand for any product that we may develop. Our pipeline of SL small molecule inhibitor product candidates could result in a greater quantity of reportable adverse events or other reportable negative clinical outcomes, manufacturing reportable events or material clinical events that could lead to clinical delays or holds by the FDA or applicable regulatory authority or other clinical delays, any of which could negatively impact the perception of one or more of our SL programs, as well as our business as a whole. In addition, responses by U.S. federal or foreign governments to negative public perception may result in new legislation or regulations that could limit our ability to develop any product candidates or commercialize any approved products, obtain, or maintain regulatory approval, or otherwise achieve profitability. More restrictive statutory regimes, government regulations, or negative public opinion would have an adverse effect on our business, financial condition, results of operations, and prospects, and may delay or impair the development of our product candidates and commercialization of any approved products or demand for any products we may develop.

We may not be successful in applying our SNIPRx platform to discover SL targets with therapeutic and commercial potential or in the discovery and development of commercially viable product candidates for us or our collaborators.

Our scientific approach focuses on applying our proprietary SNIPRx platform to identify SL targets across the human genome. Our drug discovery team then chooses targets identified by SNIPRx and develops potent and selective inhibitors of these targets. We use these inhibitors to further validate our SL findings before advancing them into clinical development.

We believe the results of our SNIPRx screen campaigns suggest that our platform is capable of identifying high quality product candidates, but past success in identifying potential product candidates does not assure future success for us with our internal drug discovery programs. Our SNIPRx platform is novel, and we may not succeed in applying our SNIPRx platform to identify targets for product candidates. We therefore cannot provide any assurance that we or our collaborators will be able to successfully identify additional product candidates or advance any of these additional product candidates. In addition, others may have discovered and prosecuted targets that we believe are undiscovered. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our SNIPRx platform will result in the identification, development, and regulatory approval of any products. In addition, we may not succeed in applying our STEP² screens to expand the potential patient populations that can be treated with our product candidates.

Efforts to identify, acquire or in-license, and then develop product candidates require substantial technical, financial, and human resources, whether or not any product candidates are ultimately identified. We apply our SNIPRx technology and STEP² screening in our efforts to discover potential precision targets for which our product candidates may be developed. Our efforts may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development, approved products, or commercial revenues for many reasons, including the following:

- the methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render any product candidates we develop obsolete;
- any product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by physicians, patients, the medical community or third-party payors.

Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates. We may find it difficult to enroll patients in our ongoing and planned clinical trials with the genomic alterations that these trials are designed to target.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of completion of our clinical trials depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In particular, because we are focused on patients with specific genomic alterations identified by our STEP² screens, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. Certain genes identified by our STEP² screens may not yet be included in commercially available panels or CLIA-validated panels used in large academic centers. We cannot be certain how many patients will have each of the genomic alterations that the applicable product candidate is designed to target or that the number of patients enrolled for each mutation will suffice for regulatory approval and inclusion of each such mutation in the approved label. We may be unsuccessful in our efforts to work with our clinical partners to identify patients who are eligible for our clinical trials.

In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same or similar populations as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

We are engaging third parties to develop patient selection tools for use in our clinical trials, but such third parties may not be successful in developing such tools, furthering the difficulty in identifying patients with the targeted genomic alterations for our clinical trials and risking enrollment into our trials. Next Generation Sequencing panels may not include genes required for screening for our clinical trials or may not be broadly commercially available. The optimal method of diagnosis is not yet known and the availability of third party payment for diagnostic tests may limit our clinical trials as well. Further, if we are unable to include patients with the targeted genomic alterations, this could compromise our ability to seek participation in FDA's expedited review and development programs or otherwise seek to accelerate clinical development and regulatory timelines.

The enrollment of patients further depends on many factors, including:

- the risks and benefits of the product candidate under trial;
- the availability and efficacy of competing therapies and clinical trials;
- the availability of genetic sequencing information for patient tumors so that we can identify patients with the targeted genomic alterations;
- the patient referral practices of physicians;
- the proximity of patients to clinical trial sites;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the ability of any current or future license partner to execute on its development commitments and responsibilities for any product candidate to which it has acquired development rights in a given geography;
- our ability to obtain and maintain patient consents;
- reporting of the preliminary results of any of our clinical trials; and
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion.

Our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us

because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. Moreover, because our product candidates represent a departure from more commonly used methods for cancer treatment and because our product candidates have not been tested in humans before, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy, rather than enroll patients in any future clinical trial.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

Serious adverse events or undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA, or other authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, toxicities, or unexpected characteristics, including death.

If unacceptable side effects or deaths arise in the development of our product candidates, we, the IRBs at the institutions in which our studies are conducted, the FDA or any comparable foreign regulatory authority could suspend or terminate our clinical trials or the FDA or other regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Undesirable side effects or deaths in clinical trials with our product candidates may cause the FDA or comparable foreign regulatory authorities to place a clinical hold on the associated clinical trials, to require additional studies, or otherwise to delay or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition, and prospects significantly.

If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, including during any long-term follow-up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture and distribution;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product;
- regulatory authorities may require additional warnings on the label, such as a boxed warning or contraindication, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- the product could become less competitive;
- a strategic collaborator for the product may choose to terminate its agreement and compromise our ability to commercialize such product in the collaborator's geography;

- we may be subject to fines, injunctions, or the imposition of civil or criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

We may in the future conduct clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We currently expect, and may in the future choose, to conduct one or more clinical trials outside the United States, including in Europe. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. Results for our clinical trials may differ by jurisdiction as a result of varying standards of care or local restrictions on reimbursement from third-party payors for clinical trials, thereby affecting the willingness of the FDA or any comparable foreign regulatory authority to accept such data. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

If it is determined that companion diagnostics are needed, we may be unable to successfully develop companion diagnostics for biomarkers that enable patient selection, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

A key component of our strategy includes the use of diagnostic tools to guide patient selection of our product candidates. In some cases, a diagnostic tool may be commercially available, for example, on a tumor-profiling panel. If not already commercially available, we may be required to seek collaborations with diagnostic companies for the development of diagnostics for biomarkers associated with our product candidates. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations. Furthermore, even if a diagnostic is commercially available, we may not be able to obtain reimbursement for its use without obtaining regulatory approval.

There are also several risks associated with biomarker identification and validation. We, in collaboration with any diagnostic partners, may not be able to identify predictive biomarkers or pharmacodynamic biomarkers for one or more of our programs. We may not be able to validate potential biomarkers (e.g., certain genomic alterations) or their functional relevance preclinically in relevant *in vitro* or *in vivo* models. Data analytics and information from databases that we rely on for identifying or validating some of our biomarker-target relationships may not accurately reflect potential patient populations or may be based on incorrect methodology. Potential biomarkers, even if validated preclinically, may not be functionally validated in human clinical trials.

If it is determined that companion diagnostics are needed, we may, in collaboration with these parties, be unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so, which may adversely affect the development of our product candidates. The development of companion diagnostic products requires a significant investment of working capital, and may not result in any future income. This could require us to raise additional funds, which could dilute our current investors or impact our ability to continue our operations in the future.

There are also risks associated with diagnostics that are commercially available, including that we may not have access to reliable supply for such diagnostics.

The failure to obtain required regulatory approvals for any companion diagnostic tests that may be required and that we may pursue may prevent or delay approval of our product candidates. Moreover, the commercial success of any of our product candidates may be tied to the regulatory approval, market acceptance and continued availability of a companion diagnostic.

The FDA and other comparable regulatory authorities regulate *in vitro* companion diagnostics as medical devices that will likely be subject to clinical trials in conjunction with the clinical trials for our product candidates, and which will require regulatory clearance or approval prior to commercialization. If it is determined that companion diagnostics are needed, we plan to collaborate with third parties for the development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory clearances or approvals, and the commercial supply of these companion diagnostics. Our third-party collaborators may fail to obtain the required regulatory clearances or approvals, which could prevent or delay approval of our product candidates. In addition, the commercial success of any of our product candidates may be tied to and dependent upon the receipt of required regulatory clearances or approvals of the companion diagnostic.

For example, the genomic alterations our compounds are addressing, such as ATM loss and CCNE1 amplification, are uncommon genetic alterations in tumors, or their subsets and their prognostic significance has not been fully validated for the patient populations that we are targeting. Such development risk contributes to the costs that we may need to bear in validating the alterations as well as the optimal method of diagnostic screening for our clinical trial populations.

Even if a companion diagnostic is approved, we will rely on the continued ability of any third-party collaborator to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies. Market acceptance of the companion diagnostic may be low as a result of the cost and complexity of utilizing such companion diagnostic. Furthermore, if commercial tumor profiling panels are not able to be updated to include additional tumor-associated genes, or if clinical oncologists do not incorporate molecular or genetic sequencing into their clinical practice, we may not be successful in developing or commercializing our existing product candidates or any future product candidates.

We intend to pursue the development of certain of our product candidates in combination with other therapies, and regulatory approval, safety or supply issues with these other therapies may delay or prevent the development and approval of our product candidates.

We may explore the use of our product candidates in combination with other therapies, including those that are not yet approved. For example, pursuant to the terms of the Roche Agreement, we have retained the right to conduct specified clinical trials of camonsertib in combination with RP-6306. If we choose to develop a product candidate for use in combination with an approved therapy, we are subject to the risk that the FDA or comparable foreign regulatory authorities could revoke approval of, or that safety, efficacy, manufacturing, or supply issues could arise with, the therapy used in combination with our product candidate. If the therapies we use in combination with our product candidates are replaced as the standard of care, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials, or we may not be able to obtain adequate reimbursement from third-party payors. The occurrence of any of these risks could result in our product candidates, if approved, being removed from the market or being less successful commercially.

Where we develop a product candidate for use in combination with a therapy that has not been approved by the FDA or comparable foreign regulatory authorities, we will not be able to market our product candidate for use in combination with such an unapproved therapy, unless and until the unapproved therapy receives regulatory approval. These unapproved therapies face the same risks described with respect to our product candidates currently in development, including serious adverse effects and delays in their clinical trials. In addition, other companies may also develop their products or product candidates in combination with the unapproved therapies with which we are developing our product candidates for use in combination. Any setbacks in these companies' clinical trials, including the emergence of serious adverse effects, may delay or prevent the development and approval of our product candidates.

If the FDA or comparable foreign regulatory authorities do not approve or revoke their approval of, or if safety, efficacy, manufacturing, or supply issues arise with, therapies we choose to evaluate in combination with any of our product candidates, we may be unable to obtain regulatory approval of or to commercialize such product candidates in combination with these therapies.

Risks Related to the Commercialization of Our Product Candidates

We have never commercialized a product candidate and may experience delays or unexpected difficulties in obtaining regulatory approval for our current or future product candidates for our initial or potential additional indications.

We have never obtained regulatory approval for, or commercialized, a drug. It is possible that the FDA may refuse to accept any or all of our planned NDAs for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any product candidates. If the FDA does not approve any of our planned NDAs, it may require that we conduct additional costly clinical, nonclinical, or manufacturing validation studies before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. Any failure or delay in obtaining regulatory approvals would prevent us from commercializing our current or future product candidates, generating revenues, and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any NDA or other application that we submit. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in foreign jurisdictions.

We currently have no marketing and sales organization and have no experience as a company in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. We intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, and retain marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing, and distribution capabilities, we will pursue arrangements with third-party sales, marketing, and distribution collaborators regarding the sales and marketing of our products, if approved. However, there can be no assurance that we will be able to establish or maintain such arrangements on favorable terms or if at all, or if we are able to do so, that these third-party arrangements will provide effective sales forces or marketing and distribution capabilities. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

Due to our limited resources and access to capital, we must, and have in the past decided to, prioritize development of certain product candidates over other potential product candidates. These decisions may prove to have been wrong and may adversely affect our ability to develop our own programs, our attractiveness as a commercial partner and may ultimately have an impact on our commercial success.

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each. Our decisions concerning the allocation of research, collaboration, management, and financial resources toward particular proprietary molecules in our library,

product candidates or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from better opportunities. Similarly, our decisions to delay, terminate or collaborate with third parties in respect of certain product development programs may also prove not to be optimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the market potential of our product candidates or misread trends in the biopharmaceutical industry, in particular for our lead product candidate, our business, financial condition and results of operations could be materially adversely affected.

Even if we obtain regulatory approval of our product candidates, the products may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers and others in the medical community.

The use of precision medicines as a potential cancer treatment is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers and others in the medical community. Various factors will influence whether our product candidates are accepted in the market, including:

- the clinical indications for which our product candidates are approved;
- physicians, hospitals, cancer treatment centers and patients considering our product candidates as a safe and effective treatment;
- the potential and perceived advantages of our product candidates over current or future alternative treatments;
- our ability to demonstrate the advantages of our product candidates over other cancer medicines;
- the prevalence and severity of any side effects;
- the prevalence and severity of any side effects for other precision medicines and public perception of other precision medicines;
- product labeling or product insert requirements of the FDA or comparable foreign regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or comparable foreign regulatory authorities;
- the timing of market introduction of our product candidates as well as competitive products;
- the cost of treatment, including with respect to diagnostic tools for our product candidates, and the availability of testing for patient selection;
- the pricing of our products, if approved, and the availability of adequate coverage and reimbursement by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage or adequate reimbursement by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

If our product candidates are approved for commercialization but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue.

In addition, although our product candidates differ in certain ways from other precision medicine approaches, serious adverse events or deaths in other clinical trials involving precision medicines, even if not ultimately attributable to our product or product candidates, could result in increased government regulation, unfavorable public perception and publicity, potential regulatory delays in the testing or licensing of our product candidates, stricter labeling requirements for those product candidates that are licensed, and a decrease in demand for any such product candidates.

Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

The market opportunities for our product candidates may be relatively small as it will be limited to those patients who are ineligible for or have failed prior treatments and our estimates of the prevalence of our target patient populations may be inaccurate.

Cancer therapies are sometimes characterized as first line, second line, or third line, and the FDA often approves new therapies initially only for a particular line of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect to initially seek approval of our product candidates in most instances at least as a second or third line therapy. Subsequently, for those product candidates that prove to be sufficiently safe and beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our product candidates, even if approved as a second or third or subsequent line of therapy, would be approved for an earlier line of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

We rely on various sources, including published literature and public or proprietary databases, to ascertain an estimate of the number of patients having particular genomic alterations, such as mutations, deletions or fusions. The determinable prevalence may vary depending on the source and quality of the underlying data and in some cases, insufficient data or poorly curated data may impact our ability to accurately estimate the prevalence of our target patient populations for each indication and in the aggregate across multiple indications both in the clinical trial setting, as well as in the commercial setting, if our product is approved. If the market opportunities for our product candidates are smaller than we estimate, our business, financial position, results of operations and prospects may be harmed. In addition, upon treatment with our product candidates, patients may have or develop resistance to our product candidates, reducing the addressable patient population and duration of treatment.

We face substantial competition, which may result in others developing or commercializing drugs before or more successfully than us.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical, and other resources, such a larger research and development team and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly as they develop novel approaches to treating disease indications that our product candidates are also focused on treating. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel therapeutics or to in-license novel therapeutics that could make the product candidates that we develop obsolete. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring, or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, tolerability, reliability, convenience of use, price, and reimbursement.

We face competition from segments of the pharmaceutical, biotechnology and other related markets that pursue the development of precision oncology therapies for patients with genetically-defined cancers. Several

biopharmaceutical companies, including Loxo Oncology, Inc. (acquired by Eli Lilly and Company), Blueprint Medicines Corporation, SpringWorks Therapeutics, Inc., Black Diamond Therapeutics, Inc., Deciphera Pharmaceuticals, Inc., Tango Therapeutics, Inc., Zentalis Pharmaceuticals, Inc., Turning Point Therapeutics, Inc. (acquired by Bristol Myers Squibb), and Exelixis, Inc. are developing precision oncology medicines. In addition, we may face competition from companies developing product candidates that are based on SL, including AstraZeneca, GlaxoSmithKline, Pfizer, Bayer, Merck Serono, Schrodinger, Inc., Exelixis, Inc., Artios Pharma Ltd., IDEAYA Biosciences, Inc, Impact Therapeutics, Aprea Therapeutics, Acrivon Therapeutics, Treadwell Therapeutics, Debiopharm Group, Varsity Pharma, Breakpoint Therapeutics, and Rhizen Pharmaceuticals AG.

We anticipate that we will continue to face intense and increasing competition as new treatments enter the market and advanced technologies become available. There can be no assurance that our competitors are not currently developing, or will not in the future develop, products that are equally or more effective or are more economically attractive than any of our current or future product candidates. Competing products may gain faster or greater market acceptance than our products, if any, and medical advances or rapid technological development by competitors may result in our product candidates becoming non-competitive or obsolete before we are able to recover our research and development and commercialization expenses. If we or our product candidates do not compete effectively, it may have a material adverse effect on our business, financial condition, and results of operations.

If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could adversely affect our business.

If any of our product candidates are approved for commercialization, we may seek to enter into agreements with third parties to market them in certain jurisdictions outside the United States. We expect that we would be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug approvals and rules governing drug commercialization in foreign countries;
- reduced protection for intellectual property rights;
- foreign reimbursement, pricing and insurance regimes;
- unexpected changes in tariffs, export controls, sanctions, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- business interruptions resulting from geopolitical actions, including war, such as the military conflict involving Russia and Ukraine, and terrorism, natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability, or public health emergencies, such as the novel COVID-19 coronavirus and related shelter-in-place orders, travel, social distancing and quarantine policies, boycotts, curtailment of trade and other business restrictions;
- greater difficulty with enforcing our contracts;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

As an organization, we have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by individual countries in Europe with which we may need to comply. If we are unable to successfully manage the challenges of international expansion and operations, our business and operating results could be harmed.

Coverage and adequate reimbursement may not be available for our product candidates, which could make it difficult for us to sell profitably or at all, if approved.

Market acceptance and sales of any product candidates that we commercialize, if approved, will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from third-party payors, including government health administration authorities, managed care organizations and other private health insurers. Our ability to commercialize any products successfully will also depend in part on the extent to which coverage and adequate reimbursement for the procedures utilizing our product candidates, performed by health care providers, once approved, will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, determine which procedures, and the products utilized in such procedures, they will cover and establish reimbursement levels. Assuming coverage is obtained for procedures utilizing a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who undergo procedures for the treatment of their conditions, and their treating physicians, generally rely on third-party payors to reimburse all or part of the costs associated with the procedures which utilize our products. Treating physicians are unlikely to use and order our products unless coverage is provided and the reimbursement is adequate to cover all or a significant portion of the cost of the procedures which utilize our products. Therefore, coverage and adequate reimbursement for procedures which utilize new products is critical to the acceptance of such new products. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

While no uniform policy for coverage and reimbursement exists in the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor-by-payor basis. Therefore, one payor's determination to provide coverage for a drug does not assure that other payors will also provide coverage, and adequate reimbursement, for the drug. Additionally, a third-party payor's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each payor determines whether or not it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its formulary it will be placed. The position on a payor's list of covered drugs, or formulary, generally determines the co-payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. Additionally, we or our collaborators may develop companion diagnostic tests for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical products, will apply to companion diagnostics. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize any product candidates that we develop.

Even if we are successful in obtaining regulatory approval, commercial success of any approved products will also depend in large part on the availability of insurance coverage and adequate reimbursement from third-party payors, including government payors, such as the Medicare and Medicaid programs, and managed care organizations, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost-effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide adequate insurance coverage and reimbursement levels for any of our products once approved, market acceptance and commercial success would be limited.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the current and future use of product candidates by us and our collaborators in clinical trials, and the potential sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients who use the product, healthcare providers, pharmaceutical companies, our collaborators, or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially adversely affect the market for our product candidates or any prospects for commercialization of our product candidates. Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a product, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products due to negative public perception;
- injury to our reputation;
- withdrawal of clinical trial participants or difficulties in recruiting new trial participants;
- initiation of investigations by regulators;
- costs to defend or settle the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenues from product sales; and
- the inability to commercialize any of our product candidates, if approved.

Although we believe we maintain adequate product liability insurance for our product candidates, it is possible that our liabilities could exceed our insurance coverage. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any of our product candidates. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Should any of the events described above occur, this could have a material adverse effect on our business, financial condition, and results of operations.

Risks Related to Regulatory Matters

Even if we obtain FDA approval for any of our product candidates in the United States, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential.

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy.

Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, other marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Comparable foreign regulatory authorities may also have programs similar to REMS. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments, but the FDA does restrict manufacturer's communications on the subject of off-label use of their products. The policies of the FDA and of comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Our relationships with customers, physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, transparency, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers, and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws that may constrain the business or financial arrangements and relationships through which we research, sell, market, and distribute our product candidates, if we obtain marketing approval. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced by private individuals on behalf of the government through civil whistleblower or qui tam actions, and civil monetary penalties laws prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or

approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- the Health Insurance Portability and Accountability Act, or HIPAA, which created additional federal civil and criminal liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which impose certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers and their business associates, independent contractors of a covered entity that perform certain services involving the use or disclosure of individually identifiable health information, as well as their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions;
- the Federal Food, Drug, and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which require certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to certain payments and other transfers of value to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physicians assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to drug pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- analogous laws in other jurisdictions including, but not limited to, laws relating to interactions with government officials, privacy laws, transparency laws, laws relating to reimbursement, competition,

consumer protection laws, laws relating to the marketing of health products and other healthcare-related laws.

In addition, we are also subject to federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm customers.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations.

If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing, or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have a material adverse effect on our ability to compete in the marketplace.

Enacted and future healthcare legislation may increase the difficulty and cost for us to progress our clinical programs and obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. For example, in March 2010, the Patient Protection and Affordable Care Act, or the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a licensure framework for follow on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and

- establishment of a Center for Medicare & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been judicial, Congressional and executive branch challenges to certain aspects of the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. Moreover, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the “donut-hole” under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is also unclear how any such challenges and other litigation, and further healthcare reform measures of the Biden administration will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute will remain in effect until 2031 unless additional action is taken by Congress. These Medicare sequester reductions had been suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug’s average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. For example, in July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at prescription drugs. In response to Biden’s executive order, on September 9, 2021, the U.S. Department of Health and Human Services, or HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented, but it is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of

which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition, and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In markets outside of the United States, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. The price control regulations outside of the United States can have a significant impact on the profitability of a given market, and further uncertainty is introduced if and when these laws change. For example, in Canada, price control legislation for patented medicines is currently undergoing significant change that may have significant effects on profitability in Canada.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

We may face potential liability if we obtain identifiable patient health information from clinical trials sponsored by us.

Most healthcare providers, including certain research institutions from which we may obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the HITECH. We are not currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, in the future, we may maintain sensitive personally identifiable information, including health information, that we receive throughout the clinical trial process, in the course of our research collaborations, and directly from individuals (or their healthcare providers) who may enroll in patient assistance programs if we choose to implement such programs. As such, we may be subject to state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

The EU General Data Protection Regulation, or GDPR, also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's decision to leave the European Union, referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated now that the United Kingdom has left the European Union.

Furthermore, certain health privacy laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators may obtain health information, as well as the providers who may share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we or third-party CMOs, CROs or other contractors or consultants fail to comply with applicable federal, state/provincial or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our therapeutic candidates and could harm or prevent sales of any affected therapeutics that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing and marketing our therapeutics. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor.

If we or our third-party manufacturers and suppliers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development activities involve the use of biological and hazardous materials and produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development, or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Trade controls may restrict or prohibit altogether the sale or supply of certain products and services to certain governments, persons, entities, countries, and territories, including those that are the target of comprehensive sanctions, unless there are license exceptions that apply or specific licenses are obtained. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We may also have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties, including independent clinical investigators, contracted laboratories and CROs, to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators, contracted laboratories and third-party CROs, to conduct our preclinical studies and clinical trials in accordance with applicable regulatory requirements and to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third party contractors and CROs are required to comply with good laboratory practices, or GLPs, as applicable, and GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GLPs and GCPs through periodic inspections of laboratories conducting GLP studies, trial sponsors, principal investigators, and trial sites. If we, our investigators, or any of our CROs or contracted laboratories fail to comply with applicable GLPs and GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our preclinical studies or clinical trials comply with applicable GLP or GCP regulations. In addition, our clinical trials must be conducted with product, including biologic product, produced in compliance with applicable cGMP regulations. Our failure to comply with these regulations may require us to repeat preclinical studies or clinical trials, which would delay the regulatory approval process.

Further, these laboratories, investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent laboratories, investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for

approval and commercialization of any product candidates that we develop. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third-party laboratories, CROs or clinical investigators terminate, we may not be able to enter into arrangements with alternative laboratories, CROs or investigators or to do so in a timely manner or on commercially reasonable terms. If laboratories, CROs or clinical investigators do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our preclinical or clinical protocols, regulatory requirements or for other reasons, our preclinical or clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional laboratories or CROs (or investigators) involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new laboratory or CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our contracted laboratories and CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and results of operations.

In addition, clinical investigators may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the preclinical study or clinical trial, the integrity of the data generated at the applicable preclinical study or clinical trial site may be questioned and the utility of the preclinical study or clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA. Any such delay or rejection could prevent us from commercializing our clinical-stage product candidate or any future product candidates.

We rely on third parties to supply and manufacture our product candidates, and we expect to continue to rely on third parties to manufacture our products, if approved. The development of such product candidates and the commercialization of any products, if approved, could be stopped, delayed, or made less profitable if any such third party fails to provide us with sufficient quantities of product candidates or products or fails to do so at acceptable quality levels or prices or fails to maintain or achieve satisfactory regulatory compliance.

We do not currently have the infrastructure or capability internally to manufacture all our product candidates for use in the conduct of our preclinical studies and clinical trials or for commercial supply, if our products are approved. We rely on, and expect to continue to rely on, contract manufacturing organizations, or CMOs. Any replacement of our CMOs could require significant effort and expertise because there may be a limited number of qualified CMOs. This could be particularly problematic where we rely on a single-source supplier. Reliance on third-party providers may expose us to more risk than if we were to manufacture our product candidates ourselves. We are dependent on our CMOs for the production of our product candidates in accordance with relevant regulations, such as cGMP, which includes, among other things, quality control, quality assurance and the maintenance of records and documentation. Moreover, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting product development activities that could harm our competitive position.

Our third-party manufacturers may be subject to damage or interruption from, among other things, fire, natural or man-made disaster, war, disease outbreaks or public health pandemics, power loss, telecommunications failure, unauthorized entry, computer viruses, denial-of-service attacks, acts of terrorism, human error, vandalism or sabotage, financial insolvency, bankruptcy, and similar events. For example, the COVID-19 pandemic has impacted our supply chain, in particular our vendors' ability to find staff, and may in the future impact our manufacturing activities.

If we were to experience an unexpected loss of supply of or if any supplier were unable to meet our demand for any of our product candidates, we could experience delays in our research or ongoing and planned clinical trials or commercialization. We could be unable to find alternative suppliers of acceptable quality, in the appropriate volumes who could meet our timelines at an acceptable cost. Moreover, our suppliers are often subject to strict manufacturing requirements and rigorous testing requirements, which could limit or delay production. The long transition periods necessary to switch manufacturers and suppliers, if necessary, could significantly delay our preclinical studies, our clinical trials, and the commercialization of our products, if approved, which could materially adversely affect our business, financial condition, and results of operation.

In complying with the applicable manufacturing regulations of the FDA and comparable foreign regulatory authorities, we and our third-party suppliers must spend significant time, money, and effort in the areas of design and development, testing, production, record-keeping, and quality control to assure that the products meet applicable specifications and other regulatory requirements. The failure to comply with these requirements could result in an enforcement action against us, including the seizure of products and shutting down of production. We and any of these third-party suppliers may also be subject to audits by the FDA and comparable foreign regulatory authorities. If any of our third-party suppliers fails to comply with cGMP or other applicable manufacturing regulations, our ability to develop and commercialize the products could suffer significant interruptions. We face risks inherent in relying on CMOs, as any disruption, such as a fire, natural hazards, vandalism, or an outbreak of contagious disease affecting the CMO or any supplier of the CMO could significantly interrupt our manufacturing capability. In case of a disruption, we will have to establish alternative manufacturing sources. This would require substantial capital on our part, which we may not be able to obtain on commercially acceptable terms or at all. Additionally, we would likely experience months of manufacturing delays as the CMO builds or locates replacement facilities and seeks and obtains necessary regulatory approvals. If this occurs, we will be unable to satisfy manufacturing needs on a timely basis, if at all.

Our current and future collaborations will be important to our business. If we are unable to enter into new collaborations as appropriate, or if these collaborations are not successful, our business could be adversely affected.

A part of our strategy is to strategically evaluate and, as deemed appropriate, enter into partnerships in the future when strategically attractive, including potentially with major biotechnology or pharmaceutical companies. We have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we may enter into collaborations with other companies to provide us with important technologies and funding for our programs and technology. If we fail to enter into or maintain collaborations on reasonable terms or at all, our ability to develop our existing or future research programs and product candidates could be delayed, the commercial potential of our product could change, and our costs of development and commercialization could increase. Furthermore, we may find that our programs require the use of intellectual property rights held by third parties, and the growth of our business may depend in part on our ability to acquire or in-license these intellectual property rights.

For example, we are currently party to a collaboration agreement with Ono Pharmaceutical Co., or Ono, pursuant to which we and Ono have agreed to collaborate in the research of potential product candidates targeting Pol θ and the development of our small molecule Pol θ inhibitor program. Similarly, in May 2020, we entered into a collaboration and license agreement with Bristol Myers Squibb pursuant to which we and Bristol Myers Squibb have agreed to collaborate in the research and development of potential new product candidates for the treatment of cancer. In June 2022, we entered into a collaboration and license agreement with Roche regarding the development and commercialization of our product candidate camonsertib and other specified ATR inhibitors. These and any future collaborations we enter into may pose a number of risks, including, but not limited to, the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- collaborators may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- collaborators with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- a collaborator may choose to deemphasize the development or commercialization of a product candidate licensed to it by us;
- if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our collaborations do not result in the successful discovery, development, and commercialization of product candidates or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under such collaboration. Moreover, we may not receive all of the milestone or royalty payments we are entitled to receive under our current and future collaboration agreements. For example, pursuant to the terms of our collaboration and license agreement with Bristol Myers Squibb, we are entitled to receive up to \$301.0 million in total milestones per each program subject to the agreement. However, given the overlapping nature of the triggers for these milestone payments, as well as the uncertainty associated with achieving any of such milestones, it is unlikely that we will receive the entire \$301.0 million in milestone payments with respect to each program subject to the agreement.

All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report also apply to the activities of our therapeutic collaborators. Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

We face significant competition in seeking appropriate collaborative partners. Our ability to reach a definitive agreement for a partnership will depend, among other things, upon an assessment of the collaborator's resources and

expertise, the terms and conditions of the proposed partnership and the proposed collaborator's evaluation of a number of factors. These factors may include the design or results of preclinical studies or clinical trials, the likelihood of regulatory approval, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of any uncertainty with respect to our ownership of technology (which can exist if there is a challenge to such ownership regardless of the merits of the challenge) and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a partnership could be more attractive than the one with us.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization, reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

Risks Related to Our Intellectual Property

Our success depends in part on our ability to obtain intellectual property rights for our proprietary technologies and product candidates, as well as our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected. Moreover, we may not be able to obtain intellectual property protection with respect to the SL pairs that we identify which are the targets of our current and future product candidates. Although we expect that the compounds underlying our product candidates will be protectable through intellectual property rights, our competitors could develop their own inhibitors based on the SL pairs we identify that might not be protected by our intellectual property rights.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees. Roche controls prosecution of patents related to their in-license on camonsertib.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our

clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States patent office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that we have had issued that cover our products.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or America Invents Act, enacted in 2013, the United States moved from a "first to invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds or cells that are similar to the biological compositions of our product candidates but that are not covered by the claims of our patents;
- the active biological ingredients in our current product candidates will eventually become commercially available in biosimilar drug products, and no patent protection may be available with regard to formulation or method of use;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will have to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned patents and/or applications and any patent rights we may own or license in the future. We rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or technologies, we may not be able to stop a competitor from marketing products that are the same as or similar to our product candidates, which would have a material adverse effect on our business. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

We rely in part on trade secrets to protect our technology, and our failure to obtain or maintain trade secret protection could harm our business.

We rely on trade secrets to protect some of our technology and proprietary information, especially where we believe patent protection is not appropriate or obtainable as is the case for our SNIPRx platform. However, trade secrets are difficult to protect. Litigating a claim that a third party had illegally obtained and was using our trade secrets would be expensive and time consuming, and the outcome would be unpredictable. Moreover, if our competitors independently develop similar knowledge, methods, and know-how, it will be difficult for us to enforce our rights and our business could be harmed.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their drug earlier than might otherwise be the case.

Patent term extensions in other countries may also be subject to certain procedural or administrative requirements including adherence to certain strict timelines. A failure to meet such requirements may result in a loss of the extension in those countries.

Intellectual property rights do not necessarily address all potential threats to our business.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds or formulations that are similar to our product candidates but that are not covered by the claims of any patents, should they issue, that we own or control;
- we or any strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or control;
- we might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or control may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our issued patents, future trademarks, copyrights, or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, trademarks, copyrights, or other intellectual property. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a negative impact on our ability to compete in the marketplace.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability and the ability of future collaborators, if any, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO or equivalent foreign regulatory authority. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could have a negative impact on our ability to commercialize our current and any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Foreign courts will have similar burdens to overcome in order to successfully challenge a third party claim of patent infringement. If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing our product

candidate(s) and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some or all of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

We depend on intellectual property licensed from a third party and termination of this license could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. In particular, we are dependent on our license agreement with New York University. Any termination of this license could result in the loss of significant rights and could harm our ability to commercialize our product candidates.

Disputes may also arise between us and our current licensor or future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current or future licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we, New York University or any future licensors fail to adequately protect any licensed intellectual property, our ability to commercialize products could suffer.

We may be subject to claims asserting that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our future product candidates.

The United States has recently enacted and implemented wide ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain technology outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial

costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Reliance on third parties requires us to share our proprietary information, which increases the possibility that such information will be misappropriated or disclosed.

Because we rely on third parties to develop and manufacture our product candidates, or if we collaborate with third parties for the development or commercialization of our future product candidates, we must, at times, share proprietary information with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share confidential information increases the risk that such information become known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how, a competitor's discovery of our know-how or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors, and consultants to publish data potentially relating to our know-how. Despite our efforts to protect our know-how, we may not be able to prevent the unauthorized disclosure or use of our technical know-how by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors, and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third-party illegally obtained and is using our proprietary information, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect proprietary information.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. While we have a registered a trademark for our SNIPRx platform and SNIPDX biomarker platform technology, we have not yet selected trademarks for RP-6306 and have not yet begun the process of applying to register trademarks for RP-6306 or any other product candidate. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with RP-6306 or any future product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable

to the FDA. Comparable foreign regulators may have similar requirements, and it is possible that different proprietary or non-proprietary names may be required in different jurisdictions.

If we are unable to protect the confidentiality of our proprietary information, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for our product candidate, we also rely on unpatented know-how, technology, and other proprietary information, to maintain our competitive position. We seek to protect our proprietary information, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated proprietary information is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods, and know-how equivalent to our proprietary information. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our proprietary information were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive, and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us.

If we do not obtain patent term extension for patents covering our product candidates, our business may be materially harmed, and in any case, the terms of our patents may not be sufficient to effectively protect our product candidates and business.

Patents have a limited term. In most countries, including the United States, the expiration of a patent is generally 20 years after its first effective non-provisional filing date. However, depending upon the timing, duration, and specifics of FDA marketing approval of our product candidates, one or more of any U.S. patents we may be issued or have licensed may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments.

The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA-approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the

scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our competitive position, business, financial condition, results of operations, and prospects could be harmed, possibly materially.

If there are delays in obtaining regulatory approvals or other additional delays, the period of time during which we can market our product candidates under patent protection could be further reduced. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. Once the patent term has expired, we may be open to competition from similar or generic products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for that product, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on our management team, including Lloyd Segal, our President and Chief Executive Officer, Michael Zinda, Ph.D., our Chief Scientific Officer, and Maria Koehler, M.D., Ph.D., our Chief Medical Officer. Each of them may currently terminate their employment with us at any time. The loss of the services of any of these persons could impede the achievement of our research, development, and commercialization objectives. We do not currently maintain “key person” life insurance on the lives of our executives or any of our employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high-quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of February 24, 2023, we had 180 full-time employees, including 148 employees engaged in research and development and 32 engaged in management or general and administrative activities. As our clinical development and commercialization plans and strategies develop, we expect we will need additional managerial, operational, sales, marketing, financial, legal and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our development efforts effectively, including the ongoing Phase 1 clinical trials of RP-6306, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services. The services include substantially all aspects of clinical trial management and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our preclinical studies or clinical trials may be extended, delayed, or terminated, and we may not be able to obtain marketing approval of our product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring qualified new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a significant disruption of our product development programs and our ability to operate our business effectively.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cyber-attacks are increasing in their frequency, sophistication, and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced any significant system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials by us or our CROs could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal and/or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, such measures may not prevent service interruptions or security breaches that could adversely affect our business and to the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our CROs, CMOs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm

our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Our international operations pose currency risks, which may adversely affect our operating results.

Our reporting and functional currency is the U.S. dollar. Assets and liabilities denominated in currencies other than the U.S. dollar are translated into U.S. dollars at exchange rates in effect at each balance sheet date. Income items and expenses are translated using the average exchange rate in effect for the relevant period.

Our operating results may be affected by volatility in currency exchange rates and our ability to manage effectively our currency transaction risks. Although we report, and will continue to report, our results in U.S. dollars, a portion our expenses are incurred in Canadian dollars as a result of our operations in Canada, as well as other currencies to a lesser extent. For example, we are also exposed to currency risk through our collaboration agreement with Ono as future payments receivable under our collaboration agreement, if any, are denominated in Japanese yen.

In addition, we maintain a significant portion of our cash in Canadian dollar-denominated reserves. We do not currently manage our foreign currency exposure in a manner that would eliminate the effects of changes in foreign exchange rates. For example, we have not engaged in any active hedging techniques, and we have not employed any derivative instruments to date. Therefore, unfavorable fluctuations in the exchange rate between the Canadian dollar and U.S. dollar could have a negative impact on our business and financial results. We do, however, keep expected Canadian dollar cash requirements in Canadian dollars to form a natural hedge.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions, including civil or criminal penalties, private litigation, and adverse publicity and could negatively affect our operating results and business.

We and any current and future collaborators may be subject to federal, state/provincial, municipal and foreign data protection laws and regulations, such as laws and regulations that address privacy and data security. In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws, including Section 5 of the Federal Trade Commission Act, that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties, including research institutions from which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, as amended by HITECH. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we violate HIPAA.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal, and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees, and other individuals about whom we or our current or future collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Data collection is governed by restrictive regulations governing the use, processing, and cross-border transfer of personal information.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to

the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR increased our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's vote in favor of exiting the European Union, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

In addition, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA went into effect on January 1, 2020, and the California Attorney General may bring enforcement actions for violations beginning July 1, 2020. The CCPA was amended on September 23, 2018, and it remains unclear what, if any, further modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our current or future collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

Our employees, principal investigators, consultants, and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants, and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in other jurisdictions, provide accurate information to the FDA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory

sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations, any of which could have a negative impact on our business, financial condition, results of operations and prospects.

Risks Related to Ownership of Our Common Shares

The trading price of our common shares has been and is likely to continue to be volatile and fluctuate substantially.

The trading price of our common shares has been and is likely to continue to be highly volatile. Furthermore, the stock market in general and the market for biopharmaceutical and pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our shareholders may not be able to sell their common shares at or above the price they paid for their common shares. The market price of our common shares may be influenced by many factors, including:

- the ongoing COVID-19 pandemic and its impact on the global markets;
- the commencement, enrollment, timing and results of our ongoing clinical trials of RP-6306, camonsertib and any future product candidates or those of our competitors;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we or our collaborators receive marketing approval;
- our success or failure in identifying new drug candidates to pursue in clinical development;
- the success or failure of our SNIPRx platform in identification of new druggable SL targets;
- the success of competitive drugs, therapies or technologies;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- failure or discontinuation of any of our research or development programs;
- developments related to any existing or future collaborations;
- regulatory or legal developments in the United States and other countries;
- the success of competitive products or technologies;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to camonsertib, RP-6306 and any future product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices;

- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or shareholder litigation;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved drug;
- sales of common shares by us, our executive officers, directors or principal shareholders, or others;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States and abroad;
- investors' general perception of us and our business; and
- the other factors described in this "Risk Factors" section and elsewhere in this Annual Report.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming, and could divert our management's attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common shares.

Concentration of ownership of our common shares among our existing executive officers, directors and principal shareholders may prevent new investors from influencing significant corporate decisions.

Based upon our common shares outstanding as of December 31, 2022, our executive officers, directors, and shareholders who owned more than 5% of our outstanding common shares beneficially own shares, in the aggregate, representing approximately 66% of our common shares. If our executive officers, directors, and shareholders who owned more than 5% of our outstanding common shares acted together, they would be able to significantly influence all matters requiring shareholder approval, including the election and removal of directors and approval of any merger, consolidation, or sale of all or substantially all of our assets. The concentration of voting power and transfer restrictions could delay or prevent an acquisition of our company on terms that other shareholders may desire or result in the management of our company in ways with which other shareholders disagree.

If research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our share price and trading volume could decline.

The trading market for our common shares will be influenced by the research and reports that industry or financial analysts publish about us or our business. We will not have any control over these equity research analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research about us. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our shares could decrease, which in turn could cause the trading price or trading volume of our common shares to decline.

The sale of a substantial number of our common shares in the public market could cause the market price of our shares to drop significantly, even if our business is doing well.

Sales of a substantial number of our common shares in the public market could occur at any time. If our shareholders sell, or the market perceived that our shareholders intend to sell, substantial amounts of our common shares in the public market, the market price of our common shares could decline significantly.

We have filed registration statements on Form S-8 to register our common shares that are issuable pursuant to our equity incentive plans. Shares registered under these registration statements on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options, as well as, in the case of our affiliates, the restrictions of Rule 144 under the Securities Act. Furthermore, in August 2022, we entered into the Sales Agreement with Cowen and Company, LLC as sales agent, pursuant to which we may issue and sell from time to time common shares up to a maximum aggregate amount of \$125.0 million in sales deemed to be an “at the market offering,” as defined by the Securities Act.

Additionally, as of December 31, 2022, certain holders of an aggregate of 17,894,178 common shares, or their transferees, have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other shareholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common shares could decline.

Because we do not anticipate paying any cash dividends on our share capital in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

You should not rely on an investment in our common shares to provide dividend income. We have never declared or paid cash dividends on our share capital. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements or preferred equity may preclude us from paying dividends. As a result, capital appreciation, if any, of our common shares will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common shares.

Our articles of continuance permit us to issue an unlimited number of common shares and preferred shares without additional shareholder approval.

Our articles of continuance permit us to issue an unlimited number of common shares. We anticipate that we will, from time to time, issue additional common shares in the future. Any further issuances of common shares will result in immediate dilution to existing shareholders and may have an adverse effect on the value of their holdings.

Our articles of continuance also permit us to issue an unlimited number of preferred shares, issuable in one or more series and, subject to the provisions of the Business Corporations Act (Québec), or QBCA, having such designations, rights, privileges, restrictions and conditions, including dividend and voting rights, as our board of directors may determine and which may be superior to those of the common shares. The issuance of preferred shares, while providing flexibility in connection with possible acquisitions, financings, and other corporate purposes, could, among other things, have the effect of delaying, deferring, or preventing a change in control of Repare and might adversely affect the market price of our common shares and the voting and other rights of the holders of common shares. We have no current or immediate plans to issue any preferred shares.

Subject to Nasdaq listing rules, we will not be required to obtain the approval of shareholders for the issuance of additional common shares and preferred shares.

We are a “smaller reporting company” and cannot predict if the reduced reporting requirements applicable to smaller reporting companies will make our common shares less attractive to investors.

We are a “smaller reporting company” under the Exchange Act as of June 30, 2022. We may continue to be a smaller reporting company if either (i) the market value of our common shares held by non-affiliates is less than \$250

million or (ii) our annual revenue was less than \$100.0 million during the most recently completed fiscal year and the market value of our common shares held by non-affiliates is less than \$700.0 million. As a smaller reporting company, we may rely on exemptions from certain disclosure requirements that are available to smaller reporting companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. For so long as we remain a smaller reporting company, we are permitted and intend to rely on such exemptions from certain disclosure and other requirements that are applicable to other public companies that are not smaller reporting companies.

We cannot predict if investors will find our common shares less attractive because we may rely on the exemptions and reduced disclosure obligations applicable to smaller reporting companies. If some investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and our share price may be more volatile.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common shares.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as amended and the rules and regulations of The Nasdaq Global Market. Pursuant to Section 404 of the Sarbanes-Oxley Act, we are now required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting. Furthermore, if at such time we no longer qualify as a “smaller reporting company”, our independent registered public accounting firm will be required to issue an annual report that attests the effectiveness of our internal control over financial reporting.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. Further, we may in the future discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Moreover, our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Moreover, we are aware that the remote working arrangements implemented in connection with the COVID-19 pandemic potentially present new areas of risk, and we are carefully monitoring any impact to our internal controls and procedures.

If we are unable to assert that our internal control over financial reporting is effective, investors could lose confidence in the reliability of our financial statements, the market price of our common shares could decline and we could be subject to sanctions or investigations by The Nasdaq Global Market, the SEC or other regulatory authorities.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or

more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. Holders.

Under the Internal Revenue Code of 1986, as amended, or the Code, we will be a passive foreign investment company, or PFIC, for any taxable year in which (1) 75% or more of our gross income consists of passive income or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income, including cash. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets and received directly its proportionate share of the income of such other corporation.

Based on the nature of our activities and the composition of our income and assets, we believe we were not classified as a PFIC for the taxable year ended December 31, 2022. No assurances regarding our PFIC status can be provided for any past, current, or future taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation. In particular, the characterization of our assets as active or passive may depend in part on our current and intended future business plans, which are subject to change. In addition, for our current and future taxable years, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our common shares from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into in the future and our corporate structure. The composition of our income and assets is also affected by how, and how quickly, we spend the cash we raise in any offering. Accordingly, our U.S. counsel expresses no opinion with respect to our PFIC status.

If we are a PFIC, a U.S. Holder (as defined below) of our common shares would be subject to adverse U.S. federal income tax consequences, such as ineligibility for any preferential tax rates for individuals on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements under U.S. federal income tax laws and regulations. Each U.S. Holder should consult its own tax advisors with respect to the potential adverse U.S. tax consequences to it if we are or were to become a PFIC. A “U.S. Holder” is a holder who, for U.S. federal income tax purposes, is a beneficial owner of our common shares and is:

- (1) a citizen or individual resident of the United States;
- (2) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- (3) an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- (4) a trust that (a) is subject to the primary supervision of a U.S. court and the control of one or more “United States persons” (within the meaning of Section 7701(a)(30) of the Code) or (b) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

If we are a controlled foreign corporation, there could be materially adverse U.S. federal income tax consequences to certain U.S. Holders of our common shares.

If a U.S. Holder is treated as owning (directly, indirectly or constructively) at least 10% of the value or voting power of our common shares, such U.S. Holder may be treated as a “United States shareholder” with respect to each “controlled foreign corporation” in our group (if any) as such term is defined in the Code. We refer to this holder as a “Ten Percent Shareholder”.

Each “Ten Percent Shareholder” in a non-U.S. corporation that is classified as a controlled foreign corporation, or a CFC, for U.S. federal income tax purposes generally is required to include in income for U.S. federal tax purposes such Ten Percent Shareholder’s pro rata share of the CFC’s “Subpart F income,” global intangible low taxed income, and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Subpart F income generally includes dividends, interest, rents, royalties, gains from the sale of securities and income from certain

transactions with related parties. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. An individual that is a Ten Percent Shareholder with respect to a CFC generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a Ten Percent Shareholder that is a U.S. corporation. Failure to comply with these reporting obligations may subject a Ten Percent Shareholder to significant monetary penalties and may prevent the statute of limitations with respect to such Ten Percent Shareholder's U.S. federal income tax return for the year for which reporting was due from starting.

A non-U.S. corporation generally will be classified as a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the Code) who owns or is considered to own 10% or more of the total combined voting power of all classes of stock entitled to vote or 10% or more of the total value of all classes of stock of such corporation.

Each U.S. Holder should consult its own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a PFIC, we generally will not be treated as a PFIC with respect to those U.S. Holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

Our ability to use our non-capital loss carryforwards to offset future taxable income may be subject to certain limitations.

In general, where control of a corporation has been acquired by a person or group of persons, subsection 111(5) of the Income Tax Act (Canada), or the Canadian Tax Act, and equivalent provincial income tax legislation restrict the corporation's ability to carry forward non-capital losses from preceding taxation years. We have not performed a detailed analysis to determine whether an acquisition of control for the purposes of subsection 111(5) of the Canadian Tax Act has occurred after each of our previous issuances of common shares or preferred shares. In addition, if we undergo an acquisition of control, our ability to utilize non-capital losses could be limited by subsection 111(5) of the Canadian Tax Act. As of December 31, 2022, we had Canadian federal and provincial non-capital loss carry forwards of \$158.5 million, which expire beginning in 2037 through 2042. In addition, we also have scientific research and experimental development expenditures of approximately \$54.6 million for Canadian federal and provincial income tax purposes, which have not been deducted. These expenditures are available to reduce future taxable income and have an unlimited carry-forward period. We also have scientific research and experimental development tax credit carry forwards of approximately \$9.0 million for Canadian federal income tax purposes, which expire beginning in 2036 through 2042. Research and development tax credits and expenditures are subject to verification by the tax authorities, and, accordingly, these amounts may vary. Future changes in our share ownership, some of which are outside of our control, could result in an acquisition of control for the purposes of subsection 111(5) of the Canadian Tax Act. Furthermore, our ability to utilize non-capital losses (or U.S. equivalents) of companies that we may acquire in the future may be subject to limitations. As a result, even if we attain profitability, we may be unable to use a material portion of our non-capital losses and other tax attributes, which could negatively impact our future cash flows.

Changes to the tax treatment of research and experimental expenditures as a result of U.S. federal tax reform could increase our tax burden and adversely affect our business and financial condition.

In December 2017, the U.S. government enacted comprehensive tax legislation, the Tax Cuts and Jobs Act of 2017, or TCJA, significantly reformed the Internal Revenue Code of 1986, as amended. As a result of this legislation beginning in 2022, our research and experimental expenditures are no longer deductible in the year they are incurred for US tax purposes. Instead, US-based research and experimental expenditures are required to be capitalized and amortized ratably over a five-year period. Any such expenditures attributable to research conducted outside the United States must be capitalized and amortized over a 15-year period. Although Congress is considering legislation that would defer the amortization requirement to later years, we have no assurance that the provision will be repealed or otherwise modified, or that any future repeal or modification would be retroactive. The requirement has materially reduced our cash flows in 2022 and is expected to materially reduce our cash flows going forward. Changes in our tax provisions or an increase in our tax liabilities, whether due to changes in applicable laws and regulations or our

interpretation or application thereof, could have a material adverse effect on our financial position, results of operations and/or cash flows.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes, or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, the Canada Revenue Agency, the U.S. Internal Revenue Service, or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a “permanent establishment” under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Our deductions and credits in respect of scientific research and experimental development expenditures may be challenged by tax authorities.

Tax authorities in Canada and the United States may not necessarily agree with our determinations of the expenses and tax credits claimed by us, including scientific research and experimental development expenses and related tax credits. If tax authorities successfully challenge such expenses or the correctness of such income tax credits claimed, our operating results could be adversely affected. Furthermore, if the tax authorities reduce the tax credit by reducing either the rate of the credit or the eligibility of some scientific research and experimental development expenses in the future, our operating results could be adversely affected.

We have and will continue to incur significantly increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we have and will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain and maintain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees, or as executive officers. The increased costs may require us to reduce costs in other areas of our business or increase the prices of our services. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Our amended and restated bylaws designate specific courts in Canada and the United States as the exclusive forum for certain litigation that may be initiated by our shareholders, which could limit our shareholders’ ability to obtain a favorable judicial forum for disputes with us.

Pursuant to our amended and restated bylaws, unless we consent in writing to the selection of an alternative forum, the courts of the Province of Québec and the appellate courts therefrom shall, to the fullest extent permitted by

law, be the sole and exclusive forum for: (a) any derivative action or proceeding brought on our behalf; (b) any action or proceeding asserting a claim for breach of fiduciary duty owed to us by any of our directors, officers or other employees; (c) any action or proceeding asserting a claim arising out of any provision of the Business Corporations Act (Québec) or the articles or our bylaws (as either may be amended from time to time); or (d) any action or proceeding asserting a claim otherwise related to our affairs, or the Canadian Forum Provision. The Canadian Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act, or the U.S. Federal Forum Provision. In addition, our amended and restated bylaws provide that any person or entity holding, owning, or otherwise acquiring any interest in any of our securities is deemed to have notice of and consented to the Canadian Forum Provision and the U.S. Federal Forum Provision.

The Canadian Forum Provision and the U.S. Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on shareholders in pursuing any such claims. Additionally, the forum selection clauses in our amended and restated bylaws may limit our shareholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our shareholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts, including courts in Canada and other courts within the United States, will enforce our U.S. Federal Forum Provision. If the U.S. Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The U.S. Federal Forum Provision may also impose additional litigation costs on shareholders who assert that the provision is not enforceable or invalid. The courts of the Province of Québec and the federal district courts of the United States of America may also reach different judgments or results than would other courts, including courts where a shareholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our shareholders.

Because we are a Canadian company, it may be difficult to serve legal process or enforce judgments against us.

We are incorporated and have our corporate headquarters in Québec, Canada. In addition, while many of our directors and officers reside in the United States, several of them reside outside of the United States. Accordingly, service of process upon us may be difficult to obtain within the United States. Furthermore, because substantially all of our assets are located outside the United States, any judgment obtained in the United States against us, including one predicated on the civil liability provisions of the U.S. federal securities laws, may not be collectible within the United States. Therefore, it may not be possible to enforce those actions against us.

In addition, it may be difficult to assert U.S. securities law claims in original actions instituted in Canada. Canadian courts may refuse to hear a claim based on an alleged violation of U.S. securities laws against us or these persons on the grounds that Canada is not the most appropriate forum in which to bring such a claim. Even if a Canadian court agrees to hear a claim, it may determine that Canadian law and not U.S. law is applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process. Certain matters of procedure will also be governed by Canadian law. Furthermore, it may not be possible to subject foreign persons or entities to the jurisdiction of the courts in Canada. Similarly, to the extent that our assets are located in Canada, investors may have difficulty collecting from us any judgments obtained in the U.S. courts and predicated on the civil liability provisions of U.S. securities provisions.

We are governed by the corporate laws of Québec, which in some cases have a different effect on shareholders than the corporate laws of Delaware.

We are governed by the QBCA and other relevant laws, which may affect the rights of shareholders differently than those of a company governed by the laws of a U.S. jurisdiction, and may, together with our charter documents, have the effect of delaying, deferring, or discouraging another party from acquiring control of us by means of a tender offer, a proxy contest or otherwise, or may affect the price an acquiring party would be willing to offer in such an

instance. The material differences between the QBCA and Delaware General Corporation Law, or the DGCL, that may have the greatest such effect include but are not limited to the following: (i) for material corporate transactions (such as mergers and amalgamations, other extraordinary corporate transactions or amendments to our articles), the QBCA generally requires a two-thirds majority vote by shareholders, whereas the DGCL generally only requires a majority vote; and (ii) under the QBCA, a holder of 10% or more of our common shares can requisition a special meeting of shareholders, whereas such right does not exist under the DGCL.

Our amended and restated bylaws and certain Canadian legislation contain provisions that may have the effect of delaying or preventing certain change in control transactions or shareholder proposals.

Certain provisions of our amended and restated bylaws and certain Canadian legislation, together or separately, could discourage or delay certain change in control transactions or shareholder proposals.

Our amended and restated bylaws contain provisions that establish certain advance notice procedures for nomination of candidates for election as directors at shareholders' meetings. The QBCA requires that any shareholder proposal that includes nominations for the election of directors must be signed by one or more holders of shares representing in the aggregate not less than 5% of the shares or 5% of the shares of a class or series of shares of the corporation entitled to vote at the meeting to which the proposal is to be presented.

The Investment Canada Act requires that a non-Canadian must file an application for review with the Minister responsible for the Investment Canada Act and obtain approval of the Minister prior to acquiring control of a "Canadian business" within the meaning of the Investment Canada Act, where prescribed financial thresholds are exceeded. Furthermore, limitations on the ability to acquire and hold our common shares may be imposed by the Competition Act (Canada). This legislation permits the Commissioner of Competition, or Commissioner, to review any acquisition or establishment, directly or indirectly, including through the acquisition of shares, of control over or of a significant interest in our company. Otherwise, there are no limitations either under the laws of Canada or Québec, or in our articles on the rights of non-Canadians to hold or vote our common shares.

Any of these provisions may discourage a potential acquirer from proposing or completing a transaction that may have otherwise presented a premium to our shareholders.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our headquarters is currently located in Montréal, Québec, Canada and consists of 9,045 square feet of leased laboratory and office space under a lease that expires in July 2025. In September 2020, we expanded our research footprint with the addition of 20,594 square feet of combined laboratory and office space in Montréal, Québec, Canada through a lease agreement that expires in August 2025. The new facility expands the laboratory capacity for our CRISPR-enabled genome-wide synthetic lethal target platform, SNIPRx[®], including dedicated space for work related to accelerating our preclinical assets, including those under our research collaboration with Bristol Myers Squibb. We also lease 11,312 square feet of office space in Cambridge, Massachusetts for our U.S.-based employees under a lease which expires in December 2024. We intend to renew our leases, move to new facilities or expand existing facilities to meet our growth, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently a party to any material legal proceedings, and we are not aware of any pending or threatened legal proceeding against us that we believe could have an adverse effect on our business, operating results or financial condition.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information for our Common Shares

Our common shares are traded on The Nasdaq Global Select Market under the symbol “RPTX” and began trading on June 20, 2020. Prior to this time, there was no public market for our common shares.

Holder

As of December 31, 2022, there were approximately 21 holders of record of our common shares. This number does not reflect the beneficial holders of our common shares for whom shares are held in “nominee” or “street” name through brokerage accounts or other nominees.

Dividends

We have never declared or paid cash dividends on our share capital, and we do not currently intend to pay any cash dividends on our share capital in the foreseeable future. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business. Any future determination related to dividend policy will be made at the discretion of our board of directors, subject to applicable laws, and will depend upon, among other factors, our results of operations, financial condition, contractual restrictions, and capital requirements. In addition, our ability to pay cash dividends on our share capital in the future may be limited by the terms of any future debt or preferred securities we issue or any credit facilities we enter into.

Recent Sales of Unregistered Equity Securities

None.

Issuer Purchases of Equity Securities

None.

Item 6. [Reserved]

Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements and related notes appearing elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the “Risk Factors” section of this Annual Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a leading clinical-stage precision oncology company enabled by our proprietary synthetic lethality approach to the discovery and development of novel therapeutics. Synthetic lethality, or SL, represents a clinically validated approach to drug development. We use our proprietary, genome-wide, CRISPR-enabled SNIPRx platform to systematically discover and develop highly targeted cancer therapies focused on genomic instability, including DNA damage repair. SL arises when a deficiency in either of two genes is tolerated in cells, but simultaneous deficiencies in both genes cause cell death. Cancer cells that contain a mutation in one gene of a SL pair are susceptible to therapeutic intervention targeting the other gene pair. Using our SNIPRx platform, we are developing our pipeline of SL product candidates, including our initial product candidate, camonsertib (also known as RP-3500 or RG6526), a potent and selective oral small molecule inhibitor of ATR (Ataxia-Telangiectasia and Rad3-related protein kinase) for the treatment of solid tumors with specific DNA damage repair-related genomic alterations, including those in the ATM gene (ataxia telangiectasia mutated kinase). In June 2022, we entered into a worldwide license and collaboration agreement with Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd, collectively referred to as Roche, for the development and commercialization of camonsertib. In July 2020, we began dosing patients in our Phase 1/2 TRESR (Treatment Enabled by SNIPRx) clinical trial of camonsertib in advanced solid tumors and, in August 2021, we began dosing patients in our Phase 1b/2 ATTACC clinical trial of camonsertib to evaluate the safety and efficacy of camonsertib in combination with approved poly (ADP-ribose) polymerase, or PARP, inhibitors, olaparib and niraparib, in patients with molecularly selected cancers.

In April 2021, we initiated our Phase 1 MYTHIC clinical trial for RP-6306, our PKMYT1 (Protein Kinase Membrane-associated tyrosine- and threonine- specific cdc-2 inhibitory kinase) SL inhibitor, as a monotherapy for the treatment of molecularly selected advanced solid tumors, and anticipate early Phase 1 read-outs from the trial in the first half of 2023. We initiated Phase 1 combination studies of RP-6306 with gemcitabine (MAGNETIC) in December 2021, camonsertib (MYTHIC) in May 2022, and FOLFIRI (MINOTAUR) in August 2022, each for the treatment of molecularly selected advanced solid tumors, and anticipate providing an update on some of these combination studies in the fourth quarter of 2023. In the fourth quarter of 2022, we received fast track designation for RP-6306 in combination with gemcitabine for the treatment of adult patients with CCNE1 amplified, or FBXW7, or PPP2R1A mutated platinum resistant ovarian cancer. Based on promising preclinical data released at the 34th EORTC-NCI-AACR Symposium in October 2022, we are working with clinical investigators to initiate clinical testing, as part of an investigator-sponsored trial (IST), of a fourth new RP-6306 combination with carboplatin, with first patient dosing expected in the first half of 2023. In the fourth quarter of 2022, we entered into an agreement with Canadian Cancer Trials Group, or CCTG, for a planned, basket Phase 2 IST to evaluate RP-6306 in patients with selected, advanced cancers receiving standard agents. We plan to modify the trial to include a sub-study, which will evaluate RP-6306 in combination with gemcitabine in patients with CD4/6i-resistant ER+/HER2- metastatic breast cancer.

We continue to focus on the advancement of our preclinical programs into clinical development. We expect to initiate IND-enabling studies in the first half of 2023 for a small molecule against an undisclosed target with potential to enter the clinic in late 2023 or early 2024, which represents an acceleration from our prior expectations for this program. We are also pursuing development of an inhibitor of polymerase theta (Polθ) in collaboration with Ono, as Polθ is SL with multiple gene deficiencies found in tumors, including BRCA alterations. In 2022, we selected a proposed inhibitor, which we designated as RP-2119. In February 2023, based on our review of ongoing preclinical studies, we elected to prioritize other Polθ inhibiting compounds in our preclinical development portfolio, which we believe have a higher probability for clinical impact relative to RP-2119. We are now guiding toward clinical entry for a Polθ inhibitor in 2024.

Since our inception in September 2016, we have focused primarily on raising capital, organizing and staffing our company, conducting discovery and research activities, identifying potential SL gene pairs, establishing and protecting our intellectual property portfolio including for our proprietary SNIPRx platform, developing and progressing our product candidates through preclinical studies and preparing for clinical trials and establishing arrangements with third parties for the manufacture of initial quantities of our product candidates and component materials. We do not have any product candidates approved for sale and have not generated any revenue from product sales. On June 23, 2020, we completed our initial public offering, or IPO, whereby we issued an aggregate of 12,650,000 common shares, which includes the exercise in full of the underwriters' option to purchase up to an additional 1,650,000 common shares, at a public offering price of \$20.00 per share. The aggregate net proceeds received by us from the IPO were approximately \$232.0 million, after deducting underwriting commissions and offering expenses of \$3.2 million. On November 1, 2021, we completed a follow-on offering, or the 2021 Offering, whereby we issued 4,600,000 common shares, including the exercise in full by the underwriters of their option to purchase up to 600,000 additional common shares, at a public offering price of \$22.00 per share, for net proceeds of \$94.3 million, after deducting underwriting commissions as well as offering expenses of \$0.8 million. Prior to our IPO, we had funded our operations primarily through equity financings, having raised an aggregate of approximately \$135.2 million of gross proceeds from the sale of our preferred shares and \$15.0 million of gross proceeds from the issuance of a warrant to acquire our common shares. As of December 31, 2022, we had cash and cash equivalents and marketable securities on hand of \$343.9 million.

Since inception, we have incurred significant operating losses. Our net losses were \$29.0 million, and \$106.9 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of \$239.3 million. We expect to continue to incur significant and increasing expenses and operating losses for the foreseeable future, as we advance our product candidates, including RP-6306, through preclinical and clinical development and seek regulatory approvals, manufacture drug product and drug supply, maintain and expand our intellectual property portfolio. Our net losses are also expected to be impacted as we hire additional personnel, pay for accounting, audit, legal, regulatory and consulting services, and pay costs associated with maintaining compliance with Nasdaq listing rules and the SEC requirements, directors and officers, or D&O, insurance, investor and public relations activities and other expenses associated with operating as a public company. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our preclinical studies, our clinical trials, our expenditures on other research and development activities, and our revenue and expenses recognized from collaboration and license agreements.

We do not have any products approved for sale. We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates, if ever. In addition, if we obtain regulatory approval for our product candidates and do not enter into a third-party commercialization partnership, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing, manufacturing and distribution activities. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity offerings and debt financings or other sources, such as potential collaboration agreements, strategic alliances and licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on acceptable terms, or at all. Our failure to raise capital or enter into such agreements as, and when, needed, could have a negative effect on our business, results of operations and financial condition.

Macroeconomic Considerations

Unfavorable conditions in the economy in the United States, Canada and abroad may negatively affect the growth of our business and our results of operations. For example, macroeconomic events, including the COVID-19 pandemic, rising inflation, the U.S. Federal Reserve raising interest rates and the Russia-Ukraine war, have led to economic uncertainty globally. The effect of macroeconomic conditions may not be fully reflected in our results of operations until future periods. If, however, economic uncertainty increases or the global economy worsens, our business, financial condition and results of operations may be harmed. For further discussion of the potential impacts of macroeconomic events on our business, financial condition, and operating results, see the section titled "Risk Factors."

Recent and Anticipated Developments

- **Advancing camonsertib, a potent and selective oral small molecule inhibitor of ATR (Ataxia-Telangiectasia and Rad3-related protein kinase) for the treatment of tumors with specific synthetic lethal genomic alterations in partnership with Roche.**
 - o Initial data from the Phase 1/2 trials evaluating camonsertib in combination with three poly (ADP-ribose) polymerase (PARP) inhibitors is expected to be presented in the first half of 2023 at a major medical meeting.
 - o We expect to report initial data from the Phase 1/2 TRESR trial evaluating camonsertib in combination with gemcitabine in the summer or fall of 2023.
- **Evaluating RP-6306, a first-in-class, oral PKMYT1 inhibitor as a monotherapy and in combinations in multiple early clinical studies.**
 - o We expect to report initial Phase 1 clinical data for RP-6306 as a monotherapy for the treatment of molecularly selected advanced solid tumors (MYTHIC) in the first half of 2023. We expect to report initial Phase 1 clinical data for RP-6306 as a combination therapy for the treatment of molecularly selected advanced solid tumors in the fourth quarter of 2023.
 - o In the fourth quarter of 2022, the U.S. Food and Drug Administration granted Fast Track designation to RP-6306 in combination with gemcitabine for the treatment of adult patients with CCNE1 amplified, or FBXW7 or PPP2R1A mutated platinum resistant ovarian cancer. Fast Track designation is intended to facilitate the development and expedite the review of drugs to treat serious conditions and fulfill an unmet medical need, enabling drugs to reach patients earlier.
 - o Based on promising preclinical data released at the 34th EORTC-NCI-AACR Symposium in October 2022, we are working with clinical investigators to initiate clinical testing, as part of an investigator sponsored trial (IST), of a fourth new RP-6306 combination with carboplatin, with first patient dosing expected in the first half of 2023.
 - o In the fourth quarter of 2022, we entered into an agreement with CCTG for a planned, basket Phase 2 IST to evaluate RP-6306 in patients with selected, advanced cancers receiving standard agents. A sub-study under the master clinical trial protocol will evaluate RP-6306 in combination with gemcitabine in patients with CD4/6i-resistant ER+/HER2- metastatic breast cancer.
- **Advancing preclinical programs into clinical development.**
 - o We expect to initiate IND-enabling studies in the first half of 2023 for a small molecule against an undisclosed target with potential to enter the clinic in late 2023 or early 2024, which represents an acceleration from our prior expectations for this program.
 - o We are pursuing development of an inhibitor of Polθ in collaboration with Ono in Japan, South Korea, Taiwan, Hong Kong, Macau and ASEAN countries, excluding mainland China. Repare retains all rights to develop and commercialize the products outside the Ono territory. In 2022, we selected a proposed inhibitor of Polθ, which we designated as RP-2119. In February 2023, based on our review of ongoing preclinical studies, we elected to prioritize other Polθ inhibiting compounds in our preclinical development portfolio, which we believe have a higher probability for clinical impact relative to RP-2119. We are now guiding toward clinical entry for a Polθ inhibitor in 2024.
 - o In January 2023, we received an approximate \$1.5 million (¥200 million) milestone payment from Ono. The payment reflected the achievement of a research milestone under our research services, license and collaboration agreement with Ono (Ono Agreement).
 - o Also, in January 2023, we and Ono amended the Ono Agreement to further extend the research term until July 31, 2023. Previously, we had entered into an amendment with Ono in October 2021 to extend the research term by one year at no additional cost to us.

Components of Results of Operations

Revenue

To date, we have not recognized any revenue from product sales, and we do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval, or license agreements with third parties, we may generate revenue in the future from product sales. However, there can be no assurance as to when we will generate such revenue, if at all.

Collaboration and License Agreement with Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd.

On June 1, 2022, we entered into a collaboration and license agreement, or the Roche Agreement, with Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd, or collectively, Roche, regarding the development and commercialization of our product candidate camonsertib (also known as RP-3500 or RG6526) and specified other ATR (Ataxia-Telangiectasia and Rad3-related protein kinase) inhibitors, which we refer to as the Licensed Products. The transaction was subject to clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 and other customary closing conditions, which were met on July 13, 2022, or Effective Date.

Under the Roche Agreement, we granted Roche a worldwide, perpetual, exclusive, sublicensable license to develop, manufacture, and commercialize the Licensed Products. Roche assumes all subsequent development of camonsertib with the potential to expand development into additional tumors and multiple combination studies. We have agreed to complete specified ongoing clinical trials at our expense. We also retained the right to conduct specified clinical trials of camonsertib in combination with our PKMYT1 compound (also known as RP-6306).

The Roche Agreement was subsequently amended in October 2022 to extend the timeline to negotiate in good faith the parties' rights and obligations with respect to the Repare Trials, as defined in the Roche Agreement, and to clarify indications included in the development plan that are subject to milestones.

Under the terms of the Roche Agreement, we received an upfront payment of \$125 million in July 2022, and are eligible to receive up to \$1.172 billion in potential clinical, regulatory, commercial and sales milestones, including up to \$55 million in potential near-term payments, and royalties on global net sales ranging from high-single-digits to high-teens. The Roche Agreement also provides us with the ability to opt-in to a 50/50 U.S. co-development and profit share arrangement, including participation in U.S. co-promotion if U.S. regulatory approval is received. If we choose to exercise its co-development and profit share option, we will continue to be eligible to receive certain clinical, regulatory, commercial and sales milestone payments, in addition to full ex-U.S. royalties.

We determined that the transaction price at the onset of the Roche Agreement was \$134.6 million, being (i) the total non-refundable upfront payment received of \$125.0 million, (ii) the additional \$4.0 million payment received, negotiated with Roche for revisions to the clinical development plan under the Roche Agreement as agreed at the time of the Effective Date, and (iii) the \$5.6 million received for the transfer of clinical trial materials.

Performance obligation	<u>Transaction price</u> <u>(in thousands)</u>
Combined licenses	\$ 105,327
Completion of Continuing Trials	26,585
Transfer of clinical trial materials	2,714
Total transaction price	<u>\$ 134,626</u>

We recognized \$116.6 million for the year ended December 31, 2022 as revenue associated with the Roche Agreement, of which \$105.3 million related to the grant of the combined licenses, \$2.7 million related to the clinical trial materials transferred, and \$8.6 million related to the partial recognition of deferred revenue for research and development services performed towards the completion of the Continuing Trials during the period.

As of December 31, 2022, there was \$18.0 million (December 31, 2021 – nil) of deferred revenue related to the Roche Agreement, of which \$15.3 million (December 31, 2021 – nil) was classified as current and \$2.7 million (December 31, 2021 – nil) was classified as non-current in the consolidated balance sheet based on the period the services to complete the Continuing Trials are expected to be performed.

Collaboration and License Agreement with Bristol-Myers Squibb Company

In May 2020, we entered into a collaboration and license agreement, or the BMS Agreement, with the Bristol Myers Squibb Company, or Bristol Myers Squibb, pursuant to which we and Bristol Myers Squibb have agreed to collaborate in the research and development of potential new product candidates for the treatment of cancer. We are providing Bristol Myers Squibb access to a selected number of our existing screening campaigns and novel campaigns. We are responsible for carrying out early-stage research activities directed to identifying potential targets for potential licensing by Bristol Myers Squibb. The collaboration consists of programs directed to both druggable targets and to targets commonly considered undruggable to traditional small molecule approaches. In the event that Bristol Myers Squibb elects to obtain an exclusive license for the subsequent development, manufacturing and commercialization of a program, Bristol Myers Squibb will then be solely responsible for all such worldwide activities.

The BMS Agreement was subsequently amended in July, September and November 2020 to include additional campaigns to the list of existing campaigns from which Bristol Myers Squibb may select campaigns under the BMS Agreement and to enable unblinding of a Bristol Myers Squibb alliance manager in order to streamline the collaboration process.

As part of the BMS Agreement, Bristol Myers Squibb paid us an initial upfront fee of \$50.0 million and made an equity investment of \$15.0 million in our company. We will also be eligible to receive up to \$3.0 billion in total milestones across all potential programs. Such milestones consist of \$301.0 million in total milestones per program subject upon the achievement of certain specified research, development, regulatory and commercial milestones.

The \$50.0 million upfront payment was recorded as deferred revenue on our consolidated balance sheet and is expected to be partially recognized at the point in time when option licenses are exercised by Bristol Myers Squibb, with the remainder being recognized on a proportional performance basis over the period of service for research services.

Performance obligation	Transaction price (in thousands)	
Research activities	\$	6,405
Options to license druggable targets		31,148
Options to license undruggable targets		12,447
Total transaction price	\$	50,000

For the years ended December 31, 2022 and 2021, we recognized, from our deferred revenue balance, \$2.7 million and \$1.1 million, respectively, as revenue associated with the BMS Agreement in relation to research activities performed during the period.

In the fourth quarter of 2022, Bristol Myers Squibb waived its rights to exercise options for druggable targets directed at two separate lesions. As a result, we recognized, from our deferred revenue balance, \$12.5 million as revenue for the year ended December 31, 2022 with regards to the amount allocated to the performance obligation from Bristol Meyers Squibb. In October 2021, we received notification from Bristol Myers Squibb of their option exercise for two druggable targets directed at a single synthetic lethal lesion, pursuant to the terms of the BMS Agreement. As a result, we recognized, from our deferred revenue balance, \$6.5 million as revenue for the year ended December 31, 2021 with regards to the achievement of the performance obligation from Bristol Myers Squibb and the option fees received.

As of December 31, 2022, there was \$27.4 million (December 31, 2021 - \$42.5 million) of deferred revenue related to the BMS Agreement, of which \$27.4 million (December 31, 2021 - \$2.9 million) was classified as current

and nil (December 31, 2021 - \$39.6 million) was classified as non-current on the consolidated balance sheet based on the period the services are expected to be performed and the expected timing of potential option exercises.

Collaboration Agreement with Ono Pharmaceutical Company Ltd.

In January 2019, we entered into a research services, license and collaboration agreement, or the Ono Agreement, with Ono Pharmaceutical Company Ltd., or Ono, pursuant to which we and Ono have agreed to collaborate in the research of potential product candidates targeting Polθ and the development of our small molecule Polθ inhibitor program. Pursuant to the terms of the agreement, we received initial upfront payments of approximately \$8.1 million. These upfront payments have been recorded as deferred revenue on our consolidated balance sheet as per our revenue recognition accounting policy and will be recognized as revenue at the point in time when a product candidate is licensed to Ono pursuant to the terms of the agreement.

In October 2021, we and Ono entered into an amendment to the Ono Agreement whereby the research term, as defined in the Ono Agreement, was extended by one year. In January 2023, we and Ono entered into a second amendment to the Ono Agreement whereby the Research Term, as defined in the Ono Agreement, was extended until July 31, 2023.

In October 2021 and December 2022, the Company achieved specified research triggers amounting to ¥100 million (\$0.9 million) and ¥200 million (\$1.5 million), respectively, as research service payments provided for in the Ono Agreement. The ¥200 million (\$1.5 million) is included in the collaboration revenue receivable at December 31, 2022 and was subsequently received in January 2023. These amounts have been added to the transaction price as the consideration was no longer constrained.

As of December 31, 2022, we classified \$10.5 million (December 31, 2021 - \$9.0 million) as current deferred revenue related to the Ono Agreement.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts and the development of our product candidates, partially offset by fully refundable Canadian research and development tax credits. We expense research and development costs as incurred, which include:

- external research and development expenses incurred under agreements with contract research organizations, or CROs, as well as investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;
- employee-related expenses, including salaries, bonuses, benefits, share-based compensation, and other related costs for those employees involved in research and development efforts;
- costs related to manufacturing material for our preclinical studies and clinical trials, including fees paid to contract manufacturing organizations, or CMOs;
- laboratory supplies and research materials;
- upfront, milestone and maintenance fees incurred under license, acquisition and other third-party agreements;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation, scientific advisory board and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities and equipment, insurance, equipment and software.

Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks using data such as information provided to us by our vendors and analyzing the progress of our studies or other services performed. Significant judgment and estimates are made in determining the accrued expense or prepaid balances at the end of any reporting period.

We characterize research and development costs incurred prior to the identification of a product candidate as discovery costs. We characterize costs incurred once a product candidate has been identified as development costs.

Our direct external research and development expenses consist primarily of fees paid to outside consultants, CROs, CMOs and research laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. Our direct external research and development expenses also include fees incurred under license, acquisition, and option agreements. We track these external research and development costs on a program-by-program basis once we have identified a product candidate.

We do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies, and facilities, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources primarily to conduct our research and discovery activities as well as for managing our preclinical development, process development, manufacturing, and clinical development activities.

The following table summarizes our research and development costs:

	Year Ended December 31,	
	2022	2021
(in thousands)		
Discovery costs		
Direct external costs	\$ 9,942	\$ 11,308
Laboratory supplies and research materials	4,072	4,398
Personnel related costs*	10,965	8,912
Facilities related costs	1,536	1,460
Other costs*	4,032	3,665
	<u>30,547</u>	<u>29,743</u>
Development		
Direct external costs		
Camonsertib program	25,434	25,350
RP-6306 program	25,241	15,962
RP-2119 program	5,152	-
Personnel related costs*	27,450	16,889
Facilities related costs	808	733
Other costs*	5,868	2,494
	<u>89,953</u>	<u>61,428</u>
R&D tax credits	(1,434)	(1,124)
Total research and development costs	<u>\$ 119,066</u>	<u>\$ 90,047</u>

*Certain amounts have been reclassified for presentation purposes.

The successful development of our product candidates is highly uncertain. We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of our product candidates and manufacturing processes and conduct discovery and research activities for our preclinical programs. We cannot determine with certainty the timing of initiation, the duration, or the completion costs of current or future preclinical studies and clinical trials of our product candidates due to the inherently unpredictable nature of preclinical and clinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments, and our ongoing assessments as to each product candidate's commercial potential. We will need to raise substantial additional capital in the future. Our clinical development costs are expected to increase significantly as we commence clinical trials. We

anticipate that our expenses will increase substantially, particularly due to the numerous risks and uncertainties associated with developing product candidates, including the uncertainty of:

- the scope, rate of progress, and expenses of our ongoing research activities as well as any preclinical studies, clinical trials and other research and development activities;
- establishing an appropriate safety profile;
- successful enrollment in and completion of clinical trials;
- whether our product candidates show safety and efficacy in our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- commercializing product candidates, if and when approved, whether alone or in collaboration with others; and
- continued acceptable safety profile of products following any regulatory approval.

Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on other product candidates. For example, if the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or EMA, or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our ongoing and planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

General and Administrative Expenses

General and administrative expense consists primarily of employee related costs, including salaries, bonuses, benefits, share-based compensation and other related costs, as well as expenses for outside professional services, including legal, accounting and audit services and other consulting fees, rent expense, directors and officers insurance expenses, investor and public relations expenses and other general administrative expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will continue to incur significant accounting, audit, legal, regulatory, compliance and directors and officers insurance costs as well as investor and public relations expenses associated with operating as a public company.

Other Income (Expense), Net

Other income (expense), net consists primarily of realized and unrealized gains and losses on foreign exchange, interest income earned on cash and cash equivalents and marketable securities, and other expenses such as interest and bank charges.

Realized and unrealized gains and losses on foreign exchange consist of realized and unrealized gains and losses from holding cash and foreign currency denominated other receivables, accounts payable, accrued expenses and other current liabilities as well as operating lease liabilities.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	YEAR ENDED DECEMBER 31,		CHANGE
	2022	2021	
			(in thousands)
Revenue:			
Collaboration agreements	\$ 131,830	\$ 7,600	\$ 124,230
Operating expenses:			
Research and development, net of tax credits	119,066	90,047	29,019
General and administrative	32,560	26,213	6,347
Total operating expenses	151,626	116,260	35,366
Loss from operations	(19,796)	(108,660)	88,864
Other income (expense), net:			
Realized and unrealized gain (loss) on foreign exchange	308	(144)	452
Interest income	5,631	259	5,372
Other expense, net	(43)	(41)	(2)
Total other income, net	5,896	74	5,822
Loss before income taxes	(13,900)	(108,586)	94,686
Income tax benefit (expense)	(15,147)	1,678	(16,825)
Net loss	\$ (29,047)	\$ (106,908)	\$ 77,861

Revenue

Revenue was \$131.8 million for the year ended December 31, 2022. Of this amount, \$116.6 million related to the recognition of revenue associated with the Roche Agreement, of which \$105.3 million related to the grant of the combined licenses, \$2.7 million related to the clinical trial materials transferred, and \$8.6 million related to the partial recognition of deferred revenue for research and development services performed towards the completion of the Continuing Trials during the period.

We also recognized \$15.2 million for the year ended December 31, 2022 as revenue associated with the BMS Agreement. Of this amount, \$12.5 million relates to the recognition of deferred revenue related to druggable targets as Bristol Myers Squibb waived its rights to exercise options for druggable targets directed at two separate lesions, and \$2.7 million was a result of the partial recognition of the deferred revenue from the BMS Agreement, in proportion to the level of research and development services performed during the period.

Revenue was \$7.6 million for the year ended December 31, 2021. Of this amount, \$6.5 million related to the recognition of deferred revenue from the exercise by Bristol Myers Squibb of their option exercise for druggable targets directed at synthetic lethal lesion, pursuant to the terms of the BMS Agreement, and the related option fees received, and \$1.1 million was a result of the partial recognition of the deferred revenue from the BMS Agreement, in proportion to the level of research and development services performed during the period.

Research and Development Expenses, Net of Tax Credits

Research and development expenses were \$119.1 million for the year ended December 31, 2022, compared to \$90.0 million for the year ended December 31, 2021. The increase of \$29.1 million in research and development expenses was primarily due to:

- a \$13.1 million increase in direct external costs related to the advancement of the RP-6306 program, and the advancement of preclinical programs into IND-enabling studies;

- a \$12.6 million increase in personnel-related costs, including a \$4.3 million increase in share-based compensation, primarily related to increased headcount in support of our discovery and development activities;
- a \$0.3 million decrease in laboratory supplies and research materials; and
- a \$3.7 million increase in other research and development costs, including travel, depreciation, facilities, and external costs not involved in the RP-6306, camonsertib or the advancement of preclinical programs into IND-enabling studies.

General and Administrative Expenses

General and administrative expenses were \$32.6 million for the year ended December 31, 2022, compared to \$26.2 million for the year ended December 31, 2021. The increase of \$6.4 million in general and administrative expenses consisted of:

- a \$4.0 million increase in personnel related costs, including a \$2.5 million increase in share-based compensation, primarily related to increased headcount as we scale the organization;
- a \$2.8 million increase in professional fees associated with the Roche collaboration and the establishment of our at-the-market facility program with Cowen and Company, LLC, as well as timing of audit and Sarbanes-Oxley Act of 2002 related compliance efforts;
- a \$0.8 million increase in other general and administrative expenses mainly related to facilities and IT costs; and
- a \$1.2 million decrease in our D&O insurance premium.

Other Income (Expense), Net

Other income, net was \$5.9 million for the year ended December 31, 2022, compared to \$0.1 million for the year ended December 31, 2021. The increase of \$5.8 million in other income was primarily attributable to higher sums invested in cash and cash equivalents and marketable securities as well as higher interest rates.

Income Tax (Expense) Benefit

Income tax expense was \$15.1 million for the year ended December 31, 2022, primarily due to the taxable income in our U.S. subsidiary and utilization of federal and state research and development tax credit carry forwards.

Income tax benefit was \$1.7 million for the year ended December 31, 2021, primarily due to U.S. federal and state research and development tax credits generated, offset by taxable income in our U.S. subsidiary.

The decrease of \$16.8 million in the income tax benefit was primarily driven by the Tax Cuts and Jobs Act effective January 1, 2022 requiring capitalization and amortization of all IRC 174 costs associated with research and development costs, offset by the utilization of federal and state research and development tax credit carry forwards.

Liquidity and Capital Resources

Since our inception, we have not recognized any revenue from product sales and have incurred operating losses and negative cash flows from our operations. We have not yet commercialized any product and we do not expect to generate revenue from sales of any products for several years, if at all. On June 23, 2020, we completed our IPO whereby we issued an aggregate of 12,650,000 common shares, which includes the exercise in full of the underwriters' option to purchase up to an additional 1,650,000 common shares, at a public offering price of \$20.00 per share. The aggregate net proceeds received by us from the IPO were \$232.0 million, after deducting underwriting commissions, and offering expenses of \$3.2 million. In November 2021, we completed a follow-on offering whereby we issued 4,600,000 common shares, including the exercise in full by the underwriters of their option to purchase up to 600,000 additional common shares, at a public offering price of \$22.00 per share, for net proceeds of \$94.3 million, after deducting underwriting commissions as well as offering expenses of \$0.8 million.

In August 2022, we entered into a Common Shares Sale Agreement, or the Sales Agreement, with Cowen and Company, LLC as sales agent, pursuant to which we may issue and sell common shares from time to time, or the ATM Shares. The ATM Shares to be sold under the Sales Agreement, if any, will be issued and sold pursuant to our shelf registration statement on Form S-3 (File No. 333-257668), up to a maximum aggregate amount of \$125.0 million. No shares have been issued under the Sales Agreement as of the date of this Annual Report on Form 10-K.

Prior to our IPO, we had funded our operations primarily through equity financings, having raised an aggregate of approximately \$135.2 million of gross proceeds from the sale of our preferred shares and \$15.0 million of gross proceeds from the issuance of a warrant to acquire our common shares. We have also partnered with Ono for our Polθ inhibitor program and Bristol Myers Squibb for research and development of potential new product candidates for the treatment of cancer and received initial upfront and additional payments of approximately \$60.5 million in the aggregate. In June 2022, we entered into a collaboration and license agreement with Roche for camonsertib and have received initial payments under the terms of the collaboration in the aggregate amount of \$134.6 million.

We expect to incur significant expenses and operating losses for the foreseeable future as we advance our product candidates through preclinical and clinical development, seek regulatory approval and pursue commercialization of any approved product candidates and we will continue to incur additional costs associated with operating as a public company. We expect that our research and development and general and administrative costs will increase in connection with our planned research and development activities.

Beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminates the option to deduct U.S.-based research and development expenditures in the current fiscal year and requires taxpayers to amortize them over five years pursuant to Internal Revenue Code Section 174. This provision has increased our 2022 cash payments of income taxes significantly as compared to 2021. Although Congress is considering legislation that would defer the amortization requirement to later years, we have no assurance that the provision will be repealed or otherwise modified. If the requirement is not modified, it will materially reduce our cash flows. Changes in our tax provisions or an increase in our tax liabilities, whether due to changes in applicable laws and regulations or our interpretation or application thereof, could have a material adverse effect on our financial position, results of operations and/or cash flows.

As of December 31, 2022, our cash and cash equivalents and marketable securities on hand was \$343.9 million. We believe that our existing cash and cash equivalents, and marketable securities on hand will be sufficient to fund our anticipated operating and capital expenditure requirements into 2026. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our capital resources sooner than we expect. If we receive regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing, and distribution, depending on where we choose to commercialize. We may also require additional capital to pursue in-licenses or acquisitions of other product candidates.

Because of the numerous risks and uncertainties associated with research, development, and commercialization of our product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future capital requirements will depend on many factors, including:

- the initiation, timing, costs, progress and results of our product candidates, including our ongoing Phase 1 clinical trials of RP-6306;
- the progress of preclinical development and possible clinical trials of our current earlier-stage programs;
- the scope, progress, results and costs of our research programs and preclinical development of any additional product candidates that we may pursue;
- the development requirements of other product candidates that we may pursue;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the timing and amount of milestone and royalty payments that we are required to make or eligible to receive under our current or future collaboration agreements, including the Roche Agreement;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA and other regulatory authorities;

- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we or our collaborators receive marketing approval;
- the cost of expanding, maintaining and enforcing our intellectual property portfolio, including filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or any of our product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the extent to which we partner our programs, acquire or in-license other product candidates and technologies or enter into additional strategic collaborations;
- the revenue, if any, received from commercial sales of camonsertib, RP-6306 and any future product candidates for which we or our collaborators receive marketing approval; and
- the costs of operating as a public company.

Until such time, if ever, as we can generate substantial product revenues to support our cost structure, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our shareholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common shareholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common shares. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Cash Flows

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our cash flows for each of the years presented:

	YEAR ENDED DECEMBER 31,		
	2022	2021	CHANGE
	(in thousands)		
Net cash provided by (used in) operating activities	\$ 322	\$ (85,796)	\$ 86,118
Net cash used in investing activities	(175,778)	(1,676)	(174,102)
Net cash provided by financing activities	880	95,557	(94,677)
Effect of exchange rate fluctuations on cash held	(330)	(54)	(276)
Net (decrease) increase in cash and cash equivalents	<u>\$ (174,906)</u>	<u>\$ 8,031</u>	<u>\$ (182,937)</u>

Operating Activities

Net cash provided by operating activities was \$0.3 million for the year ended December 31, 2022, reflecting a net loss of \$29.0 million, offset by a net change of \$4.4 million in our net operating assets and non-cash charges of \$25.0 million. The non-cash charges primarily consist of share-based compensation for option grants to employees, as well as depreciation expense and non-cash lease expense offset by the net accretion/amortization of marketable securities and deferred tax assets. The change in our net operating assets was due to a decrease of \$1.9 million in prepaid expenses and research development tax credits receivable, as well as an increase of \$7.9 million in accrued

expenses and other current liabilities, income taxes payable and deferred revenue, offset by an increase of \$2.7 million in collaboration revenue receivable and other receivables, as well as a \$2.8 million decrease in accounts payable and operating lease liabilities.

Net cash used in operating activities was \$85.8 million for the year ended December 31, 2021, reflecting a net loss of \$106.9 million, offset by a net change of \$7.0 million in our net operating assets and non-cash charges of \$14.1 million. The non-cash charges primarily consist of share-based compensation for option grants to employees, as well as depreciation expense and non-cash lease expense offset by deferred tax assets. The change in our net operating assets was due to a decrease of \$3.6 million in other receivables, as well as an increase of \$11.9 million in accounts payable, income tax payable and accrued expenses and other current liabilities, offset by an increase of \$0.9 million in research and development tax credits receivable and other non-current assets, as well as a \$7.6 million decrease in operating lease liabilities and deferred revenue.

The \$86.1 million decrease in cash used in operating activities for the year ended December 31, 2022 compared to December 31, 2021 is primarily due to the \$134.6 million upfront payment received under the Roche Agreement offset by an increase in operating expenses, specifically direct external costs and personnel-related costs, as we advance the development of our product candidates.

Investing Activities

Net cash used in investing activities was \$175.8 million for the year ended December 31, 2022 and resulted primarily from purchases of marketable securities offset by proceeds from maturities of marketable securities.

Net cash used in investing activities was \$1.7 million for the year ended December 31, 2021 and resulted primarily from purchases of property and equipment.

Financing Activities

Net cash provided by financing activities was \$0.9 million for the year ended December 31, 2022, consisting of net proceeds from the exercise of stock options and issuance of common shares under the ESPP.

Net cash provided by financing activities was \$95.6 million for the year ended December 31, 2021, consisting primarily of \$94.3 million from the November 2021 issuance of shares in the follow-on offering, net of underwriting commissions and offering expenses.

Material Cash Requirements

As of December 31, 2022, we anticipate the aggregate of our cash and cash equivalents and marketable securities will be sufficient to fund our contractual obligations, as well as cash requirements to support our ongoing operations and capital expenditures. Our contractual obligations as of December 31, 2022 primarily consist of:

Collaboration and Research Agreements

Collaboration and research agreement obligations primarily relate to a strategic collaboration agreement that we entered into with the University of Texas M. D. Anderson Cancer Center, or MDACC, in March 2020. The collaboration consists of preclinical studies and clinical trials designed by us and MDACC with the research to be completed by MDACC. We have agreed to commit \$10.0 million in the aggregate to fund the collaboration, with payments to be made over a period of five years, of which \$5.4 million was paid as of December 31, 2022.

We also entered into an agreement with the Broad Institute, Inc., or Broad, in July 2022, under which Broad will perform specialty screening services at our request over the course of a three-year term in exchange for payments of \$0.8 million per year, beginning in July 2022, totaling \$2.3 million in the aggregate.

Purchase and Other Obligations

In the normal course of business, we enter into contracts with CROs and other third parties for preclinical studies and clinical trials, research and development supplies and other testing and manufacturing services. These contracts generally do not contain minimum purchase commitments and provide for termination 30 to 90 days' prior written notice, and therefore are cancellable contracts. The amount and timing of such payments are not known as of December 31, 2022.

We have further entered into license agreements under which we are obligated to make milestone and royalty payments and incur annual maintenance fees. The future milestone or royalty payment obligations under the agreement are contingent upon future events, such as achieving certain clinical and commercial milestones or generating product sales. As of December 31, 2022, we were unable to estimate the timing or likelihood of achieving these clinical and commercial milestones or generating future product sales. See the section titled "License and Collaboration Agreements" elsewhere in this Annual Report as well as Note 7 to our annual consolidated financial statements appearing elsewhere in this Annual Report for a description of our license agreements.

Indemnification agreements

In the ordinary course of business, we may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, we have entered into indemnification agreements with members of our board of directors and executive officers that will require us, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments we could be required to make under these indemnification agreements is, in many cases, unlimited. To date, we have not incurred any material costs as a result of such indemnifications. We are not aware of any indemnification arrangements could have a material effect on our financial position, results of operations or cash flows, and we have not accrued any liabilities related to such obligations in our consolidated financial statements as of December 31, 2022.

Critical Accounting Estimates

This management's discussion and analysis is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reported periods. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates. See Note 2 to our annual consolidated financial statements included elsewhere in this Annual Report for a description of our other significant accounting policies.

Revenue Recognition

In the year ended December 31, 2022, our revenue was generated from our Bristol Myers Squibb collaboration agreement and the Roche collaboration and license agreement. We also have a collaboration agreement with Ono, from which revenue has yet to be recognized.

We recognize revenue in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers, or ASC 606. We enter into collaboration and license agreements, which are within the scope of ASC 606, to discover, develop, manufacture, and

commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (i) licenses to compounds directed to specific targets (referred to as “exclusive licenses”) and (ii) research and development activities to be performed on behalf of the collaboration partner related to the licensed targets. Payments to us under these agreements may include non-refundable license fees, customer option exercise fees, payments for research activities, reimbursement of certain costs, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, we perform the following five steps: (i) we identify the contract(s) with a customer; (ii) we identify the performance obligations in the contract; (iii) we determine the transaction price; (iv) we allocate the transaction price to the performance obligations in the contract; and (v) we recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

As part of the accounting for these arrangements, we must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above and whether those performance obligations are distinct from other performance obligations in the contract; b) the transaction price under step (iii) above; and c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. We use judgment to determine whether milestones or other variable consideration, except for sales-based royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. In determining the stand-alone selling price of a license to our proprietary technology or a material right provided by a customer option, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed estimates that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating estimated stand-alone selling price, we evaluate whether changes in the key assumptions used to determine estimated stand-alone selling price will have a significant effect on the allocation of arrangement consideration between performance obligations.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within one year following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within one year following the balance sheet date are classified as deferred revenue, net of current portion. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

Exclusive Licenses – If the license to our intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, we recognize revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, we consider relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promises, whether the value of the license is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, we utilize judgment to assess the nature of the combined performance obligation and whether the license is the predominant promise within the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. If the license is the predominant promise, and it is determined that the license represents

functional intellectual property, revenue is recognized at the point in time when control of the license is transferred. If it is determined that the license does not represent functional intellectual property, revenue is recognized over time using an appropriate method of measuring progress. We have recognized revenue related to such licenses from our Roche collaboration and license agreement.

Research and Development Services – The obligations under our collaboration and license agreements generally include research and development services to be performed by us to benefit the collaboration partner. For performance obligations that include research and development services, we generally recognize revenue allocated to such performance obligations based on an appropriate measure of progress. We utilize judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure such as costs incurred. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. The measure of progress, and thereby periods of which revenue should be recognized, are subject to estimates by management and may change over the course of the contract. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense. We have recognized revenue related to such research and development services from our Bristol Myers Squibb collaboration agreement and our Roche collaboration and license agreement.

Customer Options – Our arrangements may provide a collaborator with the right to acquire additional goods or services in the future. Under these agreements, fees may be due to us (i) at the inception of the arrangement as an upfront fee or payment or (ii) upon the exercise of the customer option. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. We evaluate the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. We allocate the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires. We have recognized revenue related to such customer options from our Bristol Myers Squibb collaboration agreement.

Milestone Payments – At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the control of the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. We evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to our efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, we generally allocate the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur. To date, we have not recognized any revenue related to the achievement of such milestones.

Royalties – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty

has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of our licensing arrangements.

Accrued and Prepaid Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued and prepaid research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued and prepaid expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid balance accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period.

Share-Based Compensation

We measure share-based compensation based on the grant date fair value of the share-based awards and recognize share-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award. For non-employee awards, compensation expense is recognized as the services are provided, which is generally ratably over the vesting period.

Share-based compensation expense is classified in our consolidated statements of operations and comprehensive loss based on the function to which the related services are provided. We recognize share-based compensation expense for the portion of awards that have vested. Forfeitures are accounted for as they occur.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected share price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. The fair value of each restricted share unit is estimated on the date of grant based on the fair value of our common share on that same date. Prior to our IPO, as there was no public market for our common shares, we determined the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies blended with the historical volatility of the Company's common shares. We expect to continue using such methodology until we have adequate historical data regarding the volatility of the trading price of our common shares on Nasdaq. The expected term of our options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. With the adoption of ASU 2018-07, we applied the nonpublic entity practical expedient for calculating the expected term of non-employee awards, using the midpoint between the vesting date and the contractual term, which is consistent with the method used for employee awards. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods

approximately equal to the expected term of the award. We have not paid, and do not anticipate paying, cash dividends on our common shares; therefore, the expected dividend yield is assumed to be zero.

Recently Adopted Accounting Pronouncements

See note 2 to our annual consolidated financial statements appearing elsewhere in this Annual Report for a description of recently adopted accounting pronouncements applicable to our financial statements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Under SEC rules and regulations, because we are considered to be a “smaller reporting company”, we are not required to provide the information required by this item in this report.

Item 8. Financial Statements and Supplementary Data.

REPARE THERAPEUTICS INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	<u>Page</u>
<u>Report of Independent Registered Public Accounting Firm (PCAOB ID: 1263)</u>	126
<u>Consolidated Balance Sheets as of December 31, 2022 and 2021</u>	129
<u>Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2022 and 2021</u>	130
<u>Consolidated Statements of Shareholders' Equity for the years ended December 31, 2022 and 2021</u>	131
<u>Consolidated Statements of Cash Flows for the years ended December 31, 2022 and 2021</u>	132
<u>Notes to Consolidated Financial Statements</u>	133

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of **Repare Therapeutics Inc.**

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of **Repare Therapeutics Inc.** (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, shareholders' equity, and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021 and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Accrued and Prepaid Research and Development Expenses

Description of the matter

As described in note 2 to the consolidated financial statements, the Company has entered into various research and development contracts with third parties and is required to record its accrued and prepaid research and development expenses resulting from these contracts at the end of each reporting period. When evaluating the adequacy of the accrued and prepaid expenses, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. As of December 31, 2022, the Company has recorded \$15.1 million of accrued research and development expenses and has also recorded total prepaid expenses of \$5.7 million, which included amounts for

prepayments of research and development expenses. The Company's determination of the amount of accrued or prepaid expenses at each reporting period requires significant judgment and estimates by management in certain circumstances, as estimates are based on management's knowledge of the level of service performed by the third parties to date.

Auditing the Company's accrued and prepaid research and development expenses is challenging and required significant auditor effort in performing appropriate procedures to evaluate the completeness and accuracy of the information management utilizes in these estimates.

How we addressed the matter in our audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls over the Company's process used in accounting for accrued and prepaid research and development expenses.

To test the accrued and prepaid research and development expenses, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used by management to estimate the accrual or prepaid balance. To corroborate management's estimates, we inspected a sample of contracts with third parties, discussed and obtained information regarding the progress of clinical trials from the Company's research and development personnel that oversee the clinical trials, and inspected a sample of data obtained from the third parties. We confirmed information directly with a sample of the third parties, such as the services provided and costs incurred, and the number of sites in the clinical trials. We also inspected subsequent invoices received from the third parties and cash disbursements made to these parties, to the extent such invoices were received, or payments were made prior to the date that the consolidated financial statements were issued.

Determining Standalone Selling Prices for the Roche Agreement

Description of the matter

As described in Note 12 to the consolidated financial statements, the Company entered into a collaboration and license agreement (the "Roche Agreement") with Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd (collectively, "Roche"). The Company accounted for the Roche Agreement under ASC 606, Revenue from Contracts with Customers and identified several performance obligations, being (i) the combination of the exclusive perpetual license to the licensed products and the non-exclusive license to certain companion diagnostics (the "License"), (ii) the research and development activities related to the completion of the continuing trials (the "Continuing Trials"), as well as (iii) the transfer of clinical trial materials on hand. The transaction price of \$134.6 million was allocated to each performance obligation based on their relative standalone selling prices, which included \$105.3 million being allocated to the License and recognized at a point in time upon the transfer of the License to Roche, and \$26.6 million allocated to the Continuing Trials which will be deferred and recognized over the period of time to complete the Continuing Trials. The standalone selling price of the License was determined by applying a probability adjusted discounted cashflow model which forecasts future cash flows related to the License. The standalone selling price of the Continuing Trials was based on internal estimates of the costs to perform the services, inclusive of a reasonable profit margin.

Auditing management's estimates of standalone selling prices for the performance obligations related to the License and the Continuing Trials was challenging as certain assumptions used by management required significant judgment and estimation. These assumptions include the probability of success and the discount rate for the License and the cost per patient for the Continuing Trials. Changes to these assumptions can have a material effect on the allocation of the transaction price to the performance obligations as well as the amount and timing of revenue recognized.

How we addressed the matter in our audit

To audit the Company's estimates of the standalone selling prices for the License and the Continuing Trials as described above, we performed audit procedures that included, among others, obtaining and assessing management's analysis to support their conclusion of the allocation of the transaction price under ASC 606. We involved our valuation professionals to assist in the assessment of the estimation methodology used by management and to assess the discount rate used by management by comparing it to current industry trends using available information from other comparable companies. We compared the probability of success used by the Company in developing the estimate of standalone selling price of the License with external data. We obtained management's schedules for cost per patient and tested the accuracy and completeness of the underlying data, and compared inputs with approved budgets and with historical data for comparable clinical trials.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Montréal, Canada
February 28, 2023

Repare Therapeutics Inc.
Consolidated Balance Sheets
(In thousands of U.S. dollars, except share data)

	As of December 31,	
	2022	2021
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 159,521	\$ 334,427
Marketable securities	184,420	7,439
Research and development tax credits receivable	1,280	2,580
Collaboration revenue receivable	1,525	—
Other receivables	1,518	654
Prepaid expenses	5,715	6,314
Total current assets	353,979	351,414
Property and equipment, net	4,228	5,604
Operating lease right-of-use assets	5,371	7,491
Other assets	497	586
Deferred tax assets	—	3,620
TOTAL ASSETS	\$ 364,075	\$ 368,715
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 461	\$ 2,302
Accrued expenses and other current liabilities	21,645	18,622
Operating lease liabilities, current portion	2,171	1,721
Deferred revenue, current portion	53,102	11,921
Income tax payable	1,240	523
Total current liabilities	78,619	35,089
Operating lease liabilities, net of current portion	3,257	5,592
Deferred revenue, net of current portion	2,682	39,613
TOTAL LIABILITIES	84,558	80,294
Commitments and Contingencies		
SHAREHOLDERS' EQUITY:		
Preferred shares, no par value per share; unlimited shares authorized as of December 31, 2022 and December 31, 2021, respectively; 0 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	—	—
Common shares, no par value per share; unlimited shares authorized as of December 31, 2022 and December 31, 2021; 42,036,193 and 41,850,162 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively	482,032	480,699
Additional paid-in capital	37,226	17,988
Accumulated other comprehensive loss	(428)	—
Accumulated deficit	(239,313)	(210,266)
TOTAL SHAREHOLDERS' EQUITY	279,517	288,421
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	\$ 364,075	\$ 368,715

The accompanying notes are an integral part of these consolidated financial statements

Repare Therapeutics Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands of U.S. dollars, except share and per share data)

	Year Ended December 31,	
	2022	2021
Revenue:		
Collaboration agreements	\$ 131,830	\$ 7,600
Operating expenses:		
Research and development, net of tax credits	119,066	90,047
General and administrative	32,560	26,213
Total operating expenses	151,626	116,260
Loss from operations	(19,796)	(108,660)
Other income (expense), net		
Realized and unrealized gain (loss) on foreign exchange	308	(144)
Interest income	5,631	259
Other expense, net	(43)	(41)
Total other income, net	5,896	74
Loss before income taxes	(13,900)	(108,586)
Income tax (expense) benefit	(15,147)	1,678
Net loss	\$ (29,047)	\$ (106,908)
Other comprehensive loss:		
Unrealized loss on available-for-sale marketable securities	(428)	—
Total other comprehensive loss	\$ (428)	\$ —
Comprehensive loss	\$ (29,475)	\$ (106,908)
Net loss per share attributable to common shareholders—basic and diluted	\$ (0.69)	\$ (2.83)
Weighted-average common shares outstanding—basic and diluted	41,922,042	37,818,115

The accompanying notes are an integral part of these consolidated financial statements

Repare Therapeutics Inc.
Consolidated Statements of Shareholders' Equity
(In thousands of U.S. dollars, except share data)

	Common Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount				
Balance, January 1, 2021	36,902,924	\$ 384,313	\$ 5,875	\$ —	\$ (103,358)	\$ 286,830
Exercise of vested stock options	333,996	1,578	(592)	—	—	986
Share-based compensation expense	—	—	12,829	—	—	12,829
Issuance of common shares upon follow-on offering, net of issuance costs of \$840	4,600,000	94,288	—	—	—	94,288
Issuance of common shares	3,299	113	—	—	—	113
Issuance of common shares under the 2020 Employee Share Purchase Plan	9,943	407	(124)	—	—	283
Net loss and comprehensive loss	—	—	—	—	(106,908)	(106,908)
Balance, December 31, 2021	<u>41,850,162</u>	<u>\$ 480,699</u>	<u>\$ 17,988</u>	<u>\$ —</u>	<u>\$ (210,266)</u>	<u>\$ 288,421</u>
Exercise of vested stock options	148,116	708	(261)	—	—	447
Share-based compensation expense	—	—	19,691	—	—	19,691
Issuance of common shares under the 2020 Employee Share Purchase Plan	37,915	625	(192)	—	—	433
Other comprehensive loss	—	—	—	(428)	—	(428)
Net loss	—	—	—	—	(29,047)	(29,047)
Balance, December 31, 2022	<u>42,036,193</u>	<u>\$ 482,032</u>	<u>\$ 37,226</u>	<u>\$ (428)</u>	<u>\$ (239,313)</u>	<u>\$ 279,517</u>

The accompanying notes are an integral part of these consolidated financial statements

Repare Therapeutics Inc.
Consolidated Statements of Cash Flows
(In thousands of U.S. dollars)

	Year Ended December 31,	
	2022	2021
Cash Flows From Operating Activities:		
Net loss for the year	\$ (29,047)	\$ (106,908)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation expense	19,691	12,829
Depreciation expense	1,978	1,471
Non-cash lease expense	2,206	1,873
Loss on disposal of property and equipment	—	24
Foreign exchange loss (gain)	(298)	12
Net (accretion)/amortization of marketable securities	(2,233)	113
Deferred tax asset	3,620	(2,208)
Changes in operating assets and liabilities:		
Prepaid expenses	593	(32)
Research and development tax credits receivable	1,287	(556)
Collaboration revenue receivable	(1,525)	—
Other receivables	(1,147)	3,554
Other non-current assets	89	(298)
Accounts payable	(1,348)	152
Accrued expenses and other current liabilities	3,020	11,166
Operating lease liabilities, current portion	615	98
Income tax payable	717	505
Operating lease liabilities, net of current portion	(2,146)	(1,118)
Deferred revenue	4,250	(6,473)
Net cash provided by (used in) operating activities	322	(85,796)
Cash Flows From Investing Activities:		
Purchase of property and equipment	(602)	(1,690)
Proceeds on disposal of property and equipment	—	40
Proceeds from maturities of marketable securities	81,400	7,450
Purchase of marketable securities	(256,576)	(7,476)
Net cash used in investing activities	(175,778)	(1,676)
Cash Flows From Financing Activities:		
Proceeds from exercise of stock options	447	986
Proceeds from issuance of common shares under the 2020 Employee Share Purchase Plan	433	283
Net proceeds from issuance of common shares in follow-on offering	—	94,288
Net cash provided by financing activities	880	95,557
Effect of exchange rate fluctuations on cash held	(330)	(54)
Net (Decrease) Increase In Cash And Cash Equivalents	(174,906)	8,031
Cash and cash equivalents cash at beginning of year	334,427	326,396
Cash and cash equivalents at end of year	\$ 159,521	\$ 334,427
Supplemental Disclosure Of Cash Flow Information:		
Cash interest received	\$ 1,966	\$ 240
Cash taxes paid, net	\$ 10,810	\$ 25
Property and equipment purchases incurred but not yet paid	\$ —	\$ 1,719
Right-of-use assets obtained in exchange for new operating lease liability	\$ 86	\$ 4,690

The accompanying notes are an integral part of these consolidated financial statements

REPARE THERAPEUTICS INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
(Amounts in U.S. dollars, except per share data, unless otherwise specified)

1. Organization and Nature of Business

Repare Therapeutics Inc. (“Repare” or the “Company”) is a precision medicine oncology company focused on the development of synthetic lethality-based therapies to patients with cancer. The Company was incorporated under the *Canada Business Corporations Act* on September 6, 2016. On June 23, 2020, immediately prior to the completion of its initial public offering (the “IPO”), the Company was continued as a corporation under the *Business Corporations Act (Québec)*.

On June 12, 2020, the Company effected a 1-for-6.062 reverse stock split of the Company’s share capital. Accordingly, all common shares, Series A and B convertible preferred shares, stock options and per share amounts in these consolidated financial statements have been retroactively adjusted to reflect the reverse stock split on a retroactive basis for all periods presented.

On June 23, 2020, the Company completed its IPO of 12,650,000 of its common shares, including the exercise in full by the underwriters of their option to purchase up to 1,650,000 additional common shares, for aggregate gross proceeds of \$253.0 million. The Company’s shares began trading on the Nasdaq Global Select Market under the ticker symbol “RPTX” on June 19, 2020. The Company received \$232.0 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by the Company. Upon closing of the IPO, all outstanding convertible preferred shares converted into 21,558,393 common shares and the outstanding warrant was automatically exercised into 750,000 common shares.

In November 2021, the Company completed a follow-on offering of 4,600,000 of its common shares, including the exercise in full by the underwriters of their option to purchase up to 600,000 additional common shares, at a public offering price of \$22.00 per share, for net proceeds of \$94.3 million, after deducting underwriting commissions as well as offering expenses of \$0.8 million payable by the Company.

Since inception, the Company has incurred operating losses. As of December 31, 2022, the Company had an accumulated deficit of \$239.3 million. The Company does not have any products approved for sale and has financed its operations primarily through equity financings and funding from its collaboration and license agreements. Based on its current operating plan, the Company expects that its existing cash and cash equivalents and marketable securities on hand will be sufficient to fund its operating and capital expenditures into 2026.

There can be no assurance that the Company will be able to obtain additional debt or equity financing, or generate product revenue or revenue from collaboration agreements, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company’s business, results of operations and financial condition.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America (“U.S. GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification (“ASC”) and as amended by Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”).

Principles of Consolidation

The accompanying consolidated financial statements of the Company include the accounts of the Company and its wholly-owned subsidiary, Repare Therapeutics USA Inc. (“Repare USA”), which was incorporated under the laws of Delaware on June 1, 2017. The financial statements of Repare USA are prepared for the same reporting period as the

parent company, using consistent accounting policies. All intra-group transactions, balances, income, and expenses are eliminated in full upon consolidation.

Smaller Reporting Company

The Company qualifies as a “smaller reporting company” under the Exchange Act as of December 31, 2022 because the market value of its common shares held by non-affiliates was less than \$560 million as of June 30, 2022 and its revenue for the year ended December 31, 2021 was less than \$100 million. As a smaller reporting company, the Company may rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. For so long as the Company remains a smaller reporting company, it is permitted and the Company intends to rely on such exemptions from certain disclosure and other requirements that are applicable to other public companies that are not smaller reporting companies.

Foreign Currencies

The functional currency for the Company and Repare USA is the U.S. dollar (“USD”). Accordingly, transactions denominated in currencies other than the functional currency are measured and recorded in the functional currency at the exchange rate in effect on the date of the transactions. At each consolidated balance sheet date, monetary assets and liabilities denominated in currencies other than the functional currency are remeasured using the exchange rate in effect at that date. Non-monetary assets and liabilities and revenue and expense items denominated in foreign currencies are translated into the functional currency using the exchange rate prevailing at the dates of the respective transactions. Any gains or losses arising on remeasurement are included in the consolidated statement of operations.

Segment Information

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company’s singular focus is the research, development and commercialization of precision oncology drugs targeting specific vulnerabilities of tumors in genetically defined patient populations.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in consolidated financial statements and accompanying notes. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, estimates related to revenue recognition, accrued research and development expenses, share-based compensation, right-of-use assets and lease liabilities and income taxes. The Company bases its estimates on historical experience and other market specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results could differ from those estimates. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds.

Marketable Securities

The Company classifies marketable debt securities with a remaining maturity of greater than three months when purchased as available-for-sale. Marketable debt securities with a remaining maturity date greater than one year are classified as non-current where the Company has the intent and ability to hold these securities for at least the next 12 months.

The Company’s marketable securities consist of U.S. treasury bills and U.S. treasury notes with original maturities greater than 90 days. All of the Company’s marketable securities have a contractual maturity of one year or less. The

Company considers its investment portfolio of U.S. treasury bills and U.S. treasury notes to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on observable inputs, other than quoted market prices. Unrealized gains and losses are reported in accumulated other comprehensive items in shareholders' equity. Amortization and accretion of premiums and discounts are recorded in interest income (expense). Realized gains or losses on debt securities are included in other income (expense).

The Company reviews investments whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. In connection therewith, the Company evaluates whether the decline in fair value has resulted from credit losses or other factors, considering the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss exists, the present value of cash flows expected to be collected from the security is compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses is recorded for the credit loss on the consolidated balance sheet, limited by the amount that the fair value is less than the amortized cost basis. Any impairment that is not related to credit is recognized in other comprehensive loss. Changes in the allowance for credit losses are recorded as a provision for (or reversal of) credit loss expense in other (expense) income, net within the consolidated statement of operations. Losses are charged against the allowance when the Company believes the uncollectibility of an available-for-sale security is confirmed or when either of the criteria regarding intent or requirement to sell is met.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and marketable securities. Our investment portfolio comprises money market funds, U.S. treasury bills and U.S. treasury notes. Our investment policy limits investment instruments to investment-grade securities with the objective to preserve capital and to maintain liquidity until the funds can be used in business operations.

The Company maintains deposits in accredited financial institutions which exceed insured limits. The Company deposits its cash in financial institutions that it believes have high credit quality and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company's exposure to foreign exchange risk is primarily related to fluctuations between the Canadian dollar and the U.S. dollar. There are balances in Canadian dollars which are subject to foreign currency fluctuations relating to the impact of translating to U.S. dollars for financial statement presentation.

As of December 31, 2022 and 2021, the Company had no significant off-balance sheet risk, such as foreign exchange contracts, option contracts or other foreign hedging arrangements.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in shareholders' equity that result from transactions and economic events other than those with shareholders. Other comprehensive loss consists of unrealized losses on available-for-sale marketable securities. Total comprehensive loss for all periods presented has been disclosed in the consolidated statements of operations and comprehensive loss.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under U.S. GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and

disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 – Quoted prices in active markets for identical assets or liabilities.
- Level 2 – Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3 – Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

An entity may choose to measure financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings.

The estimated fair values of the Company's cash and cash equivalents, collaboration revenue receivable, other receivables, other assets and accounts payable and accrued expenses approximate their carrying values.

The Company's marketable securities are carried at fair value, determined according to Level 2 inputs in the fair value hierarchy described above.

Property and Equipment, Net

Property and equipment is stated at historical cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which are as follows:

Asset Category	Estimated Useful Lives
Computer equipment	3 years
Office equipment	5 years
Laboratory equipment	5 years
Leasehold improvements	the shorter of the lease term and the useful life

When assets are retired or disposed of, the assets and related accumulated depreciation are derecognized from the accounts, and any resulting gain or loss is included in the determination of net loss. Expenditures for maintenance and repairs are recorded to expense as incurred.

Impairment of Long-Lived Assets

The Company evaluates its finite-lived intangible assets for impairment whenever events or changes in circumstances indicate that the carrying value of assets may not be recoverable. Recoverability of these assets is measured by comparing their carrying value to the future net undiscounted cash flows the assets are expected to generate over their remaining economic life. If such assets are considered impaired, the impairment to be recognized is measured by the amount by which the carrying value of the assets exceeds their fair value. Indefinite-lived intangible assets are tested for impairment annually, or more frequently if indicators of impairment are present. To date, no such impairment losses have been recorded.

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the consolidated balance sheet as a right-of-use asset and current and non-current lease liabilities, as applicable.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Prospectively, the Company will adjust the right-of-use assets for straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew.

Assumptions made by the Company at the commencement date are re-evaluated upon occurrence of certain events, including a lease modification. A lease modification results in a separate contract when the modification grants the lessee an additional right of use not included in the original lease and when lease payments increase commensurate with the standalone price for the additional right of use. When a lease modification results in a separate contract, it is accounted for in the same manner as a new lease.

In accordance with ASC 842, components of a lease should be split into three categories: lease components, non-lease components and non-components. The fixed and in-substance fixed contract consideration (including any consideration related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components.

Entities may elect not to separate lease and non-lease components. The Company has elected to account for lease and non-lease components together as a single lease component for all underlying assets and allocate all of the contract consideration to the lease component only.

Revenue Recognition

The Company recognizes revenue in accordance with ASC 606, Revenue from Contracts with Customers ("ASC 606"). This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company enters into collaboration and license agreements, which are within the scope of ASC 606, to discover, develop, manufacture, and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (i) licenses to compounds directed to specific targets (referred to as "exclusive licenses") and (ii) research and development activities to be performed on behalf of the collaboration partner related to the licensed targets. Payments to the Company under these agreements may include non-refundable

license fees, customer option exercise fees, payments for research activities, reimbursement of certain costs, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

The Company first evaluates license and/or collaboration arrangements to determine whether the arrangement (or part of the arrangement) represents a collaborative arrangement pursuant to ASC 808, Collaborative Arrangements (“ASC 808”), based on the risks and rewards and activities of the parties pursuant to the contractual arrangement. The Company accounts for collaborative arrangements (or elements within the contract that are deemed part of a collaborative arrangement), which represent a collaborative relationship and not a customer relationship, outside the scope of ASC 606.

The Company’s collaborations primarily represent revenue arrangements. For the arrangements or arrangement components that are subject to revenue accounting guidance, in determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company applies the five-step model. As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above and whether those performance obligations are distinct from other performance obligations in the contract; b) the transaction price under step (iii) above; and c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company uses judgment to determine whether milestones or other variable consideration, except for sales-based royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. In determining the stand-alone selling price of a license to the Company’s proprietary technology or a material right provided by a customer option, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed estimates that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating its estimated stand-alone selling price, the Company evaluates whether changes in the key assumptions used to determine its estimated stand-alone selling price will have a significant effect on the allocation of arrangement consideration between performance obligations.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within one year following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within one year following the balance sheet date are classified as deferred revenue, net of current portion. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

Exclusive Licenses – If the license to the Company’s intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, the Company considers relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promises, whether the value of the license is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation and whether the license is the predominant promise within the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. If the license is the predominant promise, and it is determined that the license represents functional intellectual property (“IP”), revenue is recognized at the point in time when control of the license is transferred. If it is determined that the license does not represent functional IP, revenue is recognized over time using an appropriate method of measuring progress.

Research and Development Services – The obligations under the Company’s collaboration and license agreements generally include research and development services to be performed by the Company to benefit the collaboration partner. For performance obligations that include research and development services, the Company generally

recognizes revenue allocated to such performance obligations based on an appropriate measure of progress. The Company utilizes judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure such as costs incurred. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods of which revenue should be recognized, are subject to estimates by management and may change over the course of the contract. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense.

Customer Options – The Company’s arrangements may provide a collaborator with the right to acquire additional goods or services in the future. Under these agreements, fees may be due to the Company (i) at the inception of the arrangement as an upfront fee or payment or (ii) upon the exercise of the customer option. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. The Company allocates the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments – At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to the Company’s efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Royalties – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

For a complete discussion of accounting for collaboration revenues, see Note 12.

Research and Development Expenses

Research and development costs are expensed as incurred. The Company’s research and development expenses consist primarily of costs incurred in performing research and development activities, including salaries and other compensation, share-based compensation, fees paid to external service providers, laboratory supplies and costs for facilities and equipment, partially offset by fully refundable research and development tax credits. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are expensed as the goods are delivered or the services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered.

Accrued and Prepaid Research and Development Expenses

The Company has entered into various research and development contracts. The payments to these agreements are recorded as research and development expenses as incurred. The Company records accrued liabilities and prepaid expenses for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities and prepaid expenses, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgements and estimates are made in determining the accrued and prepaid balances at the end of any reporting period. Actual results could differ from the Company's estimates.

Share-Based Compensation

The Company accounts for all share-based awards granted to employees and non-employees as share-based compensation expense at fair value.

The measurement date for employee and non-employee awards is the date of grant, and share-based compensation costs are recognized over the employees' requisite service period, which is the vesting period, on a straight-line basis. Forfeitures are accounted for as they occur.

The fair value of each restricted share unit is estimated on the date of grant based on the fair value of our common share on that same date. The fair value of each stock option grant or purchases under our 2020 Employee Share Purchase Plan ("ESPP") is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected share price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option and the Company's expected dividend yield. As there was no public market for its common shares prior to its IPO in June 2020, the Company determined the volatility for stock option awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies blended with the historical volatility of the Company's common shares. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. For purchases under our ESPP, only the historical volatility of the Company's common shares is used when developing an estimate of expected volatility. The expected term of the Company's stock options granted to employees and non-employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. In connection with the adoption of ASU No. 2018-07, Compensation—Stock Compensation ("ASU No. 2018-07"), the Company calculated the expected term of non-employee awards using the midpoint between the vesting date and the contractual term, which is consistent with the method used for employee awards. For purchases under our ESPP, the expected term is based on the length of the offering period. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award, for time periods approximately equal to the expected term of the award. The Company has not paid, and does not anticipate paying, cash dividends on its common shares; therefore, the expected dividend yield is assumed to be zero.

Share-based compensation is classified in the accompanying consolidated statements of operations and comprehensive loss based on the function to which the related services are provided. Any consideration paid by employees on exercising stock options or the purchases under our ESPP and the corresponding portion previously credited to additional paid-in capital are credited to share capital.

Share Issuance Costs

Share issuance costs applicable to the issuance of equity instruments are recorded as a reduction of the financing equity proceeds.

Net Loss per Share

Basic net loss per share attributable to common shareholders is computed by dividing the net loss attributable to common shareholders by the weighted-average number of common shares outstanding during the reporting period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common shareholders by the weighted-average number of common shares and potentially dilutive

securities outstanding during the period determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share calculation, shares issuable under the ESPP and options to purchase common shares considered to be potentially dilutive securities were excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive and therefore, basic and diluted net loss per share were the same for all reporting periods presented.

Income Taxes

The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's consolidated financial statements. Under this method, deferred tax assets and liabilities are determined based on differences between the consolidated financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Research and Development Tax Credits

The Company recognizes the benefit of refundable Canadian research and development tax credits as a reduction of research and development costs when there is reasonable assurance that the amount claimed will be recovered.

Recently Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments (ASU 2016-13). Certain amendments thereto were also issued by the FASB. ASU 2016-13 and the related amendments implement an impairment model, known as the current expected credit loss model, that is based on expected losses rather than incurred losses. The Company adopted ASU 2016-13 and the related amendments thereto on January 1, 2022. The adoption of ASU 2016-13 and the related amendments thereto did not have a material impact on the Company's consolidated financial statements or disclosures as of and for the year ended December 31, 2022.

Recently Issued Accounting Pronouncements Not Yet Adopted

There were no new accounting pronouncements issued which could have a significant effect on the Company's consolidated financial statements.

3. Fair Value Measurements

The following table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values:

Description	Financial Assets	Level 1	Level 2	Level 3
	(in thousands)			
As at December 31, 2022				
Assets				
Money market funds included in cash and cash equivalents	\$ 42,995	\$ 42,995	\$ —	\$ —
Marketable securities				
U.S. Treasury notes	58,362	—	58,362	—
U.S. Treasury bills	126,058	—	126,058	—
Total marketable securities	184,420	—	184,420	—
Total financial assets	\$ 227,415	\$ 42,995	\$ 184,420	\$ —
As at December 31, 2021				
Assets				
Money market funds included in cash and cash equivalents	\$ 2,535	\$ 2,535	\$ —	\$ —
Marketable securities				
U.S. Treasury notes	7,439	7,439	—	—
Total financial assets	\$ 9,974	\$ 9,974	\$ —	\$ —

When developing fair value estimates, the Company maximizes the use of observable inputs and minimizes the use of unobservable inputs. When available, the Company uses quoted market prices to measure the fair value. In determining the fair values at each date presented above, the Company relied on quoted prices for similar securities in active markets or using other inputs that are observable or can be corroborated by observable market data.

During the years ended December 31, 2022 and 2021, there were no transfers between fair value measure levels.

4. Cash and Cash Equivalents and Marketable Securities

As of December 31, 2022 and 2021, cash and cash equivalents and marketable securities were comprised of the following:

	<u>Amortized Cost</u>	<u>Unrealized Gains</u>	<u>Unrealized Losses</u>	<u>Fair Value</u>
	(in thousands)			
As at December 31, 2022				
Cash and cash equivalents:				
Cash	\$ 116,526	\$ —	\$ —	\$ 116,526
Money market funds	42,995	—	—	42,995
Total cash and cash equivalents	\$ 159,521	\$ —	\$ —	\$ 159,521
Marketable securities:				
U.S. Treasury notes	\$ 58,641	\$ 1	\$ (280)	\$ 58,362
U.S. Treasury bills	126,207	4	(153)	126,058
Total marketable securities	\$ 184,848	\$ 5	\$ (433)	\$ 184,420
As at December 31, 2021				
Cash and cash equivalents:				
Cash	\$ 331,892	\$ —	\$ —	\$ 331,892
Money market funds	2,535	—	—	2,535
Total cash and cash equivalents	\$ 334,427	\$ —	\$ —	\$ 334,427
Marketable securities:				
U.S. Treasury notes	\$ 7,439	\$ —	\$ —	\$ 7,439
Total marketable securities	\$ 7,439	\$ —	\$ —	\$ 7,439

Interest receivable was \$0.4 million and nil as of December 31, 2022 and 2021, respectively, and is included in other receivables.

The Company held 28 and nil available-for-sale marketable securities with an aggregate fair value of \$157.9 million and nil that were in an unrealized loss position as of December 31, 2022 and 2021, respectively. These marketable securities have been in an unrealized loss position for less than twelve months. The unrealized losses as of December 31, 2022 were not attributed to credit risk but were primarily associated with changes in interest rates and market liquidity. The Company does not intend to sell these securities and it is more likely than not that it will hold these investments for a period of time sufficient to recover the amortized cost. As a result, the Company did not record

an allowance for credit losses or other impairment charges for its marketable securities for the year ended December 31, 2022.

The Company recognized \$0.4 million and nil in net unrealized losses in other comprehensive loss for the years ended December 31, 2022 and 2021, respectively.

The maturities of the Company's marketable securities as of December 31, 2022 and 2021 are less than one year.

5. Property and Equipment, Net

Property and equipment, net as of December 31, 2022 and 2021 consisted of the following:

	December 31,	
	2022	2021
	(in thousands)	
Computer equipment	\$ 473	\$ 469
Office equipment	514	509
Laboratory equipment	6,075	5,536
Leasehold improvements	2,519	2,465
Total	9,581	8,979
Less: Accumulated depreciation	(5,353)	(3,375)
Property and equipment, net	<u>\$ 4,228</u>	<u>\$ 5,604</u>

Depreciation expense recognized was allocated as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Research and development	\$ 1,837	\$ 1,325
General and administration	141	146
Depreciation expense	<u>\$ 1,978</u>	<u>\$ 1,471</u>

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities as of December 31, 2022 and 2021 consisted of the following:

	December 31,	
	2022	2021
	(in thousands)	
Accrued compensation and benefits	\$ 5,616	\$ 4,867
Accrued research and development expense	15,078	11,272
Accrued professional services	680	387
Accrued property and equipment purchases	-	1,719
Other	271	377
Total accrued expenses and other current liabilities	<u>\$ 21,645</u>	<u>\$ 18,622</u>

7. License Agreements

In December 2016, as further amended in February 2017 and amended and restated in July 2018, the Company entered into a license agreement (the "NYU Agreement") with New York University, pursuant to which the Company obtained a worldwide, royalty-bearing, exclusive license under certain patents and know-how of New York University to research, develop and commercialize products covered by such licensed patents. The Company is required to pay New York University an annual non-refundable license fee, which is creditable against future milestone and royalty payments. The Company is required to pay amounts up to approximately \$6.7 million in the aggregate upon

achievement of certain clinical and commercial milestones and pay a low single digit royalty on future net sales of any product covered by a licensed product and a lower-single digit royalty on future net sales of any product not covered by a licensed product. The NYU Agreement expires on the date of expiration of all royalty obligations.

Any potential future milestone or royalty payment amounts have not been accrued at December 31, 2022 and 2021 due to the uncertainty related to the successful achievement of these milestones.

8. Leases

The Company has historically entered into lease arrangements for its facilities and certain equipment. As of December 31, 2022, the Company had four operating leases with required future minimum payments. The Company's leases generally do not include termination or purchase options.

Operating Leases

In June 2017, and as further amended in 2021, the Company entered into a lease agreement for office and laboratory space in Montréal, Québec, for a four-year term, ending in July 2021. In August 2021, the lease was extended through July 2025.

In November 2017, and as further amended throughout 2018, 2019, 2020, 2021 and 2022, the Company entered into a lease agreement for office and laboratory space located in Montréal, Québec, for a three-year term ending in October 2020, which was extended through December 2022. The Company entered into a new lease agreement, effective January 2023, which will result in \$0.2 million of minimum lease payments over the thirty-two month lease term.

In July 2021, the Company entered into a lease agreement for office space in Cambridge, Massachusetts, for a three-year term ending in December 2024, which commenced in December 2021. The Company has an option for a three year renewal, which has not been recognized in the Company's right-of-use asset or lease liability.

In November 2019, and as further amended in July 2021, the Company entered into a lease agreement for office and laboratory space for a five-year term located in Montréal, Québec which commenced in September 2020. The Company has an option for a five year renewal, which has not been recognized in the Company's right-of-use asset or lease liability. As required under the terms of the lease agreement, the Company incurred prepaid rent of \$1.0 million prior to commencement of the lease term, with the current portion previously accounted for within prepaid expenses and other current assets and the long-term portion accounted for within other assets. As well, as required under the terms of the amended lease agreement, the Company incurred prepaid rent of \$0.4 million prior to commencement of the lease term which was accounted for within prepaid expenses. As of the commencement of the lease term, this prepaid rent has been reclassified to the right-of-use asset.

The following tables contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's operating leases for the years ended December 31, 2022 and 2021:

	December 31,	
	2022	2021
	(in thousands)	
Operating Leases		
Lease Cost		
Operating lease cost	\$ 2,456	\$ 2,101
Short-term lease cost	33	25
Variable lease cost	278	163
Total lease cost	<u>\$ 2,767</u>	<u>\$ 2,289</u>

	December 31,	
	2022	2021
	(in thousands, except as specified otherwise)	
Other Operating Lease Information		
Operating cash flows for operating leases	\$ 1,948	\$ 1,240
Right-of-use assets obtained in exchange for lease obligations	\$ 86	\$ 4,690
Weighted-average remaining lease term (in years)	2.43	3.35
Weighted-average discount rate	4.0%	4.0%

Variable lease costs for the years ended December 31, 2022 and 2021 include contingent rental usage, common area maintenance and other operating charges. As the Company's leases do not provide an implicit rate, the Company utilized its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment.

Future minimum lease payments under the Company's operating leases as of December 31, 2022 were as follows:

	December 31, 2022
	(in thousands)
Maturity of Lease Liabilities	
2023	\$ 2,342
2024	2,395
2025	957
Total lease payments	\$ 5,694
Less: interest	(266)
Total lease liabilities	\$ 5,428

9. Shareholders' Equity

Preferred Shares

Effective upon the closing of the IPO, the Company authorized for issue an unlimited number of preferred shares, issuable in series, having such designations, rights, privileges, restrictions and conditions, including dividend and voting rights as the board of directors of the Company may determine, and such rights and privileges, including dividend and voting rights, may be superior to those of the common shares. No preferred shares were issued and outstanding as of December 31, 2022 and 2021.

Common Shares

The articles of continuance of the Company authorize an unlimited number of common shares, voting and participating, without par value.

Each common share entitles the holder to one vote on all matters submitted to the shareholders for a vote. The holders of common shares are entitled to receive dividends, as may be declared by the board of directors, if any. Through December 31, 2022, no cash dividends have been declared or paid.

On November 1, 2021, the Company completed a follow-on offering of 4,600,000 of its common shares, including the exercise in full by the underwriters of their option to purchase up to 600,000 additional common shares, at a public offering price of \$22.00 per share, for net proceeds of \$94.3 million, after deducting underwriting commissions as well as offering expenses of \$0.8 million payable by the Company.

In August 2022, the Company entered into a common shares sale agreement ("the Sales Agreement"), with Cowen and Company, LLC ("Cowen") as sales agent, pursuant to which we may issue and sell common shares from time to

time, or the ATM Shares. The ATM Shares to be sold under the Sales Agreement, if any, will be issued and sold pursuant to our shelf registration statement on Form S-3 (File No. 333-257668), up to a maximum aggregate amount of \$125.0 million. No shares have been issued under the Sales Agreement as of December 31, 2022.

10. Share-Based Compensation

2020 Employee Share Purchase Plan

In June 2020, the Company's board of directors adopted, and the Company's shareholders approved the 2020 Employee Share Purchase Plan ("ESPP"). The maximum number of common shares that may be issued under the ESPP was initially 327,000. Additionally, the number of shares reserved and available for issuance under the ESPP will automatically increase each January 1, beginning on January 1, 2021 and each January 1 thereafter through January 31, 2030, by the lesser of (1) 1.0% of the total number of common shares outstanding on December 31 of the preceding calendar year, (2) 3,300,000 common shares, or (3) such smaller number of common shares as the Company's board of directors may designate. As of January 1, 2023, the number of common shares that may be issued under the ESPP is 1,487,035.

The ESPP enables eligible employees to purchase common shares of the Company at the end of each offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower. Participation in the ESPP is voluntary. Eligible employees become participants in the ESPP by enrolling in the plan and authorizing payroll deductions. At the end of each offering period, accumulated payroll deductions are used to purchase the Company's shares at the discounted price. The Company makes no contributions to the ESPP. A participant may withdraw from the ESPP or suspend contributions to the ESPP. If the participant elects to withdraw during an offering, all contributions are refunded as soon as administratively practicable. If a participant elects to withdraw or suspend contributions, they will not be able to re-enroll in the current offering but may elect to participate in future offerings. The ESPP purchases only whole shares of the Company's shares. The Company's first ESPP offering period began February 16, 2021 and ended on August 15, 2021, with a second offering period commencing on August 16, 2021. Subsequent offering periods will be on a rolling six-month basis.

For the years ended December 31, 2022 and 2021 the Company issued 37,915 and 9,943 common shares under the ESPP, respectively, at an average price per share of \$11.43 and \$28.46, respectively. Cash received from purchases under the ESPP for the years ended December 31, 2022 and 2021 was \$0.4 million and \$0.3 million, respectively. In February 2023, the Company issued 41,703 common shares under the ESPP at an average price per share of \$9.80.

The assumptions that the Company used in the Black Scholes option-pricing model to determine the grant date fair value under the ESPP offering were as follows:

	Year Ended December 31,	
	2022	2021
Risk-free interest rate	2.36 %	0.05 %
Expected term (in years)	0.50	0.50
Expected volatility	85.37 %	61.91 %
Expected dividend yield	0.00 %	0.00 %

The weighted average grant date fair value under the ESPP offering during the years ended December 31, 2022 and 2021 was \$4.91 and \$10.94, respectively.

Option Plan and 2020 Plan

In December 2016, as further amended in December 2017 and September 2019, the Company adopted the Repare Therapeutics Inc. Option Plan (the "Option Plan") for the issuance of stock options and other share-based awards to directors, officers, employees or consultants. The Option Plan authorized up to 4,074,135 shares of the Company's common shares to be issued.

In June 2020, the Company's board of directors adopted, and the Company's shareholders approved the 2020 Equity Incentive Plan (the "2020 Plan"). The 2020 Plan became effective on the effective date of the IPO, at which time the Company ceased making awards under the Option Plan. The 2020 Plan allows the Company's compensation committee to make equity-based and cash-based incentive awards to the Company's officers, employees, directors and consultants including but not limited to stock options and restricted share units. A total of 3,600,000 common shares were initially reserved for issuance under the 2020 Plan, plus the number of shares (not to exceed 3,807,448 shares) consisting of (i) 298,605 common shares that were available for issuance of awards under the Option Plan at the time the 2020 Plan became effective, which ceased to be available for future issuance under the Option Plan at such time and (ii) any shares subject to outstanding options or other share awards that were granted under the Option Plan that terminate or expire prior to exercise or settlement; are forfeited because of the failure to vest; or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price. In addition, the number of shares reserved and available for issuance under the 2020 Plan will automatically increase each January 1, beginning on January 1, 2021 and each January 1 thereafter through January 1, 2030, by 5% of the outstanding number of common shares on the immediately preceding December 31, or such lesser number of shares as determined by the Company's board of directors. As of January 1, 2023, the number of common shares reserved for issuance under the 2020 Plan is 10,025,525.

The 2020 Plan is administered by the board of directors. The exercise prices, vesting and other restrictions are determined by the board of directors, except that the exercise price per share of stock option may not be less than 100% of the fair value of the common share on the date of grant, determined based on the average of the daily volume-weighted average trading price of shares on each of the five trading days immediately preceding the date of grant.

Stock options awarded under the 2020 Plan expire 10 years after the grant and generally have vesting conditions of 25% on the first anniversary of the date of grant and 75% on a monthly basis at a rate of 1/36th unless otherwise decided by the Company's board of directors.

Option Activity

The assumptions that the Company used in the Black Scholes option-pricing model to determine the grant date fair value of stock options granted to employees and non-employees were as follows, presented on a weighted-average basis:

	Year Ended December 31,	
	2022	2021
Risk-free interest rate	2.17 %	0.80 %
Expected term (in years)	5.99	6.00
Expected volatility	78.95 %	75.99 %
Expected dividend yield	0.00 %	0.00 %

The weighted average grant date fair value of stock options granted during the years ended December 31, 2022, 2021 and 2020 was \$9.54 and \$22.49, respectively.

The following table summarizes the Company's share option activity:

	Number of shares	Weighted average exercise price	Weighted average remaining contractual term (in years)	Intrinsic value (in thousands)
Outstanding, January 1, 2022	5,322,591	\$ 14.76	8.15	\$ 55,722
Granted	3,346,567	\$ 14.41		
Exercised	(148,116)	\$ 3.02		
Forfeited	(488,140)	\$ 22.15		
Outstanding, December 31, 2022	8,032,902	\$ 14.38	7.90	\$ 37,250
Options exercisable, December 31, 2022	3,592,087	\$ 11.41	6.94	\$ 28,538
Options unvested, December 31, 2022	4,440,815	\$ 16.79	8.65	\$ 8,712

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common shares for those stock options that had an exercise price lower than the fair value of the Company's common shares.

The aggregate intrinsic value of options exercised during the years ended December 31, 2022 and 2021 was \$1.7 million and \$8.5 million, respectively.

The total fair value of options vested during the years ended December 31, 2022 and 2021 was \$20.1 million and \$7.4 million, respectively.

During the year ended December 31, 2022, an aggregate of 148,116 options were exercised at a weighted-average exercise price of \$3.02 per share, for aggregate proceeds of \$0.4 million. As a result, an amount of \$0.3 million previously included in additional paid-in-capital related to the exercised options has been credited to common shares and deducted from additional paid-in-capital.

In January and February 2023, the Company granted an aggregate of 1,495,240 stock options at a weighted average exercise price of \$12.42 per share and an aggregate of 626,260 restricted share units to employees under the 2020 Plan.

Share-Based Compensation

Share-based compensation expense for all awards was allocated as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Research and development	\$ 10,020	\$ 5,681
General and administrative	9,671	7,148
Total share-based compensation expense	<u>\$ 19,691</u>	<u>\$ 12,829</u>

Share-based compensation expense by type of award was as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Stock options	\$ 19,400	\$ 12,632
ESPP	291	197
Total share-based compensation expense	<u>\$ 19,691</u>	<u>\$ 12,829</u>

As of December 31, 2022, there was \$42.9 million of unrecognized share-based compensation expense related to unvested stock options. The unrecognized share-based compensation expense is expected to be recognized over a weighted-average remaining vesting period of 1.8 years as of December 31, 2022.

11. Employee Savings Plan

The Company has offered its employees in the United States the ability to participate in a 401(k). The Company has also offered its employees in Canada the ability to participate in a registered retirement savings plan. As of January 1, 2021, the Company started making non-matching employer contributions into both of these plans on behalf of participants equal to 3% of their base salary. The Company has recorded an expense of \$0.8 million and \$0.5 million in matching contributions for the years ended December 31, 2022 and 2021.

12. Collaborations

Roche Collaboration and License Agreement

In June 2022, the Company entered into a collaboration and license agreement (the "Roche Agreement") with Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd (collectively, "Roche") regarding the development and

commercialization of the Company's product candidate camonsertib (also known as RP-3500 or RG6526) and specified other Ataxia-Telangiectasia and Rad3-related protein kinase ("ATR") inhibitors (the "Licensed Products"). The transaction was subject to clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 and other customary closing conditions, which were met on July 13, 2022 ("Effective Date"). Pursuant to the Roche Agreement, the Company granted Roche a worldwide, perpetual, exclusive, sublicensable license to develop, manufacture, and commercialize the Licensed Products, as well as a non-exclusive, sublicensable license to certain related companion diagnostics. The Company has agreed to complete specified ongoing clinical trials in accordance with the development plan in the Roche Agreement, as well as ongoing investigator sponsored trials (together, the "Continuing Trials") at the Company's expense. Roche assumes all subsequent development of camonsertib with the potential to expand development into additional tumors and multiple combination studies. The Company retained the right to conduct specified clinical trials (the "Repare Trials") of camonsertib in combination with the Company's PKMYT1 compound (also known as RP-6306). The Roche Agreement also provides the Company, at its sole discretion, with the ability to opt-in to a 50/50 U.S. co-development and profit share arrangement, including participation in U.S. co-promotion if U.S. regulatory approval is received. If the Company chooses to exercise its co-development and profit share option, it will continue to be eligible to receive certain clinical, regulatory, commercial and sales milestone payments, in addition to full ex-U.S. royalties.

The Roche Agreement was subsequently amended in October 2022 to extend the timeline to negotiate in good faith the parties' rights and obligations with respect to the Repare Trials, as defined in the Roche Agreement, and to clarify indications included in the development plan that are subject to milestones.

Under the terms of the Roche Agreement, the Company received an upfront, nonrefundable payment of \$125.0 million in July 2022. The Company also received an additional payment of \$4.0 million negotiated with Roche for revisions to the clinical development plan under the Roche Agreement as agreed to by the parties at the time of the Effective Date. The Company further received \$5.6 million for the transfer of clinical trial material on hand to Roche, as agreed to pursuant to the Roche Agreement. The Company is eligible to receive up to \$1.172 billion in potential clinical, regulatory, commercial and sales milestones, as well as royalties on global net sales ranging from high-single-digits to high-teens, subject to certain specified reductions. Royalties are payable by Roche on a product by product and country by country basis until the later of 12 years following the first commercial sale of a licensed product in such country or the expiration of certain exclusivity rights.

The Roche Agreement will expire upon the last to expire royalty term or, as applicable, the end of the U.S. co-development and profit share arrangement. Additionally, Roche may terminate the agreement for convenience in its entirety or on a product by product or country by country basis subject to certain notice periods. Either party may terminate earlier upon the other party's uncured material breach of the agreement or insolvency. Subject to the terms of the Roche Agreement, effective upon termination of the Roche Agreement, the Company is entitled to retain specified licenses to be able to continue to exploit the Licensed Products.

The Company assessed the Roche Agreement in accordance with ASC 606, *Revenue from Contracts with Customers*, and concluded that Roche is a customer within the context of the agreement. At inception, the Company identified several performance obligations under the agreement, being (i) the combination of the exclusive perpetual license to the Licensed Products and the non-exclusive license to certain companion diagnostics, (ii) the research and development activities related to the completion of the Continuing Trials, as well as (iii) the transfer of clinical trial materials on hand. The Company determined that the exclusive license to the Licensed Products and the non-exclusive license to certain companion diagnostics should be combined into one distinct performance obligation as they were not capable of being distinct from each other within the context of the agreement given both are highly interdependent of each other. The Company determined that the combined licenses, the completion of the Continuing Trials and the transfer of clinical trial materials were all capable of being distinct and were distinct within the context of the Roche Agreement given such activities are independent of each other and Roche could benefit from either separately.

The Company determined that the transaction price at the onset of the agreement is \$134.6 million, being the total non-refundable upfront payment received of \$125.0 million, the additional \$4.0 million payment received and the \$5.6 million received for the transfer of clinical trial materials. Additional consideration is to be paid to the Company upon the achievement of multiple clinical, regulatory and sales milestones. The Company utilized the most likely method approach and concluded that these amounts were constrained based on the probability of achievement. As such, the Company excluded this additional consideration from the transaction price.

The Company has allocated the transaction price of \$134.6 million to each performance obligation based on the relative stand-alone selling price of each performance obligation at inception. The Company has determined the estimated stand-alone selling price at contract inception of the combined licenses by applying a probability adjusted discounted cashflow model which forecasts future cash flows related to the licenses. The Company considered applicable market conditions and relevant entity-specific factors, including those factors contemplated in negotiating the agreement, probability of success, discount rate and the time needed to commercialize a product pursuant to the license. The Company has determined the estimated stand-alone selling price at contract inception of the research and development activities required to complete the Continuing Trials based on internal estimates of the costs to perform the services, inclusive of a reasonable profit margin. Significant inputs used to determine the total costs to complete the Continuing Trials included the length of time required, the internal hours as well as external costs expected to be incurred, the number of patients and the number of clinical and investigator sponsored trials. The Company has determined the stand-alone selling price of the clinical trial materials transferred based on the purchase price from external vendors, without applying a markup as the materials have a built-in margin from the external vendors. Based on the relative stand-alone selling price, the allocation of the transaction price to the separate performance obligations was as follows:

Performance obligation	<u>Transaction price</u> <u>(in thousands)</u>
Combined licenses	\$ 105,327
Completion of Continuing Trials	26,585
Transfer of clinical trial materials	2,714
Total transaction price	<u>\$ 134,626</u>

Revenue associated with the combined licenses was recognized at a point in time upon the transfer of the licenses to Roche on the effective date of the Roche Agreement as the Company concluded that the combined licenses were a functional intellectual property license that Roche could benefit from as of the time of grant. Revenue associated with the completion of the Continuing Trials has been deferred and will be recognized on a proportional performance basis over the period of time to complete the Continuing Trials, being estimated at within 24 months of the effective date, using input-based measurements of total costs of research and development incurred to estimate the proportion performed. Progress towards completion is remeasured at the end of each reporting period. Revenue associated with the transfer of clinical trial materials was recognized at a point in time upon delivery of the clinical trial materials to Roche in the year ended December 31, 2022.

The Company recognized \$116.6 million for the year ended December 31, 2022 as revenue associated with the Roche Agreement, of which \$105.3 million related to the grant of the combined licenses, \$2.7 million related to the clinical trial materials transferred, and \$8.6 million related to the partial recognition of deferred revenue for research and development services performed towards the completion of the Continuing Trials during the period.

As of December 31, 2022, there was \$18.0 million (December 31, 2021 - nil) of deferred revenue related to the Roche Agreement, of which \$15.3 million (December 31, 2021 - nil) was classified as current and \$2.7 million (December 31, 2021 - nil) was classified as non-current in the consolidated balance sheet based on the period the services to complete the Continuing Trials are expected to be performed.

Bristol Myers Squibb

In May 2020, the Company entered into a collaboration and license agreement (the "BMS Agreement") with Bristol-Myers Squibb Company ("Bristol-Myers Squibb"), pursuant to which the Company and Bristol Myers Squibb have agreed to collaborate in the research and development of potential new product candidates for the treatment of cancer. The Company is providing Bristol Myers Squibb access to a selected number of its existing screening campaigns and novel campaigns. The Company is responsible for carrying out early-stage research activities directed to identifying potential targets for potential licensing by Bristol Myers Squibb, in accordance with a mutually agreed upon research plan and will be solely responsible for such costs. The collaboration consists of programs directed to both druggable targets and to targets commonly considered undruggable to traditional small molecule approaches. Upon Bristol Myers Squibb's election to exercise its option to obtain exclusive worldwide licenses for the subsequent development, manufacturing and commercialization of a program, Bristol Myers Squibb will then be solely responsible for all such worldwide activities and costs.

The BMS Agreement was subsequently amended in July, September and November 2020 to include additional campaigns to the list of existing campaigns from which Bristol Myers Squibb may select campaigns under the agreement and to enable unblinding of a Bristol Myers Squibb alliance manager in order to streamline the collaboration and selection process.

Under the terms of the BMS Agreement, Bristol Myers Squibb paid the Company an initial nonrefundable upfront fee payment of \$50.0 million in June 2020. The Company is entitled to receive, on a program-by-program basis, option exercise fees ranging in the low six figures depending on the nature of the applicable program. Bristol Myers Squibb also has the right to retain rights to certain back-up programs in exchange for a one-time payment in the low eight figures per program. The Company is also entitled to receive up to \$301.0 million in total milestones on a program-by-program basis, consisting of \$176.0 million in the aggregate for certain specified research, development and regulatory milestones and \$125.0 million in the aggregate for certain specified commercial milestones. The Company is further entitled to a tiered percentage royalty on annual net sales ranging from high-single digits to low-double digits, subject to certain specified reductions. Royalties are payable by Bristol Myers Squibb on a licensed product-by-licensed product and country-by-country basis until the later of the expiration of the last valid claim covering the licensed product in such country, expiration of all applicable regulatory exclusivities in such country for such licensed product and the tenth anniversary of the first commercial sale of such licensed product in such country.

On a program-by-program basis, prior to the earlier of such program ceasing to be included under the BMS Agreement and expiration of the last to expire royalty term for such program, the Company, alone and with third parties, is prohibited from researching, developing, manufacturing and commercializing products that are directed to the applicable target for such program.

The Company has provided Bristol Myers Squibb with certain, limited rights to first negotiation if the Company determines to divest, license or collaborate with others regarding certain existing programs, including in the event that the Company receives an unsolicited offer to do so. The right of first negotiation expressly excludes any potential change of control transaction, as defined in the agreement.

The collaboration term will expire 42 months after the effective date of the agreement. The BMS Agreement will expire, assuming that Bristol Myers Squibb has exercised at least one option for a program, on a licensed product-by-licensed product and country-by-country basis on expiration of the applicable royalty term and in its entirety upon expiration of the last royalty term. Either party may terminate earlier upon an uncured material breach of the BMS agreement by the other party, or the insolvency of the other party. Additionally, Bristol Myers Squibb may terminate the BMS Agreement for any or no reason on a program-by-program basis upon specified written notice.

The Company assessed the BMS Agreement in accordance with ASC 606, *Revenue from Contracts with Customers*, and concluded that Bristol Myers Squibb is a customer based on the agreement structure. At inception, the Company identified several performance obligations under the BMS Agreement, being (i) research activities for each campaign over the collaboration term, as well as (ii) a selected number of material rights associated with options to obtain exclusive development, manufacturing, and commercial licenses to targets identified. The Company determined that the options to obtain the exclusive development, manufacturing and commercialization licenses were material rights under ASC 606 because there are minimal amounts to be paid to the Company upon exercise of such options.

The Company determined that the transaction price at the onset of the BMS Agreement is the total non-refundable upfront payment received of \$50.0 million. Additional consideration is to be paid to the Company upon the exercise of options to license targets and future milestone payments. The Company utilized the most likely method approach and concluded that these amounts were constrained as they represent option fees and milestone payments that can only be achieved subsequent to option exercises. As such, the Company excluded this additional consideration from the transaction price.

The Company has allocated the transaction price of \$50.0 million to each performance obligation based on the relative stand-alone selling price of each performance obligation at inception, which was determined based on each performance obligation's estimated stand-alone selling price. The Company has determined the estimated stand-alone selling price at contract inception of the research activities based on internal estimates of the costs to perform the services, inclusive of a reasonable profit margin. Significant inputs used to determine the total costs to perform the research activities included the length of time required, the internal hours expected to be incurred on the services and

the number and costs of various studies that will be performed to complete the research plan. The Company determined the estimated stand-alone selling price at contract inception of the material rights associated with options to obtain exclusive licenses to druggable targets and undruggable targets based on the fees Bristol Myers Squibb would pay to exercise these options, the probability-weighted value of expected future cash flows associated with each license related to each target and the probability that these options would be exercised by Bristol Myers Squibb. In developing such estimates, the Company also considered applicable market conditions and relevant entity-specific factors, including those factors contemplated in negotiating the agreement, probability of success and the time needed to commercialize a product candidate pursuant to the associated license. Based on the relative stand-alone selling price, the allocation of the transaction price to the separate performance obligations was as follows:

Performance obligation	Transaction price	
	(in thousands)	
Research activities	\$	6,405
Options to license druggable targets		31,148
Options to license undruggable targets		12,447
Total transaction price	\$	50,000

Revenue associated with the options has been deferred and will be recognized at the point in time when options to license are exercised by Bristol Myers Squibb or upon expiry of such options. Revenue associated with the research activities has been deferred and will be recognized on a proportional performance basis over the period of service for research activities, being the collaboration term, using input-based measurements of total costs of research incurred to estimated proportion performed. Progress towards completion is remeasured at the end of each reporting period.

For the years ended December 31, 2022 and 2021, the Company recognized from deferred revenue \$2.7 million and \$1.1 million, respectively, as revenue associated with the BMS Agreement in relation to research activities performed during the period.

In the fourth quarter of fiscal 2022, Bristol Myers Squibb waived its rights to exercise options for druggable targets directed at two separate lesions. As a result, the Company recognized from deferred revenue \$12.5 million as revenue for the year ended December 31, 2022 with regards to the amount allocated to the performance obligation from Bristol Meyers Squibb. In October 2021, the Company received notification from Bristol Myers Squibb of their option exercise for two druggable targets directed at a single synthetic lethal lesion, pursuant to the terms of the BMS Agreement. As a result, the Company recognized from deferred revenue \$6.5 million as revenue for the year ended December 31, 2021 with regards to the achievement of the performance obligation from Bristol Meyers Squibb and the option fees received.

As of December 31, 2022, there was \$27.4 million (December 31, 2021 - \$42.5 million) of deferred revenue related to the BMS Agreement, of which \$27.4 million (December 31, 2021 - \$2.9 million) was classified as current and nil (December 31, 2021 - \$39.6 million) as non-current in the consolidated balance sheet based on the period the services are expected to be performed and the expected timing of potential option exercises.

Ono

In January 2019, the Company entered into a research services, license and collaboration agreement (the “Ono Agreement”) with Ono Pharmaceutical Co., Ltd. (“Ono”), a Japanese pharmaceutical company, pursuant to which the Company and Ono have agreed to collaborate in the research of potential product candidates targeting Polθ and the development of the Company’s small molecule Polθ inhibitor program. The Company is primarily responsible for carrying out research activities to identify a product candidate, to be licensed to Ono, in accordance with a mutually agreed upon research plan during a research term that will end upon the earlier of the date of the first submission of an Investigational New Drug application (“IND”) in the United States or Japan, or the end of the research term. In the event that Ono elects to collaborate on the subsequent development and commercialization of the proposed product candidate, Ono will be then responsible for such activities in Japan, South Korea, Taiwan, Hong-Kong, Macau and the Association of Southeast Asian Nations (collectively, the “Ono territory”), and the Company will be responsible for all such activities in the rest of the world outside the Ono territory, including the United States, Canada and European Union.

In October 2021, the Company and Ono entered into an amendment to the Ono Agreement whereby the research term, as defined in the Ono Agreement, was extended by one year. In January 2023, the Company and Ono entered into a second amendment to the Ono Agreement whereby the Research Term, as defined in the Ono Agreement, was extended until July 31, 2023.

Under the terms of the Ono Agreement, the Company received non-refundable upfront payments of ¥900 million (\$8.1 million), consisting of an initial upfront fee payment of ¥110 million (\$1.0 million) and an initial upfront research service payment of ¥790 million (\$7.1 million). Additionally, in connection with the research activities to be conducted pursuant to the Ono Agreement, the Company is eligible to receive additional research service payments of up to an aggregate of ¥750 million (\$6.5 million) upon the occurrence of certain specified research triggers. The Company is also entitled to receive clinical, regulatory and commercial milestone payments of up to ¥17.21 billion (\$149.5 million) in the aggregate, plus a tiered percentage royalty on annual net sales in Ono's Territory ranging from high-single digits to low teens, subject to certain specified reductions. All future milestone payments and royalties are payable in U.S. dollars after conversion from Japanese yen at the then applicable rate. Additionally, upon election by Ono to collaborate on the proposed product candidate, Ono shall be responsible for a specified percentage of research and development costs for the IND-enabling studies of the selected product candidate.

The Company assessed the arrangement in accordance with ASC 606 and concluded that Ono is a customer based on the arrangement structure. The Company identified a single performance obligation under the arrangement consisting of the combination of the license to develop and commercialize a selected product candidate targeting Polθ and associated research services.

The Company determined that the license and research services are not distinct within the context of the contract, and the license is the predominant good or service. Accordingly, revenue is recognized in accordance with guidance for licenses, and because the license represents functional IP, it is recognized at the point in time control of the license is transferred.

The Company determined that the transaction price at the onset of the arrangement is the total upfront payments received in the aggregate amount of \$8.1 million which is recorded as deferred revenue. The future milestone payments represent variable consideration that is fully constrained at inception of the arrangement as the achievement of the milestone events are highly uncertain. The Company will reevaluate the likelihood of achievement of the milestones at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price. In October 2021 and December 2022, the Company achieved specified research triggers amounting to ¥100 million (\$0.9 million) and ¥200 million (\$1.5 million), respectively, as research service payments provided for in the Ono Agreement. The ¥200 million (\$1.5 million) is included in the collaboration revenue receivable at December 31, 2022 and was subsequently received in January 2023. These amounts have been added to the transaction price as the consideration was no longer constrained. Should a product candidate be presented for selection in 2023 and Ono exercises its selection option, the Company would be entitled to receive ¥450 million (approximately \$3.4 million) as well as ¥110 million (approximately \$0.9 million) upon corresponding grant of license, for a total of approximately \$4.3 million.

As of December 31, 2022 the Company classified \$10.5 million (December 31, 2021 - \$9.0 million) as current deferred revenue related to the Ono Agreement.

13. Income Taxes

Loss before the provision for income taxes consisted of the following:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Canada	\$ (17,550)	\$ (110,433)
Foreign	\$ 3,650	\$ 1,847
Loss before provision for income taxes	<u>\$ (13,900)</u>	<u>\$ (108,586)</u>

The components of the provision for income taxes are as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Current income tax provision - foreign	\$ 11,527	\$ 530
Deferred income tax benefit - foreign	3,620	(2,208)
Total provision for income taxes	<u>\$ 15,147</u>	<u>\$ (1,678)</u>

A reconciliation between tax expense and the product of accounting income multiplied by the statutory income tax rate is as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Loss before income taxes	\$ (13,900)	\$ (108,586)
Income tax at statutory rate	26.5 %	26.5 %
Computed income tax recovery	(3,684)	(28,775)
Effect on income tax resulting from:		
Federal investment tax credit	(4,899)	(4,093)
Accounting charges not deductible for tax purposes	679	1,078
Capital gain income	(13,956)	—
Equity compensation	3,492	2,220
State taxes	(777)	(37)
Other	(142)	644
Change in valuation allowance	34,434	27,285
Tax (benefit) expense	<u>\$ 15,147</u>	<u>\$ (1,678)</u>

The Company's applicable statutory tax rate is the Canadian combined rate applicable in the jurisdictions in which the Company operates.

As of December 31, 2022, the Company had tax losses of approximately \$158.5 million, which are available to offset future taxable income in Canada. The Company has not recognized the tax benefit of these losses. These losses expire as follows:

	(in thousands)
2042	\$ 45,279
2041	93,834
2040	—
2039	11,394
2038	7,111
2037	883
Total	<u>\$ 158,501</u>

As of December 31, 2022, the Company had Scientific Research and Experimental Development (“SR&ED”) expenditures of approximately \$54.6 million for Canadian federal and Québec purposes, which have not been deducted. These expenditures are available to reduce future taxable income and have an unlimited carryforward period. SR&ED expenditures are subject to verification by the tax authorities and, accordingly, the amounts may vary.

As of December 31, 2022, the Company had non-refundable Canadian federal investment tax credits of approximately \$9.0 million, which may be utilized to reduce Canadian federal income taxes payable. The Company has not

recognized the tax benefits related to the non-refundable investment tax credits. The investment tax credits expire as follows:

	(in thousands)	
2042	\$	2,392
2041		2,253
2040		1,702
2039		1,362
2038		776
2037		455
2036		24
Total	\$	<u>8,964</u>

The Company's deferred tax assets as of December 31, 2022 and 2021 consisted of the following:

	(in thousands)	
	2022	2021
Net operating loss carryforwards	\$ 42,003	\$ 30,093
Net research and development expenditures	14,468	10,656
Share issuance costs	2,369	3,538
Net federal investment tax credits	6,589	4,805
U.S. research and development tax credits	—	1,775
Tax basis of property and equipment in excess of carrying values	(376)	—
Operating lease right-of-use assets	(1,429)	(1,995)
Operating lease liability	1,445	1,950
Accrued expense and other liabilities	785	760
Deferred revenue	14,783	13,656
Share-based compensation	2,492	988
R&D costs capitalized	13,911	—
Total deferred tax assets	<u>97,040</u>	<u>66,226</u>
Valuation allowance	(97,040)	(62,606)
Net deferred tax assets	<u>\$ —</u>	<u>\$ 3,620</u>

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets and has determined that it is more likely than not that the Company will not recognize the benefit of its net deferred tax assets, and as a result, a valuation allowance of \$97.0 million and \$62.6 million has been established at December 31, 2022 and December 31, 2021, respectively.

The Company has incurred net operating losses in Canada since inception and the Company's U.S. subsidiary operated profitably in the United States since its inception. As of December 31, 2021, the Company had U.S. federal and state research and development tax credit carry forwards of \$1.8 million which were utilized in the year ended December 31, 2022.

The Company files income tax returns in Canada and in the United States. In the normal course of business, the Company could be subject to examination by federal and provincial or state jurisdictions, where applicable. There are currently no pending tax examinations. The Company may be subject to tax examination for fiscal years 2017 to 2022 due to unexpired statute of limitation periods.

The calculation of the Company's tax liabilities involves dealing with uncertainties in the application of complex tax laws and regulations for both federal taxes and the provinces and states in which the Company operates or does business in. ASC 740 states that a tax benefit from an uncertain tax position may be recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, on the basis of the technical merits.

The Company records uncertain tax positions as liabilities in accordance with ASC 740 and adjusts these liabilities when the Company's judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from the current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available. As of December 31, 2022 and 2021, no uncertain tax positions have been recorded in the consolidated financial statements.

The Company recognizes interest and penalties related to unrecognized tax benefits on the income tax expense line in the accompanying consolidated statement of operations and comprehensive loss. As of December 31, 2022 and 2021, no accrued interest or penalties are included on the related tax liability line in the consolidated balance sheet.

14. Net Loss per Share

The following table summarizes the computation of basic and diluted net loss per share attributable to common shareholders of the Company:

	Year Ended December 31,	
	2022	2021
	(in thousands, except share and per share data)	
Numerator:		
Net loss	\$ (29,047)	\$ (106,908)
Denominator:		
Weighted-average number of common shares outstanding—basic and diluted	41,922,042	37,818,115
Net loss per share—basic and diluted	\$ (0.69)	\$ (2.83)

The Company's potentially dilutive securities, which include stock options and shares issued under the ESPP, have been excluded from the computation of diluted net loss per share attributable to common shareholders as the effect would be to reduce the net loss per share attributable to common shareholders. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common shareholders is the same.

The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common shareholders for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2022	2021
Options to purchase common shares	8,032,902	5,322,591
Estimated shares issuable under the ESPP	47,216	9,654

15. Government Assistance

The Company incurred research and development expenditures which are eligible for refundable investment tax credits. The refundable investment tax credits recorded are based on management's estimates of amounts expected to be recovered and are subject to audit by the taxation authorities. These amounts have been recorded as a reduction of research and development expenditures in the amounts of \$1.4 million, and \$1.1 million for the years ended December 31, 2022 and 2021, respectively.

16. Commitments and Contingencies

The following table summarizes the Company's commitments to settle contractual obligations at December 31, 2022, other than leases which are recognized as operating lease liabilities in the consolidated balance sheet.

Year Ending December 31,		(in thousands)
2023	\$	3,090
2024		3,106
2025		32
2026		56
2027		32
Following years		63
Total	\$	6,379

The commitment amounts in the table above are associated with contracts that are enforceable and legally binding and that specify all significant terms, including fixed or minimum services to be used, fixed, minimum or variable price provisions, and the approximate timing of the actions under the contracts.

Collaboration and Research Agreements

Collaboration and research agreement obligations primarily relate to a strategic collaboration agreement that was entered into with the University of Texas M. D. Anderson Cancer Center ("MDACC") in March 2020. The collaboration consists of preclinical studies and clinical trials designed by the Company and MDACC with the research to be completed by MDACC. The Company has agreed to commit \$10.0 million in funding for various studies over a period of five years, of which \$5.4 million was paid as of December 31, 2022.

The Company entered into an agreement with the Broad Institute, Inc. ("Broad"), in July 2022, under which Broad will perform specialty screening services at the Company's request over the course of a three-year term in exchange for payments of \$0.8 million per year, beginning in July 2022, totaling \$2.3 million in the aggregate.

Purchase and Other Obligations

In the normal course of business, the Company enters into contracts with Contract Research Organizations ("CROs") and other third parties for preclinical studies and clinical trials, research and development supplies and other testing and manufacturing services. These contracts generally do not contain minimum purchase commitments and provide for termination on 30 to 90 days' prior written notice, and therefore are cancellable contracts. These payments are not included in the table above as the amount and timing of such payments are not known as of December 31, 2022.

The Company has further entered into license agreements under which it is obligated to make milestone and royalty payments and incur annual maintenance fees. The future milestone or royalty payments under these agreements have not been included in the table above since the payment obligations are contingent upon future events, such as achieving certain clinical and commercial milestones or generating product sales. As of December 31, 2022, the Company is unable to estimate the timing or likelihood of achieving these clinical and commercial milestones or generating future product sales (see Note 7).

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date,

the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any indemnification arrangements that could have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in these consolidated financial statements as at December 31, 2022.

17. Currency Risk

The Company is exposed to the financial risk related to the fluctuation of foreign exchange rates and the degree of volatility of those rates. The foreign currency risk is limited to the portion of the Company's business transactions denominated in currency other than U.S. dollars.

The Company incurs a portion of its expenses in Canadian dollars, as well as other currencies to a lesser extent. A change in the currency exchange rates between the U.S. dollars relative to the Canadian dollar could have a significant effect on the Company's consolidated results of operations, financial position, or cash flows. The Company does not enter into arrangements to hedge its currency risk exposure, although it maintains expected Canadian dollar cash requirements in Canadian dollars to form a natural hedge.

The Company is exposed to currency risk through its cash, other receivables, accounts payable, accrued expenses and other current liabilities, as well as right-of-use lease liabilities denominated in Canadian dollars as follows:

	December 31,	
	2022	2021
	(in thousands)	
Cash	\$ 1,904	\$ 3,583
Research and development tax credits receivable	—	3,261
Other receivables	851	745
Accounts payable	(324)	(665)
Accrued expenses and other current liabilities	(2,289)	(2,116)
Lease liabilities	(4,392)	(5,564)
Net financial position exposure	<u>\$ (4,250)</u>	<u>\$ (756)</u>

Based on the above net exposure at December 31, 2022, and assuming that all other variables remain constant, a 10% depreciation of the U.S. dollar against the Canadian dollar would result in an increase of \$0.3 million in the Company's net loss for the year ended December 31, 2022.

The Company is also exposed to currency risk through the Ono Agreement as the Company has a collaboration revenue receivable balance as of December 31, 2022, and any future payments receivable under the Ono Agreement, if any, are denominated in Japanese yen.

18. Geographic Information

The Company's property and equipment, net by location was as follows:

	December 31,	
	2022	2021
	(in thousands)	
Canada	\$ 2,888	\$ 3,675
United States	1,340	1,929
Total property and equipment, net	<u>\$ 4,228</u>	<u>\$ 5,604</u>

The Company's right-of-use assets by location were as follows:

	December 31,	
	2022	2021
	(in thousands)	
Canada	\$ 3,578	\$ 4,939
United States	1,793	2,552
Total right-of-use assets, net	\$ 5,371	\$ 7,491

For the year ended December 31, 2022 the Canadian parent company recognized revenue under its collaboration agreements of \$15.2 million (2021 - \$7.6 million) with Bristol Myers Squibb, whose headquarters are located in the United States, and \$116.6 million (2021 - nil) with Roche, whose headquarters are located in Switzerland.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.**Evaluation of Disclosure Controls and Procedures**

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, no evaluation of controls and procedures can provide absolute assurance that all control issues and misstatements due to error or fraud may occur and not be, if any, have been detected.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, conducted an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2022 based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) (2013 framework). This evaluation included review of the documentation of controls, evaluation of the design effectiveness of controls, testing of the operating effectiveness of controls and a conclusion on this evaluation. Based on the results of its assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

This Annual Report does not include an attestation report of our independent registered public accounting firm regarding the effectiveness of our internal control over financial reporting due to our exemption as a smaller reporting company. Management's report was not subject to audit by the Company's registered public accounting firm pursuant to rules of the Securities and Exchange Commission that permit the Company to provide only management's report in this Annual Report.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the last fiscal quarter of 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item is incorporated by reference to the information set forth in the sections titled “Information about Our Board of Directors” and “Information about Our Executive Officers”, “Corporate Governance, “Delinquent Section 16(a) Reports”, and “Corporate Governance – Committees of the Board of Directors” in our definitive proxy statement to be filed with the SEC on Schedule 14A in connection with our 2023 Annual Meeting of Shareholders, or the Proxy Statement, which is expected to be filed no later than 120 days after December 31, 2022.

Our board of directors has adopted the Repare Therapeutics Inc. Code of Business Conduct and Ethics that applies to all officers, directors and employees. This includes our principal executive officer, principal financial officer and principal accounting officer or controller or persons performing similar functions. The nominating and corporate governance committee is responsible for overseeing the Code of Business Conduct and Ethics and must approve any waivers of the Code of Ethics for our employees, executive officers and directors. The Code of Business Conduct and Ethics is available on our website at ir.reparerx.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to the principal executive officer, principal financial officer and principal accounting officer or controller or persons performing similar functions, we will promptly disclose the nature of the amendment or waiver on our website. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K, and you should not consider information on our website to be part of this Annual Report on Form 10-K.

Item 11. Executive Compensation.

Information required by the items is incorporated by reference to the information set forth in the sections titled “Executive Compensation” and “Director Compensation” in the Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item is incorporated by reference to the information set forth in the sections titled “Securities Authorized for Issuance Under Equity Compensation Plans” and “Security Ownership of Certain Beneficial Owners and Management” in the Proxy Statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information required by this item is incorporated by reference to the information set forth in the sections titled “Information Regarding the Board of Directors and Corporate Governance – Independence of the Board of Directors” and “Transactions with Related Persons” in the Proxy Statement.

Item 14. Principal Accounting Fees and Services.

Information required by this item is incorporated by reference to the information set forth in the section titled “Independent Registered Public Accounting Firm Fees and Services” in the Proxy Statement.

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as a part of this Annual Report:

(1) Consolidated Financial Statements;

Our Consolidated Financial Statements are listed in the “Index to Consolidated Financial Statements” under Part II, Item 8 of this Annual Report.

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes herein.

(3) Exhibits:

The documents listed in the following Exhibit Index of this Annual Report are incorporated by reference or are filed with this Annual Report on Form 10-K, in each case as indicated therein (numbered in accordance with Item 601 of Regulation S-K).

Exhibit Index

Exhibit Number	Description	Incorporated by Reference			
		Schedule Form	File Number	Exhibit	Filing Date
3.1	Articles of Continuance of Repare Therapeutics Inc.	8-K	001-39335	3.1	June 23, 2020
3.2	Amended and Restated Bylaws of Repare Therapeutics Inc.	8-K	001-39335	3.2	June 23, 2020
4.1	Form of Common Share Certificate of the registrant.	S-1	333-238822	4.1	June 15, 2020
4.2	Amended and Restated Registration Rights Agreement, by and among the registrant and certain of its shareholders, dated September 3, 2019.	S-1	333-238822	4.2	May 29, 2020
4.3	Warrant Agreement by and between the registrant and BMS Strategic Portfolio Investments Holdings, Inc., dated May 26, 2020.	S-1	333-238822	4.3	May 29, 2020
4.4	Description of Registrant's Securities.	10-K	001-39335	4.4	March 4, 2021
10.1+	Repare Therapeutics Inc. Amended and Restated Option Plan.	S-1	333-238822	10.1	May 29, 2020
10.2+	Form of Option Agreement under the Repare Therapeutics Inc. Amended and Restated Option Plan.	S-1	333-238822	10.2	May 29, 2020
10.3+	Form of 2020 Equity Incentive Plan.	S-1	333-238822	10.3	June 15, 2020
10.4+	Form of Share Option Grant Notice and Share Option Agreement under the 2020 Equity Incentive Plan.	S-1	333-238822	10.4	June 15, 2020
10.5+	Form of Restricted Share Unit Grant Notice and Restricted Share Unit Award Agreement under the 2020 Equity Incentive Plan.	S-1	333-238822	10.5	June 15, 2020
10.6+	Form of 2020 Employee Share Purchase Plan.	S-1	333-238822	10.6	June 15, 2020
10.7+	Form of Indemnity Agreement by and between the registrant and its directors and officers.	S-1	333-238822	10.7	June 15, 2020
10.8+	Employment Agreement between the registrant and Lloyd M. Segal, dated June 12, 2020.	S-1	333-238822	10.8	June 15, 2020
10.9+	Employment Agreement between the registrant and Michael Zinda, dated June 12, 2020.	S-1	333-238822	10.9	June 15, 2020
10.10	Employment Agreement between the registrant and Maria Koehler, dated June 12, 2020.	S-1	333-238822	10.10	June 15, 2020

10.11	<u>Employment Agreement between the registrant and Steve Forte, dated June 12, 2020.</u>	10-K	001-39335	10.11	March 1, 2022
10.12++	<u>Lease Agreement by and between the registrant and NEOMED Institute, dated November 26, 2019, as amended June 5, 2020.</u>	S-1	333-238822	10.14	June 15, 2020
10.13†	<u>Research Services, License and Collaboration Agreement by and between the registrant and Ono Pharmaceutical Co., Ltd., dated January 31, 2019.</u>	S-1	333-238822	10.15	May 29, 2020
10.14†	<u>Amended and Restated License Agreement by and between the registrant and New York University, dated July 9, 2018.</u>	S-1	333-238822	10.16	May 29, 2020
10.15†	<u>Collaboration and License Agreement by and between the registrant, Repare Therapeutics USA Inc. and Bristol-Myers Squibb Company, dated May 26, 2020.</u>	S-1	333-238822	10.17	May 29, 2020
10.16†	<u>First Amendment to Collaboration and License Agreement by and between the registrant, Repare Therapeutics USA Inc. and Bristol-Myers Squibb Company, dated July 22, 2020.</u>	10-Q	001-39335	10.1	August 13, 2020
10.17	<u>Second Amendment to Collaboration and License Agreement by and between the registrant, Repare Therapeutics USA Inc. and Bristol-Myers Squibb Company, dated September 24, 2020.</u>	10-Q	333-238822	10.1	November 12, 2020
10.18	<u>Second Amendment to Lease Agreement by and between the registrant, the registrant and NEOMED Institute, dated June 11, 2020.</u>	10-Q	333-238822	10.2	November 12, 2020
10.19†	<u>Third Amendment to Collaboration and License Agreement by and between the registrant, Repare Therapeutics USA Inc. and Bristol-Myers Squibb Company, dated November 20, 2020.</u>	10-K	001-39335	10.20	March 4, 2021
10.20++	<u>Addendum to Lease Agreement by and between the registrant, Repare Therapeutics Inc. and NEOMED Institute, dated June 1, 2021.</u>	10-Q	001-39335	10.1	August 12, 2021
10.21++	<u>Third Amendment to Lease Agreement by and between the registrant, Repare Therapeutics Inc. and NEOMED Institute, dated June 1, 2021.</u>	10-Q	001-39335	10.2	August 12, 2021
10.22	<u>Fourth Amendment to Lease Agreement by and between the registrant, Repare Therapeutics Inc. and The Manufacturers Life Insurance Company, dated June 22, 2021.</u>	10-Q	001-39335	10.3	August 12, 2021

10.23++	<u>Lease Agreement by and between the registrant, Repare Therapeutics Inc. and RREEF America REIT II Corp. PPP, dated July 31, 2021.</u>	10-Q	001-39335	10.4	August 12, 2021
10.24	<u>First Amendment to Research Services, License and Collaboration Agreement by and between the registrant and Ono Pharmaceutical Co., Ltd., dated October 29, 2021.</u>	10-Q	001-39335	10.1	August 12, 2021
10.25	<u>Fifth Amendment to Lease Agreement by and between the registrant, Repare Therapeutics Inc. and The Manufacturers Life Insurance Company, dated January 17, 2022.</u>	10-K	001-39335	10.27	March 1, 2022
10.26	<u>Commencement Date Memorandum to the Lease Agreement by and between the registrant, Repare Therapeutics Inc. and RREF America REIT II Corp. PPP, dated February 25, 2022.</u>	10-K	001-39335	10.28	March 1, 2022
10.27	<u>Collaboration and License Agreement by and between the registrant, Repare Therapeutics Inc. and Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd. dated June 1, 2022.</u>	10-Q	001-39335	10.1	August 4, 2022
10.28	<u>Common Shares Sales Agreement, dated August 4, 2022, by and between and between Repare Therapeutics Inc. and Cowen and Company, LLC.</u>	10-Q	001-39335	10.2	August 4, 2022
10.29	<u>First Amendment to Collaboration and License Agreement by and between the registrant, Repare Therapeutics Inc. and Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd. dated October 7, 2022.</u>	10-Q	001-39335	10.1	November 9, 2022
10.30	<u>Second Amendment to Collaboration and License Agreement by and between the registrant, Repare Therapeutics Inc. and Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd. dated October 7, 2022.</u>	10-Q	001-39335	10.2	November 9, 2022
10.31*	<u>Lease Amending Agreement by and between the registrant, Repare Therapeutics Inc. and NEOMED Institute, dated October 27, 2022.</u>				
10.32*++	<u>Lease Agreement by and between the registrant, Repare Therapeutics Inc. and NEOMED Institute, dated January 1, 2023.</u>				
10.33*†	<u>Second Amendment to Research Services, License and Collaboration Agreement by and between the registrant, Repare Therapeutics Inc. and Ono Pharmaceutical, Ltd., dated January 31, 2023.</u>				
21.1	<u>Subsidiaries of the registrant.</u>	S-1	333-238822	21.1	May 29, 2020

23.1*	Consent of Ernst & Young LLP, an Independent Registered Public Accounting Firm.
24.1*	Power of Attorney (incorporated by reference to the signature pages of this Annual Report on Form 10-K).
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Inline Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

* Filed herewith.

** This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

† Certain portions of this exhibit (indicated by asterisks) have been omitted because they are not material and would likely cause competitive harm to Repare Therapeutics Inc. if publicly disclosed.

+ Indicates management contract or compensatory plan.

++ Certain schedules and exhibits to this exhibit have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the SEC upon request.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

REPARE THERAPEUTICS INC.

Date: February 28, 2023

By: /s/ Lloyd M. Segal
Lloyd M. Segal
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Lloyd Segal and Steve Forte, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the U.S. Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and either of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Lloyd M. Segal</u> Lloyd M. Segal	President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	February 28, 2023
<u>/s/ Steve Forte</u> Steve Forte	Executive Vice President, Chief Financial Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	February 28, 2023
<u>/s/ Thomas Civik</u> Thomas Civik	Chair of the Board of Directors	February 28, 2023
<u>/s/ David Bonita, M.D.</u> David Bonita, M.D.	Director	February 28, 2023
<u>/s/ Jerel Davis, Ph.D.</u> Jerel Davis, Ph.D.	Director	February 28, 2023
<u>/s/ Todd Foley</u> Todd Foley	Director	February 28, 2023
<u>/s/ Samarth Kulkarni, Ph.D.</u> Samarth Kulkarni, Ph.D.	Director	February 28, 2023
<u>/s/ Briggs Morrison, M.D.</u> Briggs Morrison, M.D.	Director	February 28, 2023
<u>/s/ Ann D. Rhoads</u> Ann D. Rhoads	Director	February 28, 2023
<u>/s/ Carol A. Schafer</u> Carol A. Schafer	Director	February 28, 2023

LEASE AMENDING AGREEMENT

THIS AGREEMENT is entered into in the city of Montreal (Quebec) as of this October 27th, 2022 (the "**Effective Date**").

BY AND BETWEEN: **NEOMED INSTITUTE**, a corporation governed by the *Canada Not-for-profit Corporations Act*, having its principal place of business at 7171, Frederick-Banting, City of Montreal, Province of Quebec, H4S 1Z9, herein acting and represented by Matthew Carlyle, Chief Financial Officer, duly authorized as he so declares;
(Hereinafter referred to as the "**Lessor**")

AND: **REPARE THERAPEUTICS** a legal person duly incorporated under the Business Corporations Act (Québec), with its head office at 7210, Frederick-Banting, Suite #100, in the City of Montreal, judicial district of Montreal, Province of Quebec, Canada H4S 2A1 herein acting and represented by Christopher Kendall, VP Finance and FP&A, duly authorized as he so declares;

(Hereinafter referred to as the "**Lessee**" and collectively with the Lessor the "**Parties**")

WHEREAS:

A. By a lease agreement dated November 1st, 2020 (the "**Original Lease**") between the Lessor and the Lessee, the Lessee leased for and during a term of twenty-four (24) months terminating on October 31st, 2022 (the "**Initial Term**"), for various premises (the "**Leased Premises**") comprising a total rentable area of approximately two thousand, one hundred, thirty (2,130) square feet of the Building known as NEOMED INSTITUTE located at 7171, Frederick-Banting, City of Montreal, Province of Quebec, H4S 1Z9, as more particularly set out in the Original Lease.

B. By an addendum to the Original Lease signed on June 1st, 2021 (the "**First Addendum**") between the Lessor and the Lessee, the Lessee leased additional space to the Leased Premises for a total of approximately two thousand, five hundred, sixty-eight (2,568) square feet of the Building known as NEOMED INSTITUTE located at 7171, Frederick-Banting, City of Montreal, Province of Quebec, H4S 1Z9, as more particularly set out in the Original Lease.

C. By an addendum to the Original Lease signed on October 1st, 2021 (the "**Second Addendum**") between the Lessor and the Lessee, the Lessee leased additional space to the Leased Premises for a total of approximately two thousand, eight hundred, thirty-two (2,832) square feet of the Building known as NEOMED INSTITUTE located at 7171, Frederick-Banting, City of Montreal, Province of Quebec, H4S 1Z9, as more particularly set out in the Original Lease.

D. The Original Lease and the Addendums are hereinafter collectively known as the "**Lease**".

E. The Initial Term and the Extended Term are hereinafter collectively known as the "**Term**".

F. The Parties have agreed to amend the Lease as more particularly set out herein.

NOW THEREFORE, in consideration of the covenants, rights and obligations contained in this Agreement, the Parties hereto agree as follows:

1. PREAMBLE

The preamble shall form an integral part hereof, as if recited at length.

2. AMENDMENTS TO LEASE

- (a) Section 2 of Schedule A of the Lease is modified such that each termination date is deleted and replaced by December 31st, 2022, and each period is increased by two months.

3. GENERAL PROVISIONS

- (a) The Parties confirm that the Lease is in full force and effect, as modified by this Lease Amending Agreement.
- (b) All capitalized terms and expressions used in this Lease Amending Agreement have the same meaning as in the Lease, unless a contrary intention is expressed in this Lease Amending Agreement.
- (c) This Lease Amending Agreement shall enure to the benefit of the Parties hereto and their respective heirs, executors, administrators, successors and assigns.
- (d) The Parties hereby acknowledge and agree that the execution hereof may be communicated by electronic transmission and that such agreement shall be deemed to be an original hereof, and shall be legal and binding upon the Parties hereto. This Lease Amending Agreement may be executed by counterparts each of which will be deemed to be an original and all of which taken together will be deemed to constitute one and the same instrument.

BALANCE OF THIS PAGE LEFT INTENTIONALLY BLANK SEE NEXT PAGE FOR SIGNATURES

IN WITNESS WHEREOF, each of the parties has caused this Agreement to be executed on the date indicated hereinabove.

(Lessor) **NEOMED INSTITUTE**

/s/ Matthew Carlyle

By: Matthew Carlyle, CFO

(Lessee) **REPARE THERAPEUTICS INC.**

7210, Frederick-Banting
Suite #100
Montreal (Quebec)
H4S 2A1

/s/ Christopher Kendall

By: Christopher Kendall,
VP Finance and FP&A

AGREEMENT OF LEASE

MADE AND ENTERED INTO IN THE CITY OF MONTREAL, PROVINCE OF QUEBEC, THIS 1st DAY OF JANUARY 2023.

BY AND BETWEEN: **NEOMED INSTITUTE**, a corporation governed by the *Canada Not-for-profit Corporations Act*, having its principal place of business at 7171, Frederick-Banting, City of Montreal, Province of Quebec, H4S 1Z9, herein acting and represented by Matthew Carlyle, CFO, duly authorized as he so declares;

LESSOR

AND: **REPARE THERAPEUTICS INC.**, Business Corporations Act (Québec), with its head office at 7210, Frederick-Banting, Suite #100, in the City of Montreal, judicial district of Montreal, Province of Quebec, Canada H4S 2A1 herein acting and represented by Christopher Kendall, VP Finance and FP&A, duly authorized as he so declares;

LESSEE

WHICH HAVE ENTERED INTO THE FOLLOWING LEASE AGREEMENT:

ARTICLE I
DEFINITIONS

The following expressions wherever used herein shall have the following meanings:

1.1 "**ADDITIONAL RENT**" means the additional rent payable by the Lessee pursuant to the provisions of Section 3.2 herein, as well as all sums of money which are required to be paid by the Lessee pursuant to the provisions of this Lease other than the Base Rent.

1.2 "**BASE RENT**" means the base rent payable by the Lessee pursuant to the provisions of Section 3.1 herein.

1.3 "**BUILDING**" means the building known and designated as Neomed Institute located at 7171, Frederick-Banting, City of Montreal, Province of Quebec, H4S 1Z9.

1.4 "**BUSINESS DAY**" means any day other than Saturday, Sunday or legal holidays in the Province of Quebec.

1.5 "**BUSINESS HOURS**" means from 7h00 to 19h00, Montreal time, Monday to Friday.

1.6 "**ENVIRONMENTAL LAWS**" means all legally binding laws, regulations, by-laws, orders, approvals, notices, permits and directives of a governmental authority having jurisdiction over the Property or the nature of the business of the Lessee, relating to the environment, public health and safety.

1.7 "**INTEREST RATE**" means five percent (5%) per annum in excess of the prime interest rate to be charged from time to time by Bank of Montreal for commercial demand loans in Canada in Canadian funds granted to its most creditworthy borrowers, compounded monthly and reckoned from their respective due dates.

1.8 "**LEASE**" means the present Lease Agreement.

1.9 "**LEASED PREMISES**" means and comprises the premises having a total rentable square footage of three thousand four hundred and forty-five (3 445) square feet situated in the Building located on the Property, as shown on Schedule "B" and "F" attached hereto, together with 10 parking spaces, of which one parking space shall be reserved in the front parking spaces of the NEOMED INSTITUTE.

1.10 "**LESSEE**" means Repare Therapeutics Inc., its permitted successors and assigns.

1.11 "**LESSEE'S PROPORTIONATE SHARE**" is established at seven Percent (7,0%) and means the fraction having as its numerator, the rentable square footage of the Leased Premises, and as its denominator, the rentable square footage of the Building, including the rentable area of the Leased Premises, which is deemed to be 49 220 rentable square feet.

1.12 "**LESSOR**" means Neomed Institute, its successors and assigns.

1.13 "**LESSOR'S REPAIRS**" means the maintenance, repairs and replacements to (i) the structural elements of the Building, (ii) the roof of the Building, including the roof membrane, (iii) the exterior walls of the Building, (iv) the foundation of the Building (including footings and floor slab) (v) the exterior utility equipment, and (vi) repairs or restoration necessitated by a casualty (such as fire, flood or vandalism), unless any such repairs are required due to the negligence or fault of the Lessee.

1.14 "**LESSOR'S WORK**" has the meaning provided therefor at Section 4.1.

1.15 "**OPERATING EXPENSES**" means all costs, charges, impositions, expenses and outlays incurred by the Lessor in connection with the ownership, operation, maintenance, repair, renovation, replacement, insuring, management or administration of the Property and any and all installations, systems and equipment thereof. By way of example only, but without limiting the generality of the foregoing, Operating Expenses shall include all of Lessor's costs of maintaining the Property in a good and proper state of upkeep and repair as a prudent owner would do, including, without limiting the generality of the foregoing, the cost of all repairs, renovations, demisements, alterations, improvements and replacements effected in respect of the Property, including minor roof repairs, except for structural repairs, repairs to the foundations of any buildings, footings and floor slab, all other Lessor's Repairs mentioned in Section 1.14 herein, but including all snow removal and landscaping, the cost of labour, materials, services (inclusive of utilities and all applicable taxes thereto) attributable to common areas and facilities of the Property (excluding any part of such costs charged separately to lessees), utility taxes, insurance premiums and other insurance costs, deductible payments, administrative costs directly related to the operation of the Property, and all salaries, benefits and contributions in respect of the employees and other personnel engaged for the Property, any and all security services (if any), the cost of any modification, modernization, improvement or addition to the Property or to any equipment or installations or service therein or thereon, where same is required by law or where it is for the benefit or safety of the users of the Property, all reasonable expenses incurred by the Lessor in obtaining or attempting to obtain a reduction of Property Taxes, any taxes which are in

whole or in part computed as a function of the capital employed in respect of the Property, levied upon the Lessor as owner of the Property, whether characterized as a tax on capital or large corporations tax, and an annual management fee equal to Fifteen percent (15%) of the applicable annual Additional Rent. In regard to capital and/or structural repairs or replacements to the Building or the systems thereof, the cost of such repair or replacement shall be amortized over its useful life in accordance with generally accepted accounting principles and charged to Lessee hereunder. Furthermore, Operating Expenses includes all costs, charges, impositions, expenses and outlays incurred by the Lessor in connection with the utilities provided in the Building, the common facilities and the Leased Premises, including, but not limited to, electricity, heating and air conditioning, natural gas, reverse osmosis purified water and vacuum system in the laboratories.

The following costs shall be excluded or deducted, as the case may be, from the Operating Expenses and the Lessee shall not be required to pay:

- i) costs related to financing or refinancing of the Property, including payments of interest on Lessor's debt;
 - ii) any expense incurred by the Lessor for the exclusive benefit of any other lessee of the Property; or in connection with services or other benefits of a type which are not provided to Lessee but which are provided to another lessee or occupant or in connection with the leasing of space in the Property, including brokers fees or commission, legal fees and expenses, marketing and promotion costs, any lessee inducements, the cost of lease take-overs, the cost of market studies and any other fees and expenses of a similar nature;
 - iii) any costs related to the acquisition of the Property;
 - iv) any reserve for bad debt or other loss of rentals;
 - v) any costs or expenses attributable to any latent defect or construction defect in the Property or costs incurred in connection with repairs, alterations, additions, improvements, or replacements made to rectify or correct any defect in the design, materials, or workmanship of the Property;
 - vi) the cost of any work which is paid for by a person other than the Lessor under a warranty obligation owed to the Lessor by such third party;
 - vii) costs of alterations of other lessee's spaces, whether for initial occupancy or thereafter;
 - viii) costs of selling, syndicating, mortgaging, or hypothecating any of Lessor's interest in the Property;
 - ix) costs incurred in connection with any disputes, including, but not limited to, any disputes between Lessor and its employees, between Lessor and property management, or between Lessor and other lessees or prospective lessees or occupants; and
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- x) interest, fines, late fees, collection costs, legal fees, or penalties assessed as a result of Lessor's failure to make payments in a timely manner or to comply with applicable laws, including regarding the payment of taxes, or to comply with the terms of any lease, hypothec, deed of trust, ground lease, private restriction, or other agreement, except in each case where such failure of the Lessor results from the failure of the Lessee to timely comply with its obligations under this Lease.

1.16 "**PARKING AREA**" means the area adjacent to the Leased Premises shown cross-hatched in blue on Schedule "C" attached hereto which is to be used as provided for in Article 12.1 of this Lease.

1.17 "**PROPERTY**" means:

A certain emplacement fronting on Frederick-Banting Street in the Borough of Saint-Laurent, City of Montreal, Province of Quebec, known and designated as being Lot ONE MILLION ONE HUNDRED SIXTY-THREE THOUSAND SEVEN HUNDRED NINETY-SIX (1 163 796) of the Cadastre of Quebec, Registration Division of Montreal, together with the Building (as defined above) and any other improvements thereon erected and the parking facilities serving the Building and any other improvements and bearing Civic Number 7171, Frederick-Banting, Borough of Saint-Laurent, City of Montreal, Quebec, H4S 1Z9, as same may be modified from time to time.

1.18 "**PROPERTY TAXES**" means all taxes whether special or general, rates, dues and assessments whatsoever, whether under the provisions of the Charter and by By-laws of the City of Montreal, or the Borough of Saint-Laurent, or of any other competent authority whether municipal, governmental or otherwise now charged or hereafter to be charged upon or in respect of the Property or any part thereof (excepting any income or profit taxes of the Lessor), and including, but not so as to limit the foregoing, all property taxes and assessments whatsoever, all municipal taxes, whether general or special, all local improvement taxes, all business taxes, school taxes, water taxes, garbage taxes, and similar taxes. Provided, however, that Property Taxes shall and does not include any business taxes, water taxes, garbage taxes or any other tax assessed directly to, and paid for by, lessees of the Property and not the Lessor. In addition to the foregoing, Property Taxes shall and does not include any and all charges that are or may be charged by the relevant governmental authority in respect to water consumed by, on or about the Property. If any such mode or method of taxation or charge is altered or varied from that in force at the beginning of the Term or should any such new tax or charge be levied or imposed on the Lessor or should the Lessor be substituted therefor then any such new tax, charge or levy shall be included in Property Taxes. Moreover, for greater certainty, if any Property Taxes are re-assessed, the Lessee's Proportionate Share of such Property Taxes shall be adjusted to take into account such re-assessment.

1.19 "**REMAINDER PROPORTIONATE SHARE**" means the proportion, expressed as a percentage, which when added to the Lessee's Proportionate Share represents One Hundred Percent (100%). For greater certainty, the "Remainder Proportionate Share" is intended to represent the proportion of the rentable area of Building not forming part of the Leased Premises, as comprised from time to time.

1.20 "**RENT**" means the Base Rent and the Additional Rent.

1.21 "**TERM**" means the period of two (2) years and eight (8) months commencing January 1st, 2023 (the "**Commencement Date**") and terminating August 30th, 2025 (the "**Expiration of the Term**"), unless terminated prior thereto under the provisions hereof.

1.22 "**YEAR**" means a calendar year occurring in whole or in part during the Term.

ARTICLE II
GRANT AND NET LEASE INTENT

2.1 The Lessor hereby leases the Leased Premises to the Lessee, hereto present and accepting, for the Term, at the Rent, and subject to the terms and conditions herein set forth. The Lessee acknowledges that the Lease is intended to be a net net net Lease in accordance with the custom and usage prevailing for industrial buildings in the Province of Quebec and accordingly, the Base Rent payable by the Lessee in virtue of these presents shall be completely net net net to the Lessor. The Lessor shall not, be responsible for any costs, expenses, impositions, outlays, or any other disbursements of any nature whatsoever arising from or relating to the Leased Premises, to their use or occupation, their contents or to the business conducted therein, and the Lessee shall be responsible for all of these costs, expenses, outlays, or disbursements to the entire exoneration of the Lessor, unless expressly provided to the contrary herein.

ARTICLE III
RENT

3.1 Subject to Section 3.11 herein, the Lessee binds and obliges itself to pay to the Lessor, in lawful money of Canada, and in addition to any Additional Rent as may be provided for hereunder without deduction, reduction, abatement or set-off whatsoever, and without necessity of any demand therefor, the following (net net net) Base Rent:

- 3.1.1 For the First (1st) year of the Term, commencing January 1st, 2023 and terminating on December 31st, 2023, a Base Rent at the rate of twenty Dollars (\$20,00) per square foot for rooms #2217, 2272, 2208A & 2208B per annum, being a sum of two thousand and eight Dollars and thirty-three Cents (\$2 008,33) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;
 - 3.1.2 For the First (1st) year of the Term, commencing January 1st, 2023 and terminating on December 31st, 2023, a Base Rent at the rate of nine Dollars and twenty-five cents (\$9,25) per square foot for rooms #2215, 2216, 2218, 2219, 2220A & 2220B per annum, being a sum of four hundred and ninety-seven Dollars and ninety-six Cents (\$497,96) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;
 - 3.1.3 For the Second (2nd) year of the Term, commencing January 1st, 2024 and terminating on December 31st, 2024, a Base Rent at the rate of twenty Dollars (\$20,00) per square foot for rooms #2215, 2216, 2217, 2218, 2219, 2272, 2208A, 2208B, 2220A & 2220B per annum, being a sum of three
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thousand and eighty-five Dollars (\$3 085,00) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;

- 3.1.4 For the Third (3rd) year of the Term, commencing January 1st, 2025 and terminating on August 31st, 2025, a Base Rent at the rate of twenty Dollars and sixty Cents (\$20,60) per square foot for rooms #2215, 2216, 2217, 2218, 2219, 2272, 2208A, 2208B, 2220A & 2220B per annum, being a sum of three thousand one hundred and seventy-seven Dollars and fifty-five Cents (\$3 177,55) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;
 - 3.1.5 For the First (1st) and Second (2nd) years of the Term, commencing January 1st, 2023 and terminating on December 31st, 2024, a Base Rent at the rate of nine Dollars and twenty-five cents (\$9,25) per square foot for rooms #1208, 1210 & 2116 per annum, being a sum of five hundred and one Dollars and eighty-one Cents (\$501,81) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;
 - 3.1.6 For the Third (3rd) year of the Term, commencing January 1st, 2025 and terminating on August 31st, 2025, a Base Rent at the rate of nine Dollars and fifty-three cents (\$9,53) per square foot for rooms #1208, 1210 & 2116 per annum, being a sum of five hundred and seventeen Dollars (\$517,00) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;
 - 3.1.7 For the First (1st) and Second (2nd) years of the Term, commencing January 1st, 2023 and terminating on December 31st, 2024, a Base Rent at the rate of twenty-five Dollars (\$25,00) per square foot for rooms #2232, 2232A, 2233, 2243AL, 2243L & 2251 per annum, being a sum of one thousand nine hundred and sixty-four Dollars and fifty-eight Cents (\$1 964,58) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;
 - 3.1.8 For the Third (3rd) year of the Term, commencing January 1st, 2025 and terminating on August 31st, 2025, a Base Rent at the rate of twenty-five Dollars and seventy-five Cents (\$25,75) per square foot for rooms #2232, 2232A, 2233, 2243AL, 2243L & 2251 per annum, being a sum of two thousand and thirty-two Dollars and fifty-two Cents (\$2 032,52) per month, plus applicable taxes in accordance with Section 3.7 herein, payable in advance, without deduction or abatement, by way of equal and consecutive monthly instalments on the first day of each month;
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3.2 During the Term, the Lessee will pay to the Lessor the Rent, in advance, in equal monthly instalments, on the first day of every month during the Term. As such, the Lessee hereby authorizes the Lessor to withdraw, from the account described in Schedule A, every first (1st) day of each month during the Term the monthly instalment of the Rent. The first payment of the Rent will be made on the first day of the Term. If the Term begins on any day other than the first, or ends on any day other than the last, of a calendar month, Rent for the fractions of a month at the beginning and at the end of the Term will be adjusted pro rata, on the basis of the actual number of days in those calendar months.

3.3 Subject to Section 3.12 herein, in addition to the Base Rent, the Lessee binds and obliges itself to pay to the Lessor, in lawful money of Canada, in each year, without deduction, reduction, abatement or set-off whatsoever, and without necessity of any demand therefor, an Additional Rent being the aggregate of:

- 3.3.1 Lessee's Proportionate Share of Property Taxes payable in accordance with the provisions of Section 3.4 below; and
- 3.3.2 Lessee's Proportionate Share of the Operating Expenses for such year in accordance with Section 3.5 below.

The Additional Rent for the First (1st), Second (2nd) & Third (3rd) years of the Term is currently estimated at twenty-nine Dollars and eleven cents (\$29.11) per square foot for rooms ##1208, 1210 & 2116, including the management fee equal to Fifteen percent (15%) of the applicable annual Base Rent.

The Additional Rent for the First (1st), Second (2nd) & Third (3rd) years of the Term is currently estimated at thirty-eight Dollars and nineteen Cents (\$38.19) per square foot for rooms #2232, 2233, 2251, 2232A, 2243AL & 2243L, including the management fee equal to Fifteen percent (15%) of the applicable annual Base Rent.

The Additional Rent for the First (1st), Second (2nd) & Third (3rd) years of the Term is currently estimated at fifty-six Dollars and fifty-nine cents (\$56.59) per square foot for rooms #2217, 2272, 2208A & 2208B, including the management fee equal to Fifteen percent (15%) of the applicable annual Base Rent.

The Additional Rent for the First (1st) year of the Term is currently estimated at fifty Dollars (\$50.00) per square foot for rooms #2215, 2216, 2218, 2219, 2220A & 2220B, including the management fee equal to Fifteen percent (15%) of the applicable annual Base Rent.

The Additional Rent for the Second (2nd) year of the Term is currently estimated at fifty-four Dollars (\$54.00) per square foot for rooms #2215, 2216, 2218, 2219, 2220A & 2220B, including the management fee equal to Fifteen percent (15%) of the applicable annual Base Rent.

The Additional Rent for the Third (3rd) year of the Term is currently estimated at fifty-six Dollars and fifty-nine cents (\$56.59) per square foot for rooms #2215, 2216, 2218, 2219, 2220A & 2220B, including the management fee equal to Fifteen percent (15%) of the applicable annual Base Rent.

The foregoing estimate is provided to the Lessee for indicative purposes only and shall in no way limit, affect or otherwise circumscribe the provisions of this Lease concerning the calculation and payment of Additional Rent, and for greater certainty, it is understood that while the aforesaid

management fee, which is based on applicable annual Base Rent, is determinable in advance, the other elements of Additional Rent are only known as on an *ex post facto* basis.

3.4 Throughout the Term, Lessee shall pay, as Additional Rent, Lessee's Proportionate Share of the Property Taxes as herein below described:

- 3.4.1 On or about the Commencement Date, Lessor shall invoice Lessee for Lessee's Proportionate Share of the Property Taxes for the then current tax year(s) or, should actual bills not yet have been received for such taxation year(s), Lessor shall estimate the amount of the Lessee's Proportionate Share of Property Taxes for the then current taxation year(s) and shall invoice Lessee therefor in equal, consecutive, monthly instalments which Lessee shall pay to Lessor in advance on the first day of each calendar month. When actual bills for all or any portion of the Property Taxes are received, Lessor shall furnish Lessee with a statement setting forth such portion thereof that is payable by Lessee pursuant to this ARTICLE III. If such amount is greater or less than the payments on account thereof theretofore made by Lessee in respect of the applicable period pursuant to this ARTICLE III, appropriate adjustments shall be made forthwith;
- 3.4.2 In addition to Lessee's obligation to pay Lessor's invoices for Property Taxes when the actual bills are received as aforesaid, commencing with the month next following such invoicing Lessee shall make monthly instalments on account of future Property Taxes on the same basis as for the preceding tax year or on the basis of Lessor's revised reasonable estimate, as the case may be, and so on from time to time; and
- 3.4.3 During the first and last years of the Term (in the event same comprise less than complete tax years), the amount Lessee is required to pay on account of Lessee's Proportionate Share of Property Taxes shall be subject to a per diem adjustment.

3.5 Throughout the Term, Lessee shall pay, as Additional Rent, Lessee's Proportionate Share of the Operating Expenses. Prior to the commencement of each Year, or as soon thereafter as reasonably possible, the Lessor shall furnish to the Lessee an estimate of the Lessee's Proportionate Share of Operating Expenses. The Lessee shall pay to the Lessor on the first day of each month in advance during each Year, as Additional Rent, an amount equal to ONE-TWELFTH (1/12) of such estimated Operating Expenses applicable to such Year. Should the first year of the Term not commence on January 1st, or should the last year of the Term not terminate on December 31st, then prior to the commencement of the Term, or of the last year of the Term, as the case may be, or as soon thereafter as is reasonably possible, the Lessor shall furnish the Lessee an estimate of the Lessee's Proportionate Share of Operating Expenses for the part of the Year in question and the Lessee shall pay to the Lessor on the first day of each month in advance during the part of the Year in question, an amount equal to such estimates divided by the number of months during the partial Year in question.

3.6 As soon as is practicable, after the end of each Year, or after the Expiration of the Term in the case the final Year, the Lessor shall furnish the Lessee with a statement indicating the Lessee's Proportionate Share of the actual charges for Operating Expenses incurred for such Year (or part of Year, as the case may be), accompanied by a statement of the Lessor's chartered

accountant confirming such amounts, for such Year (or part of Year, as the case may be). The Lessee shall pay to the Lessor forthwith an amount equal to the excess of such actual charges incurred over the amount theretofore paid by the Lessee for such Year (or part of Year, as the case may be) as Additional Rent on account of Operating Expenses. However, should the total amount paid by the Lessee to the Lessor for such Year (or part of Year, as the case may be) as Additional Rent on account of Operating Expenses exceed the Lessee's Proportionate Share of actual charges incurred for Operating Expenses for such applicable period, the Lessee shall receive a credit, or a reimbursement in the case of the final year, for the excess. The appropriate adjustments shall be made between the parties hereto within thirty (30) days following the date on which the Lessor shall have furnished the Lessee with such statement.

3.7 Any refunds, credits or subsidies of Property Taxes for vacant premises or resulting from reductions of such taxes attributable to there being or having been vacant premises in the Property shall not be deducted from or otherwise reduce Property Taxes and the amounts of any credits (applicable against Property Taxes or other indebtedness) or reductions of such taxes for vacant premises attributable to there being or having been vacant premises on the Property shall be included in Property Taxes, as if such refunds, credits, subsidies or reductions had not been granted, it being the intention of the parties that such refunds, credits, reductions and subsidies shall be for the sole benefit of the Lessor.

3.8 The Lessee undertakes to pay to the Lessor concurrently with the payment in respect of which such taxes are assessed, all goods and services tax (G.S.T.) and Quebec sales taxes (Q.S.T.), and all other goods and services and value added taxes in respect of the Rent, and all other sums payable by the Lessee pursuant to the Lease. Such amounts shall not be considered as forming consideration for the rental of space or the provision by the Lessor of any service under this Lease, but shall be deemed for all other purposes to be Rent and the Lessor shall have all of the same remedies for and rights of recovery of such amounts as it has for the recovery of Rent under this Lease.

3.9 The Lessee agrees that it shall have no right to claim any set off, compensation or deduction in respect of any Rent, or any other sums payable by the Lessee to the Lessor pursuant to the Lease, for any reason whatsoever.

3.10 It is the intention of the parties that the lease of the Leased Premises to the Lessee pursuant to this Lease and the Rent payable by the Lessee hereunder shall be free and clear of all taxes, costs and charges arising from or relating to the Leased Premises and the Lessee shall pay all costs, charges and expenses of every kind and nature regarding the Lessee's operations in the Leased Premises or any part of the Property. For greater certainty, but without limiting the generality of the foregoing, the Lessee shall be responsible for the payment, to the complete exoneration of the Lessor, of all business taxes, if any, relating to the business carried on by the Lessee in the Leased Premises or any other similar replacement taxes and/or rates which may be levied or imposed upon the business carried on in the Leased Premises or which may be payable by the Lessee as occupant thereof, whether so levied or imposed on the Lessee or the Lessor, as well as water taxes or any other tax assessed directly to, and paid for by, tenants of the Building and not the Lessor. If the mode of collecting such taxes be so altered as to make the Lessor liable therefor instead of the Lessee, the Lessee undertakes to reimburse the Lessor the amounts to be paid by the Lessor as Additional Rent on demand.

3.11 The Lessee agrees that should its bank refuse to honour and pay any cheque which the Lessee may have given to the Lessor in respect of any Rent, or any other sums payable by the Lessee to the Lessor pursuant to the Lease, or for any reason whatsoever, then the Lessor shall

have the right to charge the Lessee for a service charge to cover the cost and inconvenience suffered by the Lessor, which the parties hereto fix at Fifty Dollars (\$50.00) for the first cheque which has not been honoured and paid, One Hundred Dollars (\$100.00) for the second cheque which has not been honoured and paid, and One Hundred and Fifty Dollars (\$150.00) for each cheque thereafter which has not been honoured and paid.

3.12 The Lessee's obligation to pay Rent shall survive the expiration or earlier termination of this Lease. Any Rent or other sum received or accepted by the Lessor and paid by anyone other than the Lessee on behalf of the Lessee shall not release or in any way affect the covenants of the Lessee set out in this Lease and shall not be deemed to constitute or evidence the Lessor's consent to a sublease or assignment under ARTICLE VIII herein. Any Rent or other sum received by the Lessor from or for the account of the Lessee while the Lessee is in default under this Lease may be applied at the Lessor's option to the satisfaction in whole or in part of any of the obligations of the Lessee then due under this Lease in such manner as the Lessor sees fit regardless of any designation or instruction of the Lessee to the contrary.

ARTICLE IV
ACCEPTANCE OF LEASED PREMISES

4.1 The Lessee accepts the Leased Premises "as is" and "where is", save only for the Lessor's work, as set out in Schedule "D" attached hereto ("**Lessor's Work**"). The Lessor's Work shall be completed by the Lessor, at its own cost, on or prior to the Commencement Date. The Lessor's Work shall be deemed to be complete on the date that all Lessor's Work has been performed, other than any details of construction, mechanical adjustment or any other similar matter, the non-completion of which does not materially interfere with the performance by Lessee of its work. However, and notwithstanding the foregoing, the Lessor shall not be liable for damages in the event Lessor's Work, if any, in the Leased Premises has not been completed by a particular date, it being understood that this Lease shall remain in full force and effect except that Base Rent and all other sums payable hereunder shall be calculated as and from the date that the Lessor's Work has been substantially completed or would have been substantially completed had the Lessee not delayed the Lessor in the completion of Lessor's Work. The Lessor shall use commercial reasonable efforts to complete the Lessor's Work with all due dispatch prior to the Commencement Date. The Lessee shall allow the Lessor to execute the Lessor's Work during the Fixturing Period (as defined below) without interference.

4.2 The Lessee acknowledges that the Lease is intended to be a net net net lease in which the Lessee is obligated to pay for and maintain the Leased Premises in the manner herein provided.

4.3 Subject to the provisions herein, the Lessee acknowledges having seen and examined the Leased Premises and declares itself to be fully content and satisfied therewith, and save and except for the completion of the Lessor's Work, the Lessee accepts the Property in its present state and condition, "as is" and "where is" and all repairs, renovations, demisements, alterations, improvements and replacements to the Leased Premises (except for Lessor's Repairs) as the Lessee may require from time to time during the Term, including such repairs as may be required or may be deemed advisable or necessary to enable the Lessee to obtain or maintain the permits referred to in Section ARTICLE VII below, shall be performed by the Lessor but at the sole cost and expense of the Lessee for which the Lessor will invoice the cost thereof plus an administration fee of fifteen percent (15%).

ARTICLE V
PLACE OF PAYMENT AND ELECTION OF DOMICILE

5.1The Lessee shall pay the Rent, and all other sums which may be owing by the Lessee to the Lessor pursuant to the Lease, without notice, demand or formality whatsoever, at the office of the Lessor, at 7171, Frederick-Banting, City of Montreal, Province of Quebec, H4S 1Z9, or as directed by the Lessor. All notices to be given to either of the parties hereto pursuant to the Lease shall be in writing and shall be validly given if either delivered personally or sent by prepaid certified mail addressed, in the case of the Lessor, at the above mentioned address, together with a copy to the Attention of Matthew Carlyle, and, to the Lessee, to the Attention: Christopher Kendall at 7210, Frederick-Banting, Suite #100, City of Montreal, Province of Quebec, H4S 2A1. Any such notice, if so mailed, shall be deemed to have been given on the fifth (5th) Business Day following the date of the mailing thereof.

ARTICLE VI
HEATING, AIR-CONDITIONING AND UTILITIES

6.1The Lessor shall be responsible for the heating and air-conditioning of the Leased Premises and for all gas, electricity and other utilities (excluding telephone) consumed in respect of the heating of the Leased Premises and for making necessary arrangements for the supply thereof. The Lessor shall pay directly to all utilities suppliers, including without limitation, Hydro-Quebec and Energir, or to any electric utility, natural gas supplier and supplier of any other utilities or, as the case may be, to their respective succeeding company, for all electricity, gas and other utilities consumed within the Leased Premises, the cost of which shall, for greater certainty, form part of Operating Expenses.

6.2The Lessor shall maintain, repair and from time to time replace the equipment relating to such utilities, the cost of which shall, for greater certainty form part of Operating Expenses.

6.3The Lessor shall heat and air-condition the Leased Premises during Normal Business Hours, excluding holidays to a reasonable degree of temperature during the appropriate seasons, but the Lessee shall hold the Lessor free and harmless from all damages, costs, losses or expenses caused directly or indirectly to the property or operations of the Lessee on the Leased Premises caused from any failure or lack of heat or air-conditioning in the Leased Premises. The Lessor must however maintain the heating and air conditioning equipment in good working order and take necessary measures to repair same when notified by the Lessee.

ARTICLE VII
USE

7.1The Leased Premises shall be used and occupied by the Lessee only for **scientific research, development activities and/or office space in connection thereof including marketing and market development**, the whole in compliance with and in conformity to all applicable governmental rules, regulations and by-laws. The Lessee shall not use the Leased Premises, nor allow the same to be used, for any purpose other than that mentioned above, without receiving the prior written consent of the Lessor, which consent shall not be unreasonably delayed or withheld. The Lessee declares that it has obtained, and shall be solely responsible for obtaining of all necessary permits to enable it to operate in the Leased Premises, and it releases and discharges the Lessor from any and all obligations in respect thereof. Nothing herein shall

be so interpreted as to imply that this Lease is in any way conditional upon the Lessee obtaining any permits or licenses for the exploitation of such business from any municipal, provincial or other authority or that the Leased Premises may otherwise be used for or be suitable for same, the Lessor making no representation and expressly disclaiming any responsibility with respect to same, and the Lessee acknowledging that the risks related to all such matters are being borne exclusively by the Lessee and at own risk and peril. The Lessee agrees and acknowledges that neither it nor any person, firm, corporation, employee, contractor or sub-contractor, whose services are retained by the Lessee, will carry on any activity in, on or about the Leased Premises that would be contrary to or in derogation from any and all federal, provincial or municipal laws, rules, regulations or by-laws including, but not restricted to, all applicable Environmental Laws.

7.2 Notwithstanding any provision to the contrary, the Lessee shall not run any business or use, allow or tolerate the use of the Leased Premises or any part thereof for any activity that in the opinion of the Lessor would tarnish the character, quality or reputation of the Lessor or the Property, or for any fraudulent or immoral practice, or carry out in the Leased Premises any activity that would be dangerous or harmful or would do anything whatsoever that could hinder the peaceable enjoyment of the other lessees or occupants of the Property or make noise or create foul odours that could inconvenience the other lessee or occupants or neighbours, or create or tolerate any losses or damages, alteration or deterioration of the Leased Premises or the Property or overload the floors in such a way as to jeopardize the structure of the Building. The Lessee, shall not, in any manner whatsoever, hold the Lessor liable for any damages or inconveniences that the Lessee may suffer due to the fault or actions of any other lessee or occupant of the Building, and the Lessee expressly waives all claims and recourses it may or could have in respect of the Lessor pursuant to Sections 1859 and 1861 of the Civil Code of Quebec.

ARTICLE VIII
SUB-LEASE AND ASSIGNMENT

8.1 Should the Lessee desire to sub-lease the Leased Premises or any part thereof, or to assign any of its rights under this Lease, then and so often as such event shall occur, the Lessee shall give to the Lessor written notice of such desire accompanied by a copy of the offer to sub-lease, or a copy of the offer to assign, together in all cases with such financial or other information in respect of the proposed sub-lessee or assignee as the Lessor may so request. The Lessor shall, acting reasonably, within thirty (30) days of receiving all the foregoing notify the Lessee in writing either (i) that it consents to such sub-lease or assignment, or (ii) that it does not consent to such sub-lease or assignment, or (iii) that it elects to terminate the Lease as of a date being ninety (90) days following the date of the Lessor's notification to the Lessee. In such latter event, the Lease shall be deemed to have terminated as of the expiration of such ninety (90) day period, unless, within ten (10) days next following the Lessor's notice electing to terminate, the Lessee shall have withdrawn, by way of written notice to such effect to the Lessor, its request to sublease or assign. Where the Lessee shall have withdrawn its request as aforesaid, the Lease shall continue in force unamended. Where any request for sublease or assignment relates to a portion only of the Leased Premises, then, in such a case, where the Lessor shall exercise his option to terminate the present Lease as aforesaid, then the Lease shall be terminated only with respect to that portion of the Leased Premises to which the proposed sublease or assignment related. It is expressly agreed and understood that the rights so conferred to the Lessor have been freely given to the Lessor by the Lessee for valid commercial reasons. Conversely, in such circumstances where the Lessor does not elect to exercise its termination rights pursuant to subparagraph (iii) of the present section, Lessor agrees that in its consent to any request of the Lessee to a sublet or assignment pursuant to the present section shall not be unreasonably withheld, conditioned or delayed.

8.2 Save as stipulated in Section 8.3, if, at any time during the Term, effective control of the Lessee is acquired or exercised by any person(s) or entity(ies) not having effective control of the Lessee on the date of execution of this Lease, whether pursuant to a sale of shares or other transaction or by operation of law, same shall be deemed an assignment of lease and shall be subject to the provisions of Section 8.1.

8.3 Provided that the Lessee is Repare Therapeutics Inc. or a Permitted Transferee (as defined below) thereof, that it is operating its business in the whole Leased Premises in accordance with the terms of this Lease and that it is not in default thereunder (save for a default of minor importance within the meaning of Article 1604 of the Civil Code of Québec), the Lessee will have the right to sublease all or any portion of the Leased Premises and/or to assign the Lease to any entity which (i) is and thereafter remains for the remainder of the Term and any extension or renewal thereof, an affiliate of the Lessee, or of the Lessee's parent company (as "affiliate" and "parent company" are defined in the *Canada Business Corporations Act*) or (ii) the resulting entity following a merger, amalgamation or *bona fide* reorganization of the Lessee pursuant to which such resulting entity is the successor in and to all or substantially all of the Lessee's assets and activities in Canada or (iii) purchases all or substantially all of the Lessee's shares or assets in Canada (each, a "**Permitted Transferee**"), without the Lessor's consent, provided the following conditions are met:

- a) a written notice is given to the Lessor within fifteen (15) days of the effective date of assignment or sublease;
- b) Lessee provides the Lessor with all relevant and reasonable documentation and information the Lessor may ask and that is available, demonstrating that the proposed assignee or sublessee complies with the foregoing conditions;
- c) Lessee and assignee or sublessee execute an agreement with the Lessor, satisfactory to the Lessor, setting forth the terms and conditions of the assignment or sublease;
- d) Lessee provides the Lessor with a copy of any such sublease or assignment to the Permitted Transferee;

The Lessor will not have the right, in the circumstances of such assignment or sublet to a Permitted Transferee, to (i) recapture any portion of the Leased Premises; (ii) to delay the Lessee's subleasing efforts; (iii) sublease the Leased Premises for the Lessee; or (iv) set any other conditions that may serve to interfere with the Lessee's rights to mitigate damages, or otherwise unreasonably inhibit the Lessee's ability to sublease or assign the Lease to such Permitted Transferee.

8.4 Where the Lessor fails to respond to the Lessee's request to an assignment or a sublet, the Lessor shall be deemed to have refused consent.

8.5 In the case of any assignment of this Lease, the assignee must unconditionally and irrevocably assume all of the Lessee's obligations under this Lease. In the case of any sublease granted for all or a portion of the Leased Premises, the sublessee must unconditionally and irrevocably assume all of the Lessee's obligations under this Lease as they apply to the portion of the Leased Premises to be sublet, for the term of such sublease. Notwithstanding the assignment or subletting, the Lessee shall remain solidarily responsible with the assignee or sublessee, without benefit of division or discussion, for the payment of the Rent and the performance of all the other obligations of the Lessee under this Lease. In no case shall an

assignment of this Lease effect novation or release the assigning Lessee from its obligations hereunder, even if the assignment is consented to by the Lessor. At the Lessor's sole option, effective whenever the Lessor gives written notice to such effect to the Lessee and to the assignee or sublessee, as the case may be, and without any further formality, all rentals, sub-rentals and other amounts payable by the assignee or sublessee to the Lessee, shall be irrevocably and unconditionally assigned to the Lessor such that all sums shall be paid directly to the Lessor by the assignee or sublessee and the amount so paid will be credited against the Lessee's Rent under this Lease. It is understood and agreed, however, that if the Lessor does not collect any such rentals, sub-rentals or other amounts from any assignee or sublessee, the Lessee will have no claim or defense against the Lessor in any manner whatsoever.

If this Lease is repudiated, disclaimed, disavowed, resiliated or otherwise terminated by whomsoever in connection with or as a result of the bankruptcy or insolvency of the original Lessee or any assignee or sublessee, the original Lessee and any assignee or sublessee, other than the bankrupt or insolvent person or entity, will enter into a lease upon notice from the Lessor given within sixty (60) days of the Lessor's knowledge of such repudiation, disclaimer, disavowal, resiliation or other termination, for a term expiring on the date this Lease would have expired but for the repudiation, disclaimer, disavowal, resiliation or other termination and upon the terms and conditions which would have applied during the remainder of the Term had this Lease not been repudiated, disclaimed, disavowed, resiliated or otherwise terminated.

8.6 Any assignment of this Lease, agreed to by the Lessor, must be prepared by the Lessor or its attorneys, and all legal fees relating to this assignment must be assumed by the Lessee.

8.7 Lessee hereby waives the provisions of Articles 1871, 1872 and 1873 of the *Civil Code of Quebec* together with the provisions of Article 1870 of the *Civil Code of Quebec*, but in this latter case, only to the extent of any inconsistency with the provisions of the present Lease.

ARTICLE IX
MAINTENANCE, REPAIRS AND ALTERATIONS

9.1 The Lessee shall protect all water, drain and gas pipes, water closets, sinks and accessories thereof, in and about the Leased Premises from all and any damage that the same may be subject to from any cause whatsoever; the Lessee shall keep the same free from all un-cleanliness or obstruction that might prevent the good working of the same. The Lessee shall ensure that the water-closets, sinks, drains and other sanitary conveniences of the Leased Premises shall be used only for those purposes for which each of said facilities were designed, and for no other purpose.

9.2 The Lessee shall deploy all reasonable commercial efforts to ensure that all equipment shall be kept at a sufficient distance from all walls, columns, doors, electrical panels and thermostats and shall further ensure that all exit doors and utility rooms are readily accessible at all times.

9.3 The Lessee shall ensure that it shall not render any portion of the Property in contravention of any of the governmental rules, regulations and by-laws, laws, orders, decisions, ordinances and rulings. The Lessee covenants and agrees to indemnify and hold the Lessor free and harmless from any penalty imposed for, or damages arising from, the breach of any of such rules, regulations and by-laws, laws, orders, decisions, ordinances, rulings by the Lessee or those for whom the Lessee is responsible.

9.4The Lessor, its agents and representatives shall have the right at all reasonable times, upon twenty-four (24) hours' written notice, during the Term to enter the Leased Premises to examine the condition thereof or for any other reasons the Lessor deems necessary, acting reasonably.

9.5The Lessee shall not make any alterations, improvements or additions to the Leased Premises. Any alterations, improvements or additions that may be required by the Lessee shall be performed by the Lessor and its contractors and the costs thereof plus an administration fee of fifteen percent (15%) of the aggregate of such costs shall be charged to Lessee as Additional Rent and shall be paid to the Lessor within ten (10) Business Days of Lessor's demand to that effect.

9.6Should any Lessor's Repairs be deemed necessary at any time during the Term by the Lessor, the Lessor shall make and complete the same with all due diligence, and the Lessee shall permit the same to be performed without demanding any reduction of the Rent, and without any claim for damages or compensation, provided that such repairs be effected and completed with due diligence and in a manner so as to minimize disruption to the Lessee's operations.

9.7The Lessee upon becoming aware of any repairs and maintenance to the Leased Premises, which shall be necessary, shall promptly furnish the Lessor with written notification thereof.

9.8Should any repairs and maintenance to the Leased Premises be required by the fault or negligence of the Lessee or those for whom it is in law responsible, the Lessee shall reimburse the Lessor as Additional Rent the cost of all such Lessor's Repairs plus an administration fee of fifteen percent (15%) of the aggregate of all such costs, within ten (10) Business Days of Lessor's demand to that effect.

9.9The Lessee agrees that should any alarm (including, but not limited to, fire alarm, any sprinkler alarm or the sprinkler system) within the Leased Premises go off due to the fault or negligence of the Lessee, then the Lessee shall be responsible for, and shall indemnify and reimburse the Lessor for, all costs, expenses, fines, charges or otherwise resulting therefrom.

9.10Upon Expiration or earlier termination of the Lease, the Lessee shall surrender vacant possession of the Leased Premises to the Lessor in good condition, reasonable wear and tear only excepted, in clean broom-swept condition, free of all effects of the Lessee.

ARTICLE X
GARBAGE REMOVAL AND EXTERMINATORS

10.1The Lessee shall not place or leave, or permit to be placed or left, in or upon any part of the exterior of the Leased Premises or the Parking Area, any debris, garbage or refuse except as allowed by the Lessor at specific times of pick up and deposited in areas indicated by the Lessor in proper receptacles provided and placed for that purpose by the Lessee. In the case of perishable refuse or garbage, the same shall be kept in a properly refrigerated area provided by the Lessee. The Lessee shall pay for the cost of any garbage, debris and refuse removal service that may be required other than that provided by the municipality without charge should the municipality provide such a service. In the event that the Lessee fails to comply with the foregoing provisions, the Lessor, subject to Section 23.1, may rectify the situation and collect all expenses and disbursements from the Lessee as Additional Rent.

ARTICLE XI
ENVIRONMENTAL CONCERNS

11.1 The Lessee undertakes, with respect to the Leased Premises:

- 11.1.1 To comply with the Environmental Laws and to ensure on a regular basis the respect of such laws by its employees, agents, representatives and other persons or entities for whom it is responsible at law, and its suppliers, customers, representatives, invitees and other persons or entities who have access to the Leased Premises or any part thereof;
 - 11.1.2 That neither it nor its employees, agents, representatives and other persons or entities for whom it is responsible at law, nor its suppliers, customers, invitees or other or other persons or entities who have access to the Leased Premises or any part thereof shall place, keep or store in, on, under or about the Leased Premises, except in compliance with Environmental Laws, any hazardous materials or any toxic, dangerous or radioactive substances, including any chemical or other products included in the definition of "hazardous materials," "hazardous waste," "highly hazardous waste," "quasi-hazardous waste," "toxic substances," "toxic pollutants," "contaminants," "pollutants," "harmful products," or terms with similar meanings in any Environmental Law (hereinafter referred to as "**Hazardous Materials**"), that are brought onto the Leased Premises after the Commencement Date.
 - 11.1.3 That it, its employees, agents, representatives and other persons or entities for whom it is responsible at law, and its suppliers, customers, invitees or other persons or entities who have access to the Leased Premises or any part thereof shall take all necessary and reasonable preventive measures in accordance with Environmental Laws to minimize the risk of leaks or spills from any Hazardous Materials used, generated, manufactured or stored in the Leased Premises by the Lessee which may in any way contaminate the Leased Premises;
 - 11.1.4 That it shall submit the list of Hazardous Materials used in carrying out its activities, if any, at the Commencement Date and updates thereto to the Lessor for approval once a year;
 - 11.1.5 That if it produces or introduces in or around the Leased Premises, any Hazardous Materials whatsoever or if the conduct of its business entails the production or presence of any Hazardous Materials whatsoever in and around the Leased Premises, then, and notwithstanding any provision to the contrary in this Lease or the law, such Hazardous Materials will be and remain its exclusive property or the exclusive property of its customers on behalf of whom it provides services and shall not become the property of the Lessor, notwithstanding the extent to which the Hazardous Materials or products containing Hazardous Materials are integrated into the Leased Premises and notwithstanding the expiration or early termination of the Lease;
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- 11.1.6 That upon expiration or early termination of the Lease, it shall, at its expense, remove and dispose of all Hazardous Materials and all storage and other containers, in accordance with the Environmental Laws to the extent required by the Lessor;
 - 11.1.7 That neither it nor its employees, agents, representatives and other persons or entities for whom it is responsible at law, nor its suppliers, customers, invitees or other persons or entities who have access to the Leased Premises or any part thereof shall in any way contaminate the Leased Premises in violation of Environmental Laws;
 - 11.1.8 To notify the Lessor in writing of any contravention of the Environmental Laws that is in any way related to the environmental condition or quality of the Leased Premises and of any situation which, with the passage of time or otherwise, would be reasonably susceptible of leading to such a contravention, with all due dispatch in each case after the Lessee becomes aware of same;
 - 11.1.9 To remedy without delay any situation for which Lessee, or its employees, agents, representatives, or other persons or entities for whom it is responsible at law, or its suppliers, customers, invitees and other persons or entities who have access to the Leased Premises or any part thereof, are responsible, and which constitutes, or, which with the passage of time or otherwise, would be reasonably susceptible of leading to, a violation of Environmental Laws;
 - 11.1.10 To provide the Lessor, upon request, with any available information and any documents relating to the Lessee's compliance with Environmental Laws as it pertains to the environmental condition or quality of the Leased Premises, including, without limitation, any relevant compliance report that is available to the Lessee;
 - 11.1.11 To give the Lessor or a representative designated by the Lessor free access to the Leased Premises upon reasonable prior notice so that the Lessor may verify, subject to the obligation of the Lessor to minimize any inconvenience to the Lessee's activities and operations as may be caused thereby and subject to the duration and frequency of such access visits being reasonable, the Lessee's complying with the obligations stipulated herein; and
 - 11.1.12 To indemnify and hold the Lessor harmless against all costs, liabilities, demands and penalties as may be incurred by the Lessor and relating directly or indirectly to any noncompliance with any Environmental Laws, or relating directly or indirectly to any breach of this ARTICLE XI, by the Lessee, its employees, agents, representatives, or other persons or entities for whom it is responsible at law, or its suppliers, customers, invitees and other persons or entities who have access to the Leased Premises or any part thereof, including, without limitation, legal costs (judicial and extra-judicial) expert fees, penalties, fines, damages and the cost of remedial work needed to conform to the Environmental Laws.
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11.2 The **Lessee** shall indemnify, defend and save harmless the **Lessor** for and against any and all costs, claims, proceedings, liabilities, obligations, losses, demands, penalties, legal costs (judicial and extra-judicial) expert fees, penalties, fines, damages and the cost of remedial work of any kind or any nature whatsoever in connection therewith asserted against or incurred by the **Lessor** with respect to any order, decision, decree, judgment, ruling, claim or the like from or by any governmental authority under any Environmental Laws or other third party claims, in each case to the extent relating to, arising from, or in connection with any environmental conditions at, on, within, about, adjacent to, near, concerning, or affecting the Leased Premises, including but not limited to any Hazardous Materials or contamination and/or release or migration occurring at, on, upon, into, within, under, migrating to or from, about, adjacent to, near, or affecting the Leased Premises and that first occurred at any time from and after the Commencement Date and during the Term that is caused or permitted by the **Lessee** or the operations of the **Lessee** or its employees, agents, contractors and those for whom it is responsible or those acting under its authority or control.

ARTICLE XII
PARKING AREA

12.1 The Lessee may occupy nine (9) parking spaces in the zone indicated in Schedule "C", and one (1) parking space in the front parking spaces of the NEOMED INSTITUTE, for its employees and visitors. The front parking space will have to be paid for by the Lessee as Additional Rent at a cost of five hundred Dollars (\$500) per month during the Term.

ARTICLE XIII

13.1 Throughout the Term, the Lessee shall take out and keep in force at its sole cost and expense:

13.1.1 An "all risks" insurance policy for two million dollars (\$2,000,000) against fire, equipment breakage, operating losses and other claims generally covered by such a policy, at all times covering the full replacement value of the Lessee's assets in the Leased Premises, leasehold and other improvements made by the Lessee to the Leased Premises as well as any other asset for which the Lessee is legally responsible or assets installed by the Lessee or on its behalf on the Property.

13.1.2 A public liability insurance policy covering bodily injury, property damage, any liability assumed by the Lessee pursuant hereto and any liability arising from activities carried out by the Lessee and any other person in the Leased Premises, and work performed by the Lessee or by any other person, including persons for whom the Lessee is legally responsible, in any part of the Property.

This policy shall be taken out for an inclusive limit of no less than two million dollars (\$2,000,000) for each claim involving bodily injury, death or property damage, or for a higher amount, which amount the Lessor may reasonably require, from time to time.

13.1.3 A business interruption insurance in such amounts as will reimburse the Lessee for direct or indirect loss of earnings attributable to all perils insured

against by the Lessee hereunder, including without limitation loss of Rent for a minimum period of indemnity of three (3) months.

13.1.4 All insurance required to cover environmental risks.

13.1.5 Any other insurance policy that the Lessor may reasonably require, from time to time.

13.2 All insurance policies shall (i) be in form satisfactory to the Lessor, (ii) be placed with insurers reasonably acceptable to the Lessor, and (iii) provide that they will not be modified, cancelled or permitted to lapse unless the insurer notifies the Lessor in writing at least thirty (30) days prior to the date of modification, cancellation or lapse.

13.3 Each insurance policy shall name the Lessor and any other party required by the Lessor as an additional insured, as its/their interest may appear. Each comprehensive general liability insurance policy shall contain a provision of cross-liability and severability of interests as between Lessor and Lessee. All other insurance policies including, without limitation, the Lessee's all risk property damage insurance shall contain a waiver of subrogation rights which the Lessee's insurers may have against the Lessor, the Lessor's insurers, and persons under the Lessor's care and control. The Lessee hereby releases and waives any and all claims against the Lessor and those for whom the Lessor is in law responsible with respect to occurrences required to be insured against by the Lessee hereunder or otherwise insured by Lessee. The Lessee shall from time to time furnish the Lessor, upon the Lessor's request, with certificates of insurance reflecting (or, where the Lessor specifically requires, certified copies of) all such insurance policies and renewals thereof.

13.4 The Lessee agrees that should the Lessee fail to take out or keep in force such insurance at any time during the Term, the Lessor shall have the right to do so and to pay the premiums therefor. In such event, the Lessee shall reimburse the Lessor the amounts paid as premiums and applicable taxes thereon as Additional Rent on demand.

13.5 Notwithstanding the express or implicit obligation of the Lessor to insure and notwithstanding any obligation on the part of the Lessee to contribute to the payment of Lessor's premiums as contemplated by the provisions of this Lease, Lessee acknowledges that no insurable interest is conferred upon the Lessee under any of the Lessor's insurance policies and that the Lessee shall have no right to recover any proceeds thereunder or to claim any right or title to such proceeds.

13.6 The Lessee shall not keep, use or store, or allow to be kept, used or stored, in the Leased Premises any materials, nor shall the Lessee commit or allow to be committed any acts, which will increase the cost or rate of insurance on the Property against fire or other perils. Should the cost or rate of insurance on the Property or any portion thereof be increased by reason of the Lessee's use or occupation of the Leased Premises or by reason of any violation of any of the foregoing provisions, the Lessee undertakes to reimburse the Lessor an amount equal to such increase and applicable taxes thereon. The Lessee further undertakes to indemnify the Lessor from all demands made by any lessee of the Property should their cost or rate of insurance be increased by reason of the Lessee's use or occupation of the Leased Premises or by reason of any violation of the foregoing by the Lessee. All monies payable by the Lessee to the Lessor pursuant hereto shall be deemed Additional Rent payable on demand.

13.7 If the occupancy of the Leased Premises or the conduct of business therein or any acts or omissions of the Lessee in the Leased Premises or any part thereof, causes or results in any

increase in premiums of the insurance carried from time to time by the Lessor with respect to the Property, the Lessee shall pay any such increase in premiums and applicable taxes thereon as Additional Rent ten (10) Business Days after invoices for such additional premiums and applicable taxes thereon are rendered by the Lessor. In determining whether increased premiums are caused by or result from the use and occupancy of the Leased Premises, a schedule issued by the organization computing the insurance rate on the Property showing the various components of such rate shall be conclusive evidence of the several items and charges which make up such rate. The Lessee shall comply promptly with all requirements and recommendations of the Insurer's Advisory Organization of Canada (or any successor thereof), or of any insurer now or hereafter in effect pertaining to or affecting the Leased Premises and the Property. The Lessee hereby acknowledges that said payment does not form part of the fixed Operating Expenses as per these presents.

13.8 The Lessee will indemnify the Lessor and save it harmless from any and all losses or claims, actions, demands, liabilities and expenses in connection with loss of life, personal injury and/or damage to or loss of property: (a) occasioned or caused wholly or in part by any act or omission of the Lessee or anyone for whom it is in law responsible; or (b) arising from any breach by the Lessee of any provisions of this Lease.

13.9 The Lessor will indemnify the Lessee and save it harmless from any and all losses or claims, actions, demands, liabilities and expenses in connection with loss of life, personal injury and/or damage to or loss of property: (a) occasional or caused wholly or in part by any act or omission of the Lessor or anyone for whom it is in law responsible; or (b) arising from any breach by the Lessor of any provisions of this Lease.

13.10 Each of the Lessor and the Lessee releases the other and waives all claims against the other and those for whom the other is in law responsible with respect to occurrences insured against or required to be insured against by the releasing party, whether any such claims arise as a result of the negligence or otherwise of the other or those for whom it is in law responsible, subject to the following:

13.10.1 such release and waiver shall be effective only to the extent of proceeds of insurance received by the releasing party or proceeds which would have been received if the releasing party had obtained all insurance required to be obtained by it under this Lease (whichever is greater) and, for this purpose, the Lessee's or the Lessor's deductible amounts under the Lessee's or Lessor's insurance shall be deemed to be proceeds of insurance received; and

13.10.2 to the extent that both parties have insurance or are required to have insurance for any occurrence, the Lessee's insurance shall be primary.

ARTICLE XIV
DAMAGE OR DESTRUCTION

Provided, and it is hereby expressly agreed that if and whenever during the Term hereby leased, or any renewal thereof, the Property or the Leased Premises shall be destroyed or damaged by fire, lightning or tempest, or any of the other perils required to be insured against under the provisions of this Lease, then and in every such event:

14.1 If the damage or destruction is such that the Leased Premises, or the Property, is rendered wholly or partially unfit for occupancy or it is impossible or unsafe to use and occupy and if in either event the damage in the opinion of the Lessor, notice of which is to be given to the Lessee within thirty (30) days of the Lessor being given access to the affected portions of the Property by the competent authorities following the happening of such damage or destruction, cannot be repaired with reasonable diligence within two hundred and seventy (270) days from the happening of such damage or destruction, then either the Lessor or the Lessee may within ten (10) days next succeeding the giving of the aforementioned notice by the Lessor, terminate this Lease by giving to the other notice in writing of such termination, in which event this Lease and the term hereby leased shall cease and be at an end as of the date of such destruction or damage and the Rent and all other payments for which the Lessee is liable under the terms of this Lease shall be apportioned and paid in full to the date of such destruction or damage. In the event that neither the Lessor nor the Lessee so terminate this Lease, the Lessor shall repair the Property with all reasonable speed and the Rent hereby reserved shall abate from the date of the happening of the damage until the damage shall be made good to the extent of enabling the Lessee to use and occupy the Leased Premises.

14.2 If the damage be such that the Leased Premises is wholly unfit for occupancy, or if it is impossible or unsafe to use or occupy it, but, if in either event, the damage, in the opinion of the Lessor, can be repaired with reasonable diligence within two hundred and seventy (270) days of the happening of such damage, the Lessor is to give notice of its decision to repair to the Lessee within thirty (30) days from the Lessor being given access to the affected portions of the Property by the competent authorities following the happening of such damage and the Rent hereby reserved shall abate from the date of the happening of such damage until the damage shall be made good to the extent of enabling the Lessee to use and occupy the Leased Premises and the Lessor shall repair the damage with all reasonable speed unless the damage or destruction is due to the acts or omissions of the Lessee or for those whom the Lessee is at law responsible in which case there shall be no abatement of Rent.

14.3 If, in the opinion of the Lessor, the damage can be made good, as aforesaid, within two hundred and seventy (270) days of the happening of such destruction or damage and the damage is such that the Leased Premises are capable of being partially used for the purposes for which it is hereby leased, then until such damage has been repaired the Rent shall abate in the proportion that the Leased Premises is rendered unfit for occupancy bears to the whole of the Leased Premises and the Lessor shall repair the damage with all reasonable speed unless the damage or destruction is due to the acts or omissions of the Lessee or for those whom the Lessee is at law responsible in which case there shall be no abatement of Rent. Nothing herein contained shall be construed to oblige the Lessor to repair or reconstruct any alterations, improvements or property of the Lessee. On the contrary, all other improvements in and to the Leased Premises shall be the responsibility of Lessee who shall be obliged to repair and re-fixture to a standard at least equivalent to that which existed prior to the date of damage or destruction, to the extent of the proceeds of insurance received by Lessee in respect to its property and improvements.

14.4 Should any hypothecary creditor who may have an interest in any insurance proceeds refuse to permit the use of such proceeds for the repair, replacement, rebuilding and/or restoration as hereinabove provided and for the payment of amounts expended for such purposes, then the Lessor's obligation to repair or rebuild as provided for hereinabove shall cease and shall be null and void and the Lease shall be cancelled effective as of the date of the damage, unless the Lessor, at the Lessor's sole option, chooses to repair and rebuild in which latter event, Rent shall abate from the date of the happening of such damage, until the damage shall be made good to the extent of enabling the Lessee to use and occupy the Leased Premises.

14.5 Should the Lessor fail to complete such repair or restoration to the Leased Premises for any reason whatsoever within the delay set forth in Paragraph 14.1 above, the Lessee may terminate the Lease by written notification to the Lessor to be given within thirty (30) days following the expiration of the two hundred and seventy (270) day period mentioned above, which termination shall become effective at the expiry of such thirty (30) days unless the repair/restoration shall have then been substantially completed.

14.6 In no event shall the Lessor be liable to the Lessee for any loss or damage caused by damage or destruction, or caused by any delay in the restoration or repair, subject to Lessee's right to terminate the Lease pursuant to section 14.5 herein.

ARTICLE XV
SIGNS

15.1 The Lessee has no right to install any sign on the exterior of the Building or on any part of the Property. The Lessee shall have the right from time to time during the Term to display and maintain a sign at the entrance of its Leased Premises to advertise its business, subject to the Lessor's prior written approval with respect to the appearance, construction and size of the sign, and which approval shall not be unreasonably withheld. Any such sign shall be dignified in appearance and shall comply with all applicable laws, by-laws, rules and regulations. The Lessor will remove the sign at the termination of the Lease, and the costs of any repair resulting from the removal of such sign shall be at the sole cost of the Tenant.

ARTICLE XVI
INTEREST

16.1 The Lessee shall pay to the Lessor interest calculated at the Interest Rate on all overdue payments of Base Rent, of Additional Rent, and of all other sums which may be owing by the Lessee to the Lessor pursuant to the Lease, calculated from the due date of the amount in question to the date of payment, compounded monthly. Overdue interest shall also bear interest at the Interest Rate.

ARTICLE XVII
NO TACIT RENEWAL

17.1 Subject to the Lessee's option to renew provided herein, the Lease shall terminate *ipso facto* without notice or demand at the Expiration of the Term or upon earlier termination in accordance with this Lease, and any continued occupation of the Leased Premises by the Lessee shall not have the effect of extending the Term or renewing the Lease for any period of time, the whole notwithstanding the provisions of Article 1879 of the *Civil Code of Quebec*. Should the Lessee continue occupation of the Leased Premises beyond the Expiration of the Term, the Lessee shall be presumed to occupy the Leased Premises under a tenancy from month to month in consideration of a monthly Rent equal to the aggregate of (i) Two Hundred (200%) of the monthly Base Rent payable by the Lessee to the Lessor during the last month of the Term, plus (ii) the Additional Rent payable by the Lessee to the Lessor during the last month of the Term, plus (iii) all other sums payable by the Lessee to the Lessor pursuant to the provisions of the Lease. The foregoing month to month tenancy is without prejudice to the Lessor's rights to evict the Lessee by force, by injunctive proceedings or otherwise.

ARTICLE XVIII
OVERLOADING

18.1The Lessee shall not bring or cause to be brought into the Leased Premises any machinery, equipment or other effects that by reason of their weight, size or otherwise might damage the Leased Premises or overload the electrical, mechanical or plumbing systems of the Leased Premises, or the floors, ceilings, walls, columns, or any other part of the Leased Premises. The Lessee hereby assumes responsibility for all damage resulting therefrom.

ARTICLE XIX
GLASS AND WINDOW PANES

19.1The Lessor shall replace any glass or window panes in the Leased Premises that may be broken, cracked or damaged during the Term and the cost thereof shall be included in the Operating Expenses.

ARTICLE XX
NO ABATEMENT OR REDUCTION OF RENT

20.1There shall be no abatement from, nor reduction of, nor compensation of any kind or nature whatsoever, with respect to the Base Rent, the Additional Rent, or any other sums payable by the Lessee to the Lessor pursuant to the Lease by reason of (i) partial or temporary interruption, failure or stoppage of light, plumbing service, sprinkler service, electric service, wiring, or anything whatsoever in and about the Leased Premises resulting from any cause whatsoever, (ii) gas, fire, water, steam, smoke, rain or snow leaking or flowing in or flooding the Leased Premises, or (iii) any delays with respect to snow removal; whether the same result to the Lessee, its employees, suppliers, customers, or to any other person, or to any property belonging to the Lessee or any other person, in or about the Leased Premises, provided the Lessor diligently proceeds to remedy the situation in question where it is its obliged to do so.

ARTICLE XXI
NON-RESPONSIBILITY OF LESSOR

21.1Except for the Lessor's fault or negligence and to the extent permitted by law, the Lessor shall not be liable for any damages, consequential or otherwise, injury or death, and the Lessee agrees to indemnify and keep the Lessor free and harmless from any damages, losses and costs in respect of any claims for damage to property or injury or death to persons occurring in, upon or about the Leased Premises, sustained by the Lessee, its employees, agents, representatives, or other persons or entities for whom it is responsible at law, or its suppliers, customers, invitees and other persons or entities who have access to the Leased Premises or any part thereof, resulting from (i) the causes mentioned in Section 20.1 above. The Lessee agrees not to hold the Lessor in any way responsible for any damage or annoyance which the Lessee may sustain through the negligence, misconduct, or otherwise of any lessees or occupants who may occupy any other premises forming part of the Property.

ARTICLE XXII
ENTRY INTO THE LEASED PREMISES

22.1The Lessee agrees to allow prospective purchasers and prospective hypothecary creditors to visit the Leased Premises during Business Hours upon twenty-four (24) hours' written notice except in cases of emergency, whereupon entry shall be immediate. During the last twelve (12)

months of the Term, the Lessee agrees to allow person or persons who may be desirous of leasing the Leased Premises to visit the same during Business Hours upon twenty-four (24) hours' written notice, and to allow for rent signs or notices to be posted on or near the Leased Premises.

ARTICLE XXIII
DEFAULT PROVISIONS

23.1 Should the Lessee fail to fulfil any covenant or obligation incurred or assumed by it in this Lease, after having received a ten (10) day prior written notice from the Lessor to such effect, or should same not be capable of being remedied in ten (10) days, if the Lessee does not diligently commence to remedy same within the ten (10) day delay or does not complete such rectification thereafter in a diligent manner, the Lessor shall have the right to cure the default on behalf of the Lessee and to charge Lessee for all sums so paid plus an administration fee of Fifteen percent (15%) on all such incurred costs, and Lessee shall forthwith repay them to the Lessor as Additional Rent. The Lessor, in addition to any other rights, shall have the same remedies and may take the same steps for the recovery of all sums which the Lessee is to pay or reimburse the Lessor pursuant to the Lease, as it may have for the recovery of rental arrears under the terms of this Lease.

23.2 In any of the following events, namely:

- 23.2.1 If the Lessee shall fail to pay to the Lessor any instalment of Base Rent or Additional Rent or any other monies owing by the Lessee to the Lessor pursuant to the Lease (it being understood that the Lessee shall no longer be entitled to the benefit of any notice of non-payment as contemplated by section 23.1 in the event that Lessee has failed to pay any such amount to Lessor when due on two (2) or more occasions falling within any period of three hundred and sixty-five (365) consecutive days, and shall on any subsequent occasion be considered in default hereunder on any subsequent occurrence of non-payment without any grace or cure period in respect thereof);
 - 23.2.2 If the Lessee be declared dissolved, bankrupt, or wound-up, or shall make any general assignment for the benefit of its creditors, or take or attempt to take the benefit of any insolvency, winding-up or bankruptcy legislation, or if a petition in bankruptcy or in winding-up, or for reorganization be filed by or against the Lessee, or if a receiver or trustee be appointed for or enter into physical possession of the property of the Lessee, or any part thereof, and if such receiver or trustee is not removed within ten (10) days of his appointment;
 - 23.2.3 If the Lessee shall assign, sublease or permit the use of the Leased Premises by others except in the manner as herein permitted;
 - 23.2.4 If the Lessee shall fail to take possession of the Leased Premises, or if the Lessee shall abandon the Leased Premises;
 - 23.2.5 If any insurance carried by the Lessor or by any lessee of the Property be cancelled in consequence of the business carried on by the Lessee or in consequence of anything brought into or stored in the Leased Premises by the Lessee;
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- 23.2.6 If the Lessee shall default in the performance of any of its other obligations under the Lease;
- 23.2.7 If any execution be issued against the property of the Lessee in or on the Property pursuant to a judgment against the Lessee unless Lessee has taken steps to satisfy the judgment or is bona fide contesting such execution and such execution has been finally satisfied, stayed or quashed within thirty (30) days from its issuance;

this Lease, may be terminated forthwith at the option of the Lessor upon written notice to the Lessee. It is expressly agreed that such right of termination is without prejudice to Lessor's other rights and recourses in the circumstances. In such event, the Lease shall expire and be at an end, and anything herein before to the contrary notwithstanding, as of the date set forth in the Lessor's aforementioned written notice, and the then current month's Base Rent and Additional Rent, plus the next ensuing twelve (12) months' Base Rent and Additional Rent shall thereupon immediately become due and payable, without prejudice to the Lessor's other rights and recourses in the circumstances, including without limitation, the Lessor's right to obtain greater damages. Furthermore, in such event, the Lessor without any further formality or judgment, may re-enter and take possession of the Leased Premises as though the Lessee or its employees, agents or representatives, or such other occupant or occupants of the Leased Premises were over-holding lessees and, to remove therefrom any persons or property occupying the Leased Premises, and to bolt the Leased Premises and change the locks thereof. The Lessor shall have the right to re-let the Leased Premises to whomsoever it may choose without further notice or demand being necessary, and may recover from the Lessee all expenses of such re-letting (including any repairs or improvements necessitated thereby), in addition to the amounts mentioned above.

23.3 In addition to the foregoing and without prejudice to the Lessor's other rights and recourses hereunder, in the event of the bankruptcy of the Lessee, there shall immediately become due and exigible in favour of the Lessor, on account of accelerated rent, an amount equal to Base Rent and Additional Rent for a period of three (3) months next following the bankruptcy or for such longer period of time as may be allowed by any applicable bankruptcy or insolvency legislation in force from time to time. Furthermore, in the event of Lessee's continued occupancy of the Leased Premises after the filing of a proposal or a notice of intention to file a proposal pursuant to the provisions of the Bankruptcy and Insolvency Act, and any amendments thereto or replacements therefore or under any other insolvency legislation and said continued occupancy commences on a day which is not the first day of any calendar month, any Rent or other amounts payable on a monthly basis hereunder for such month and for any other partial month of the Term shall be calculated on a per diem basis and be paid in advance.

23.4 In the event that the Lessor is required to retain the services of a solicitor to enforce the fulfilment by the Lessee of any obligation undertaken by it under the Lease, then in each such event the Lessor shall be entitled to demand from the Lessee, in addition to and without prejudice to judicial costs otherwise payable by the Lessee, and whether or not judicial proceedings are in fact instituted, an amount equal to all reasonable legal costs, expenses and disbursements incurred by the Lessor to enforce the fulfilment by the Lessee of any such obligation plus the cost of all inspections and environmental assessments, plus all costs incurred to enforce the fulfilment of any such obligation, plus an indemnity equal to FIFTEEN PERCENT (15%) of the amount otherwise owing by the Lessee to the Lessor. Such indemnity is to indemnify the Lessor for additional administrative expenses incurred in connection with the enforced fulfilment by the

Lessee of its obligations hereunder. Such legal costs, expenses and disbursements, and such indemnity shall be payable on demand as Additional Rent.

23.5 The Lessee hereby waives the provisions of Article 1883 of the *Civil Code of Quebec*.

ARTICLE XXIV
EXPROPRIATION

24.1 If during the Term, the whole or a substantial portion of the Leased Premises is expropriated which renders the remainder of the Leased Premises unsuitable for the purpose intended in this Lease, the Lease shall cease and terminate as of the date on which vacant occupancy of the Leased Premises or the portion thereof in question is required by the expropriating party, and the Lessee shall pay to the Lessor the Rent and all other sums which may be owing by the Lessee to the Lessor pursuant to the Lease to such date.

24.2 In the event that Thirty percent (30%) or more of the Property be expropriated, whether or not the Leased Premises are affected, then the Lessor shall have the right to terminate the Lease as of the date on which vacant occupancy of the Property or the portion thereof in question is required by the expropriating party, provided the Lessor furnishes the Lessee with a one hundred and eighty (180) day prior written notice of such termination. In such event, the Lease shall terminate as of such date and the Lessee shall pay to the Lessor the Rent and all other sums which may be owing by the Lessee to the Lessor pursuant to the Lease to such date. Should the Lessor fail to furnish the Lessee with the aforementioned notice, the Lease shall continue in full force and effect.

24.3 If the expropriation of a part of the Leased Premises does not render the remainder of the Leased Premises unsuitable for the purpose intended in this Lease, then the Rent and all other sums payable by the Lessee to the Lessor pursuant to this Lease shall abate from the date on which occupancy of the portion so expropriated is taken by the expropriating party, in the proportion that the area of the part of the Leased Premises so expropriated bears to the area of the entire Leased Premises.

24.4 The Lessor and Lessee agree that the entire expropriation proceeds payable in respect of the expropriation of the Leased Premises or any part thereof, or payable in respect of the expropriation of the Property or any part thereof, shall be paid and belong to the Lessor, subject to the provisions of section 24.5 below which may be awarded or recoverable by the Lessee.

24.5 In the event that the expropriation affects the Leased Premises but does not result in the termination of the Lease but yet requires the reconstruction or replacement of some portion of the Leased Premises, such reconstruction or replacement shall be carried out by the Lessor at its expense in a good and workmanlike manner, and as expeditiously as reasonably practical, provided that the cost thereof does not exceed the amount of compensation award payable to the Lessor in respect of the cost of such reconstruction or replacement. The Lessee hereby expressly waives any right or claim to any part thereof. The Lessee shall have the right to claim and to recover from the expropriating authority (though not from the Lessor) such compensation as may be separately awarded or recoverable by the Lessee in its own right on account of any and all damages to the Lessee's business by reason of such expropriation or on account of any and all costs, losses, disbursements or otherwise which the Lessee may suffer as the result of such expropriation.

24.6 In no event shall the Lessor be liable to the Lessee for any loss or damage caused by expropriation for any reason whatsoever.

ARTICLE XXV
SECURITY

25.1 The Lessee clearly acknowledges and understands that any security services engaged by the Lessor at the Property are strictly and exclusively for the Lessor itself. Consequently, the Lessee acknowledges that any security services at the Property may be altered or eliminated at any time during the Term and the Lessee acknowledges and agrees that the Lessor shall not in any way be liable for any damages, costs or losses of any nature whatsoever, however caused, including but not limited to due to the fault or negligence of the Lessor or any person for whom it is responsible at law and resulting from any deficiency or failure in the security services in effect for the Property or due to the lack thereof.

25.2 The Lessee undertakes and agrees not to temper with, alter, remove or otherwise disable any and all security equipment in the Leased Premises and in the Property, including, but not limited to fire prevention and detection equipment.

ARTICLE XXVI
RULES AND REGULATIONS

26.1 The Lessee undertakes to observe and apply the regulation appended hereto as Schedule "E". The Lessor shall have the right, at any time and from time to time, to make or vary such reasonable rules and regulations as may be desirable, in the sole opinion of the Lessor (but not inconsistent with the provisions of this Lease), for the safety, care, cleanliness, operation and maintenance of the Leased Premises, the Parking Area, and the Property, and for the preservation of good order therein provided that such rules and regulations apply to all of the lessees of the Property. The Lessor shall furnish the Lessee with written notice of such rules and regulations, and all such rules and regulations shall be faithfully observed and performed by the Lessee, its employees, agents and representatives. The Lessor shall not be responsible to the Lessee for the non-observance or violation of any such rules or regulations by any other lessee.

26.2 The Lessee covenants with the Lessor that it will not do, or omit to do, or permit to be done or omitted, anything upon or in respect of the Leased Premises, the doing or omission of which (as the case may be) shall be or result in any nuisance, noise, disturbance or discomfort to other lessees, nor shall it create any noxious odours, unreasonable noise, dust, fumes or smoke.

26.3 Notwithstanding the foregoing, the Lessor shall ensure that the quiet and peaceful enjoyment of the Leased Premises by the Lessee is not interrupted, disturbed or hindered by demands or claims from the Lessor or from any party for whom the Lessor is in law responsible.

ARTICLE XXVII
MORTGAGES AND SUBORDINATION

27.1 The Lease and all the rights of the Lessee hereunder are and shall be subject and subordinate at all times to any and all mortgages, hypothecs or trust deeds affecting the Property which have been executed or which may at any time hereafter be executed, and any and all extensions and renewals thereof and substitutions therefor.

27.2 The Lessee covenants and agrees that if, by reason of default by the Lessor under any hypothec, trust deed or other charge to which the Lease is subject or subordinate, the Lessor's title is terminated, the Lessee will attorn to the hypothecary creditor or trustee or the acquirer of the Property pursuant to any action taken under any such hypothec, trust deed or other charge and the Lessee will recognize such person as the Lessee's Lessor under this Lease.

27.3 The Lessee agrees to execute and deliver, at any time and from time to time, upon the request of the Lessor or of the holder of any such hypothec, trust deed or other charge, any instrument which may be necessary or appropriate to evidence such attornment. Notwithstanding the foregoing, Lessee's obligation to execute any such attornment instrument requested by the holder of any such hypothec, trust deed or other charge, shall be conditioned upon Lessee's receipt of a commercially reasonable non-disturbance agreement.

27.4 The Lessee shall upon request of the Lessor furnish to each creditor under a hypothec, trust deed or other charge, a written statement that the Lease is in full force and effect and that the Lessor has complied with all its obligations under the Lease (or state those with which it has not complied) and any other reasonable written statement, document or estoppel certificate requested by any such creditor.

ARTICLE XXVIII
RELEASE OF LESSOR

28.1 In the event of any sale or other alienation of Lessor's rights in the Property to an arm's length third party acquirer, the Lessor shall be entirely released and relieved of all covenants and obligations of the Lessor hereunder as of the date of such sale/alienation, provided such acquirer agrees to assume and carry out any and all covenants and obligations of the Lessor hereunder.

ARTICLE XXIX
AMENDMENT OF LEASE

29.1 No assent or consent to changes in or waiver of any part of this Lease shall be deemed or taken as made unless the same be done in writing and attached or endorsed hereon by the Lessor and the Lessee. No covenant or term of the Lease stipulated in favour of a party hereto shall be waived, except by express written consent of such party, whose forbearance or indulgence in any regard whatsoever shall not constitute a waiver of the covenant, term or condition to be performed by the other party and until complete performance by a party of such covenant, term or condition, the other party shall be entitled to invoke any remedies available under the Lease or by law despite forbearance or indulgence.

ARTICLE XXX
NO REPRESENTATIONS OR WARRANTIES

30.1 The Lessee agrees that the Lessor has made no representations or warranties to the Lessee whatsoever except as may be provided for in the Lease, and that the Lease constitutes the total agreement between the parties hereto.

30.2 The Lessee acknowledges that the Lease has been freely negotiated by the Lessee, and that it has had the opportunity to engage legal counsel to review the Lease and to advise it prior to the Lessee's execution of same.

30.3 Notwithstanding the foregoing, the Lessor hereby represents and guarantees that that the Leased Premises and all building systems therein shall as at the Commencement Date be in good working order and condition.

30.4 The signatories hereby declare being duly authorized to sign the present Lease Agreement and bind the company that they represent.

ARTICLE XXXI
SEVERABILITY

31.1 Should any term or provision of the Lease be deemed illegal, unenforceable, or contrary to public order and good morals, under the laws of the Province of Quebec, such provision(s) shall be considered severable, and the remainder of this Lease and its conditions shall remain in full force and effect as though such provision(s) had never been included.

ARTICLE XXXII
SUCCESSORS AND ASSIGNS

32.1 The Lease shall be binding upon, and inure to the benefit of, the respective heirs, successors, administrators and assigns of the Lessor and the Lessee, provided that nothing in this Article shall be construed as permitting the Lessee to sublet, assign or transfer any interest in the Lease other than as specifically provided in the Lease.

ARTICLE XXXIII
FORCE MAJEURE

33.1 In the event that either the Lessor or the Lessee shall be delayed or hindered in or prevented from the performance of any act required hereunder by reason of causes beyond the reasonable control of the performing party, including without limitation, strikes; lock-outs; labour troubles; inability to procure materials; failure of power; pandemics; epidemics; restrictive governmental laws or regulations; declarations of a state of emergency by the applicable governmental authority which prevent the Leased Premises from being open; public health emergencies where the Leased Premises are required or recommended by the applicable governmental authority or public health agency having jurisdiction to close along with the closure of other similar businesses within the municipality in which the Leased Premises are located; riots; insurrection; war or acts of war (a "**Force Majeure Event**"), then performance of such act shall be excused for the period of the delay caused by the Force Majeure Event and the period for the performance of any such act shall be extended for a period equivalent to the period of such delay caused by the Force Majeure Event. However, in no event shall financial inability be considered to be a cause of Force Majeure nor shall it permit any delay or waiver of the payment of Base Rent or Additional Rent. Moreover, in the event that the Lessee's fixturing is delayed due to a Force Majeure for a period of up to 90 days, and provided that the Lessee notifies the Lessor of the Force Majeure Event and takes commercially reasonable action to mitigate any delay, the Fixturing Period shall be extended on a day for day basis, and the Commencement Date and Expiration of the Term (and the dates provided increases in Base Rent as contemplated in section 3.1) shall be extended accordingly. An event or circumstance contemplated in this Section 34.1 shall be deemed not to be an eviction or disturbance of the Lessee's enjoyment of the Leased Premises and the occurrence thereof shall not render the Lessor liable in damages to the Lessee or entitle the Lessee to claim any diminution in Rent but, upon such occurrence, the Lessor shall without delay take all reasonable steps to terminate the event or circumstance in question.

ARTICLE XXXIV
APPROVAL OF LESSOR

34.1 Wherever the Lessor's consent is required to be given hereunder or wherever the Lessor must approve any act or performance by the Lessee, such consent or approval, as the case may be, shall be given in writing by the Lessor before same shall be deemed to be effective and, shall not be unreasonably withheld, conditioned or delayed.

ARTICLE XXXV
TIME TO BE OF THE ESSENCE

35.1 Time shall be of the essence of this Lease.

ARTICLE XXXVI
PUBLICATION OF LEASE

36.1 This Lease shall not be published at length but only by notice pursuant to the provisions of the *Civil Code of Quebec* and then only if the form and the terms of such notice have first been approved by the Lessor in writing, which approval shall not be unreasonable withheld. The form shall not contain any financial provisions or conditions. All costs of publication shall be assumed by the Lessee. The Lessee shall, at the expiration or earlier termination of this Lease, radiate all registrations of any such notice of lease failing which the Lessor will have the right to cause such radiation and to charge to the Lessee the cost thereof.

ARTICLE XXXVII
SCHEDULES

37.1 The Schedules attached to this Lease are included in and form an integral part of this Lease.

37.2 This Lease and such rules and regulations as may be adopted and promulgated by the Lessor and provided to the Lessee, from time to time constitute the entire agreement between the parties.

ARTICLE XXXVIII
INTERPRETATION

38.1 The singular number shall be deemed to include the plural and any gender shall be deemed to include the neuter, masculine or feminine where required. Where there is more than one Lessee, they shall be jointly and solidarily bound to the fulfilment of their obligations hereunder. The headings herein are for convenience only and shall not constitute a part of the Lease. The definition of any words used in any Article of the Lease shall apply to such words when used in any other Article hereof whenever the context is consistent.

ARTICLE XXXIX
GOVERNING LAW

39.1 The Lease shall be construed and governed by the laws of the Province of Quebec and the Parties irrevocably submit to the exclusive jurisdiction of the courts of the Province of Quebec for the settlement of any dispute that may arise in connection with the present Lease.

ARTICLE XL
LEGAL COSTS AND BROKERAGE COMMISSIONS

40.1 The Lessor and the Lessee shall each pay their own legal fees in respect of the negotiation and execution of this Lease.

40.2 The Lessee represents and warrants that no broker, agent or other intermediary was involved in this transaction and in the negotiation and preparation of this Lease. Consequently, the Lessee shall indemnify and hold the Lessor harmless from any action instituted by brokers or agents for payments of fees or commissions associated with the transaction.

ARTICLE XLI
CIVIL CODE WAIVERS

41.1 The Lessee hereby waives any rights which it may have or enjoy at any time pursuant to Article 1854 (2nd paragraph), 1859, 1861, 1867 (second paragraph, *in fine*), 1868 (second paragraph, *in fine*), 1881 and 1883 of the *Civil Code of Quebec* or any replacement legislation.

ARTICLE XLII
CONTESTATION OF TAXES

42.1 The Lessor shall have no obligation to contest, appeal, object to or litigate the levying or imposition of any Property Taxes and/or any valuation imposed with respect thereto, and Lessor may settle, compromise, consent to, waive or otherwise determine, in its sole discretion, all matters and things relating thereto.

ARTICLE XLIII
CONFIDENTIALITY

43.1 The parties will maintain all Confidential Information (as hereinafter defined) in confidence and will not disclose such information to any other party without written consent. "**Confidential Information**" includes the terms of this Lease and any and all information whether in oral, written or other form, which is communicated by Lessee to Lessor relating to Lessee's proposed development and use of the Leased Premises, including but not limited to, architectural plans, specifications, site plans and drawings (regardless of whether such information is labelled as confidential), but shall not include any information:

- 43.1.1 is in or comes into the public domain otherwise than by any breach of the present Lease;
- 43.1.2 the recipient can show that such information was in its possession by virtue of being recorded in its files or being in its use prior to receipt from the other party; or
- 43.1.3 is received by a party hereto from a third party acting in good faith, legally in possession of such information, without restrictions as to its disclosure or use of the kind provided for by this Lease.

Confidential Information may be released (i) to the parties' employees, partners, legal counsel, consultants and lenders who have a reasonable need for such Confidential Information, provided that such individuals agree to maintain the confidential nature of the information; (ii) as may

otherwise be required by law; or (iii) as may be necessary for a party to give effect to or otherwise enforce its rights under the present Lease. This provision will be binding upon execution of this Lease or the Lease is terminated.

ARTICLE XLIV
AUDIT RIGHTS

44.1 Lessee will have the right to audit the Operating Expenses and the Property Taxes. Lessee will initiate any audit by giving written notice to Lessor of Lessee's intent to audit. Lessee's notice shall be given within ninety (90) days after Lessee's receipt from Lessor of (i) an annual recalculation of the Operating Expenses and the Property Taxes, and (ii) Lessor's notice to Lessee stating the Operating Expenses and Property Taxes for any calendar year and the audit shall occur within one hundred and twenty (120) days after Lessor's receipt of Lessee's written notice, failing which Lessee shall be prescribed from auditing the period in question and shall be deemed to have accepted Lessor's calculations. Lessee's audit may be conducted only by employees or consultants of Lessee or chartered accountants retained by the Lessee for such purposes, and under no circumstances shall same be conducted by any person or entity acting on a success or recovery basis. Lessee shall provide Lessor with a copy of the audit within thirty (30) business days of receipt. Where the Lessor disagrees with any results of such audit, and the parties are unable to settle same within thirty (30) business days following Lessor's receipt thereof, then in such case, Lessor may, at any time within ten (10) business days following expiry of the aforesaid thirty (30) business day period, submit the unsettled or disputed matters for determination to a national or regional firm of chartered accountants who otherwise act for neither Lessor or Lessee for final determination, and the decision of such chartered accountants shall be binding upon the parties. The fees of such accountants shall be borne by the unsuccessful party. If the audit, finally determined, determines that Lessee overpaid Operating Expenses and/or Property Taxes, Lessor will immediately reimburse Lessee for the expenses that Lessee paid in excess of the audited Operating Expenses and Property Taxes and will reimburse the Lessee's reasonable expenses for conducting such audit in the event Lessee paid an amount of five percent (5%) or greater than the amount of the Operating Expenses Lessee should have paid. If the audit determines that Lessee underpaid the Operating Expenses and/or Property Taxes, Lessee will make payment to Lessor within thirty (30) days of Lessee's receipt of the audit.

ARTICLE XLV
LANGUAGE DECLARATION

50.1 The Parties hereto have requested that the present Agreement of Lease be drawn up in the English language. *Les Parties aux présentes ont exigé que la présente Convention de Bail soit rédigée dans la langue anglaise.*

IN WITNESS WHEREOF, the Parties hereto have signed these presents at Montreal, Province of Quebec, on the 1st day of January 2023.

**NEOMED INSTITUTE
(LESSOR)**

PER: _____ /s/ Matthew Carlyle _____

Name: Matthew Carlyle
Title: EVP & CFO

**REPARE THERAPEUTICS INC
(LESSEE)**

PER: _____ /s/ Christopher Kendall _____

Name: Christopher Kendall
Title: VP Finance & FP&A

SCHEDULE "A"

AUTOMATIC WITHDRAWAL INFORMATION

N/A – already on file

SCHEDULE "B"

PLAN OF LEASED PREMISES

Basement

SCHEDULE "B"

PLAN OF LEASED PREMISES

Ground Floor

SCHEDULE "C"

PLAN OF PARKING AREAS

SCHEDULE "D"
LESSOR'S WORK

NA

SCHEDULE "E"

Rules and Regulations

See attached document

SCHEDULE "F"

Square Footage of Leased Premises

Room #	Room Type	Square feet
1208	Office	237
1210	Office	331
2116	Office	83
2215	Office in lab suite	97
2216	Office in lab suite	97
2217	Biology lab	321
2218	Office in lab suite	97
2219	Office in lab suite	97
2232	Vivarium	156
2233	Vivarium	156
2251	Vivarium	212
2272	Biology lab	530
2208A	Biology lab	159
2208B	Biology lab	195
2220A	Office in lab suite	78
2220B	Office in lab suite	180
2232A	Vivarium	149
2243AL	Vivarium	119
2243L	Vivarium	151
	Total	3445

***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) customarily and actually treated by the registrant as private or confidential.

**SECOND AMENDMENT
TO
RESEARCH SERVICES, LICENSE AND COLLABORATION AGREEMENT**

This Second Amendment to Research Services, License and Collaboration Agreement (this “**Second Amendment**”) is entered into as of January 31, 2023 (the “**Second Amendment Effective Date**”) by and between Repare Therapeutics, Inc., a corporation organized and existing under the laws of Canada and having its principal place of business at 7210 Frederick-Banting, St-Laurent, Quebec, H4S 2A1, Canada (“**Repare**”) and Ono Pharmaceutical Co., Ltd., a corporation organized and existing under the laws of Japan and having an address of 8-2, Kyutaromachi 1-chome, Chuo-ku, Osaka 541-8564, Japan (“**Ono**”). Repare and Ono may each be referred to herein as a “**Party**” or collectively as the “**Parties**.”

WHEREAS, Repare and Ono entered into that certain Research Services, License and Collaboration Agreement, dated as of January 31, 2019, as amended by First Amendment, dated as of October 29, 2021 (the “**Agreement**”); and

WHEREAS, the Parties wish to amend the Agreement to extend the Research Term and revise the Licensed Drug Candidate selection process;

NOW, THEREFORE, the Parties, intending to be legally bound, hereby agree as follows:

1. Capitalized terms used in this Second Amendment that are not defined herein shall have the meanings ascribed to them in the Agreement.
2. Section 1.142 of the Agreement is hereby deleted in its entirety and replaced with the following:

1.142 “**Research Term**” means the period commencing on the Effective Date and ending upon the earlier of (a) July 31, 2023, or (b) the date of submission of the first IND in the United States or in Japan. Any extension of the Research Term will require the mutual written agreement of both Parties.
3. Section 3.3 of the Agreement is hereby deleted in its entirety and replaced with the following:

3.3 **DC Selection Meeting**. The Parties shall hold a meeting at the date and time agreed upon by the Parties, but no later than the earlier of (a) the date of submission of the first IND in the United States or in Japan or (b) [***], in order to discuss the selection of one potential Licensed Drug Candidate among the Drug Candidates to move toward further Development and Commercialization by the Parties (the “**DC Selection Meeting**”).
4. Notwithstanding anything to the contrary in the Agreement, except as the Parties may otherwise agree in writing, [***]
5. This Second Amendment shall be deemed incorporated into and made a part of the Agreement. The provisions of this Second Amendment shall constitute an amendment to the Agreement, and, to the extent that any term or provision of this Second Amendment may be deemed expressly inconsistent with any term or provision in the Agreement, this Second Amendment shall govern and control. Except as expressly modified by the terms of this Second Amendment, all of the terms, conditions, and provisions of the Agreement are hereby ratified, and the Agreement remains in full force and effect.

6. This Second Amendment may be executed in two (2) or more counterparts, including by facsimile or PDF signature pages or other electronic means, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

[THE REMAINDER OF THIS PAGE HAS BEEN LEFT INTENTIONALLY BLANK]

IN WITNESS WHEREOF, and intending to be legally bound hereby, the Parties have caused this Second Amendment to Research Services, License and Collaboration Agreement to be executed by their respective duly authorized officers as of the Second Amendment Effective Date.

REPARE THERAPEUTICS, INC.

By: /s/ Lloyd M. Segal

Name: Lloyd M. Segal

Title: President & CEO

ONO PHARMACEUTICAL CO., LTD

By: /s/ Takao Yoshida

Name: Takao Yoshida

Title: Senior Director, Research Center of Oncology

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statements (Form S-8 Nos. 333-239400, 333-255048 and 333-263469) pertaining to the 2020 Equity Incentive Plan and the 2020 Employee Share Purchase Plan of Repare Therapeutics Inc. and in the Registration Statement (Form S-3 No. 333-257668) of Repare Therapeutics Inc. and the related Prospectus of our report dated February 28, 2023, with respect to the consolidated financial statements of Repare Therapeutics Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2022.

/s/ Ernst & Young LLP

Montréal, Canada
February 28, 2023

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Lloyd M. Segal, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2022 of Repare Therapeutics Inc.;
 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
 4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13(a)-15(f) and 15(d)-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.
-

Date: February 28, 2023

By: /s/ Lloyd M. Segal
Lloyd M. Segal
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Steve Forte, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2022 of Repare Therapeutics Inc.;
 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
 4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13(a)-15(f) and 15(d)-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.
-

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), Lloyd M. Segal, President and Chief Executive Officer of Repare Therapeutics Inc. (the "Company"), and Steve Forte, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

- (1) The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022 (the "Report") fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: February 28, 2023

By: /s/ Lloyd M. Segal

Lloyd M. Segal
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 28, 2023

By: /s/ Steve Forte

Steve Forte
Executive Vice President, Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)
