CLEVELAND BIOLABS INC
Form 10-K
March 06, 2018
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549
FORM 10-K
(Mark One)
x Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934
For the fiscal year ended December 31, 2017
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 001-32954
CLEVELAND BIOLABS, INC.
(Exact name of registrant as specified in its charter)

DELAWARE	20-0077155
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
73 High Street, Buffalo, NY 14203	(716) 849-6810
(Address of principal executive offices)	Telephone No.

Securities Registered Pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, par value $0.005 per share	NASDAQ Capital Market

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 x
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x
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 x No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant’s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company or an emerging growth company. See definition of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	¨	Accelerated filer
Non-accelerated filer	¨	Smaller reporting company x
		Emerging growth company ¨

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No x

The aggregate market value of the voting and non-voting common equity held by non-affiliates as of the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2017, was $13,886,205. There were 11,279,834 shares of common stock outstanding as of March 5, 2018.

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DOCUMENTS INCORPORATED BY REFERENCE

The definitive proxy statement relating to the registrant's 2018 Annual Meeting of Stockholders is incorporated by reference in Part III to the extent described therein. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2017.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. Forward-looking statements give our current expectations of forecasts of future events. All statements other than statements of current or historical fact contained in this annual report, including statements regarding our future financial position, business strategy, new products, budgets, liquidity, cash flows, projected costs, regulatory approvals or the impact of any laws or regulations applicable to us, and plans and objectives of management for future operations, are forward-looking statements. The words "anticipate," "believe," "continue," "should," "estimate," "expect," "intend," "may," "plan," "project," "will," and similar expressions, as they relate to us, are intended to identify forward-looking statements.

We have based these forward-looking statements on our current expectations about future events. While we believe these expectations are reasonable, such forward-looking statements are inherently subject to risks and uncertainties, many of which are beyond our control. Our actual future results may differ materially from those discussed here for various reasons. Factors that could contribute to such differences include, but are not limited to:

- our need for additional financing to meet our business objectives;
- our history of operating losses;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our plans and expectations with respect to future clinical trials and commercial scale-up activities;
- our reliance on third-party manufacturers of our product candidates;
- future agreements with third parties in connection with the commercialization of any approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States, the European Union and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- government contracting processes and requirements;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the exercise of control over our company our by our majority stockholder;
- the geopolitical relationship between the United States and the Russian Federation, as well as general business, legal, financial and other conditions within the Russian Federation;
- our ability to obtain and maintain intellectual property protection for our product candidates; and
- the other factors discussed below in "Item 1A. "Risk Factors," in Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and in other filings we make with the Securities and Exchange Commission.

Given these risks and uncertainties, you are cautioned not to place undue reliance on such forward-looking statements. The forward-looking statements included in this report are made only as of the date hereof. We do not undertake any obligation to update any such statements or to publicly announce the results of any revisions to any of such statements to reflect future events or developments.

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PART I

Item 1. Business

When used in this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires, the terms "Cleveland BioLabs," the "Company," "CBLI," "we," "us," and "our" refer to Cleveland BioLabs, Inc. and its consolidated subsidiaries, BioLab 612, LLC and Panacela Labs, Inc.

GENERAL OVERVIEW

Cleveland BioLabs is an innovative biopharmaceutical company developing novel approaches to activate the immune system and address serious medical needs. Our proprietary platform of Toll-like immune receptor activators has applications in mitigation of radiation injury and immuno-oncology. We combine our proven scientific expertise and our depth of knowledge about our products' mechanisms of action into a passion for developing drugs to save lives. Entolimod, a Toll-like receptor 5 ("TLR5") agonist, which we are developing as a medical radiation countermeasure ("MRC") for reducing the risk of death from Acute Radiation Syndrome ("ARS") is our most advanced product canidtate. Other indications, including immunotherapy for oncology, have been or may in the future be investigated as well.

Entolimod as a MRC is being developed under the United States Food & Drug Administration's ("FDA's" or "Agency's") Animal Efficacy Rule (the "Animal Rule") for the indication of reducing the risk of death following exposure to potentially lethal irradiation occurring as a result of a radiation disaster (see "– Government Regulation – Animal Rule"). We believe that entolimod is the most efficacious MRC currently in development. The following is a summary of the clinical development of entolimod as an MRC to date and its related regulatory status.

We have completed two Good Clinical Practices ("GCP") clinical studies designed to evaluate the safety, pharmacokinetics and pharmacodynamics of entolimod in a total of 150 healthy subjects. We have completed a Good Laboratory Practices ("GLP"), randomized, blinded, placebo-controlled, pivotal study designed to evaluate the dose-dependent effect of entolimod on survival and biomarker induction in 179 non-human primates exposed to 7.2 Gy total body irradiation when entolimod or a placebo was administered at 25 hours after radiation exposure. We have also completed a GLP, randomized, open-label, placebo-controlled, pivotal study designed to evaluate the dose-dependent effect of entolimod on biomarker induction in 160 non-irradiated non-human primates.

We met with the FDA in July 2014 to present our human dose-conversion and to discuss our intent to submit an application for pre-Emergency Use Authorization ("pre-EUA"), a form of authorization granted by the FDA under certain circumstances (see "– Government Regulation – Emergency Use Authorization"). The FDA confirmed that our existing efficacy and safety data and animal-to-human dose conversion were sufficient to proceed with a pre-EUA application and agreed to accept a pre-EUA application for review. The pre-EUA application was submitted in the second quarter of 2015. As part of the Company's response to pre-EUA review comments received from the FDA, we met with the Agency in the first quarter of 2016 to discuss various aspects of entolimod manufacturing. The Agency specified that the Company needs to establish comparability between the drug formulation used in previously conducted preclinical and clinical studies and the entolimod drug formulation proposed for commercialization under the pre-EUA. The FDA also indicated that further review of the pre-EUA dossier would not proceed until these comparability data have been evaluated by the Agency.

To establish the comparability of the older formulation and the new formulation, the FDA requested that we first perform a side-by-side analytical comparability study between the two entolimod drug formulations. Thereafter, the Agency requested that we conduct an in vivo study in non-human primates ("NHP") to establish bio-comparability. The side-by-side analytical comparability analysis of the two formulations of entolimod was completed in the fourth quarter of 2016. The report of these results was submitted to the FDA in the first quarter of 2017. The FDA has reviewed this data and provided its consent to commence the bio-comparability study in NHP in the second quarter of 2017. The bio-comparability study is currently ongoing. Following completion of the study and discussion of the submitted study results with the FDA, we expect the FDA to resume the review of our pre-EUA dossier.

If the FDA authorizes the application, then Federal agencies are free to procure entolimod for stockpiling so that the drug is available to distribute in the event of an emergency, i.e., prior to the drug being formally approved by FDA under a Biologics License Application ("BLA"). Such authorization is not equivalent to full licensure through approval of a BLA, but precedes full licensure, and, importantly, would position entolimod for potential sales in

advance of full licensure in the U.S. We further believe pre-EUA status will position us to explore sales opportunities with foreign governments.

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In addition, the Company has submitted a Marketing Authorization Application ("MAA") with the European Medicines Agency ("EMA") for entolimod as a MRC in Europe. The MAA was validated by the EMA in the fourth quarter of 2017 and is currently under review by the Agency.

In September 2015, we announced two awards totaling approximately $15.8 million in funding from the United States Department of Defense ("DoD"), office of Congressionally Directed Medical Research Programs to support further development of entolimod as a MRC. These awards have funded, and will continue to fund, additional preclinical and clinical studies of entolimod, which are needed for a BLA. In October 2016, the DoD modified the original statement of work of one of these contracts (Joint Warfighter Medical Research Program ("JWMRP") contract award number W81XWH-15-C-0101) by eliminating certain tasks no longer deemed critical for the preparation of the BLA and established new tasks to address the formulation questions raised by the FDA during the review of the pre-EUA dossier, including an aim to conduct an in vivo NHP bio-comparability study along with other drug manufacturing related activities. In September 2017, the DoD further modified the contract by extending its term to 2019 on a no-cost basis.

In addition to development work on the MRC for reducing the risk of death from ARS indication, we have completed a Phase 1 open-label, dose-escalation trial of entolimod in 26 patients with advanced cancer in the U.S. The data for the U.S. study were presented at the 2015 annual meeting of the American Society of Clinical Oncology ("ASCO"). Seven (7) additional patients have been dosed with the entolimod drug formulation proposed for commercialization under the pre-EUA and MAA in an extension of this study performed in the Russian Federation ("Russia"). Based on current plans, we hope to include up to 17 additional patients under this extension study prior to its completion in 2019.

We have also completed dosing of 40 patients in a study of the safety and tolerability of entolimod when administered as a neo-adjuvant therapy before cancer surgery in treatment-naïve patients with primary colorectal cancer. This study was performed in Russia using the entolimod dug formulation proposed for commercialization under the pre-EUA and MAA. Because this study included older patients (up to 84 years) and those with other health conditions, the trial further extended our understanding of entolimod effects in broader population of study patients. The safety profile of the drug appeared generally similar to the profiles previously identified in healthy subjects and patients with cancer who participated in prior studies. Increases in plasma cytokines and alterations of blood cells were observed that appeared consistent with TLR5-mediated mobilization and trafficking of immunocytes to peripheral tissues, although changes in tumor immune cell infiltration appeared to be independent of treatment group in this exploratory study. This study was partially funded by the development contract with the Russian Federation Ministry of Industry and Trade ("MPT").

Because both oncology studies performed in Russia used the entolimod drug formulation proposed for commercialization under the pre-EUA and MAA, the safety data from these studies was included in our MAA submission to the EMA for use of entolimod as a MRC.

CBLB612 is a synthetic molecule that activates the Toll-like heterodimeric receptor 2/6 ("TLR2/TLR6") and stimulated white blood cell generation in preclinical studies. Recently we have completed dosing in a Phase 2, randomized, placebo-controlled clinical study of CBLB612 as myelosuppressive prophylaxis in patients with breast cancer receiving doxorubicin-cyclophosphamide chemotherapy. While the efficacy hypothesis of the study was not confirmed, the CBLB612 appeared to be generally well tolerated at the doses used in this clinical trial. We currently have no active clinical studies ongoing with CBLB612.

Mobilan is a recombinant non-replicating adenovirus that directs expression of TLR5 and its agonistic ligand, a secretory non-glycosylated version of entolimod we are also developing through our subsidiary, Panacela Labs, Inc. ("Panacela"). Two randomized, placebo-controlled, dose-ranging studies of Mobilan in men with prostate cancer are currently ongoing in the Russian Federation.

CORPORATE INFORMATION

We were incorporated in Delaware in June 2003 as a spin-off company from The Cleveland Clinic. We exclusively license our founding intellectual property from The Cleveland Clinic. In 2007, we relocated our operations to Buffalo, New York and became affiliated with Roswell Park Cancer Institute ("RPCI"), through technology licensing and research collaboration relationships. Our common stock is listed on the NASDAQ Capital Market under the symbol "CBLI."

Our principal executive offices are located at 73 High Street, Buffalo, New York 14203, and our telephone number at that address is (716) 849-6810.

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Since inception we have formed several subsidiaries to best capitalize on our unique ability to leverage financial and clinical development resources in Russia. In December 2009, we created Incuron LLC ("Incuron") with BioProcess Capital Ventures ("BCV") to develop Curaxin compounds (defined below). In September 2011, we created Panacela, a U.S. entity, with Joint Stock Company "Rusnano" ("Rusnano") to develop Mobilan and other product candidates (described below.) Simultaneous with the formation of Panacela, was the creation of a wholly-owned Russian subsidiary of Panacela named Panacela Labs, LLC. Finally, we have a wholly-owned Russian subsidiary, BioLab 612, LLC. Incuron was included in our consolidated financial results through November 25, 2014, and then accounted for as an equity investment through April 29, 2015, after which our remaining equity interest in Incuron was sold by June 30, 2015. Currently we no longer own equity in Incuron, but do maintain a right to royalty payments, as later described, and we conduct drug development activities on behalf of Incuron in the U.S.

CBLI and Panacela each have worldwide development and commercialization rights to product candidates in development, subject to certain financial obligations to our current licensors.

The CBLI logo and CBLI product names are proprietary trade names of CBLI, its subsidiaries. We may indicate U.S. trademark registrations and U.S. trademarks with the symbols "®" and "™", respectively. Third-party logos and product/trade names are registered trademarks or trade names of their respective owners.

PRODUCT DEVELOPMENT PIPELINE

Our product development programs arise from both internally developed and in-licensed intellectual property from our innovation partners, The Cleveland Clinic and RPCI. In building the Company’s product development pipeline, we intentionally pursued targets with applicability across multiple therapeutic areas and indications. This approach gives us multiple product opportunities and ensures that our success is not dependent on any single product or indication. Our currently ongoing product development programs and their respective development stages are illustrated below:

CBLI

PRODUCT Indication	DISCOVERY	PRECLINICAL	PIVOTAL ANIMAL STUDIES	HUMAN SAFETY / DOSE CONVERSION
ENTOLIMOD-Biodefense Acute Radiation Syndrome				

PRODUCT Indication	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PHASE III
ENTOLIMOD-Oncology Advanced Solid Tumors					

Panacela

PRODUCT Indication	DISCOVERY	PRECLINICAL	PHASE I	PHASE II	PHASE III
MOBILAN Targeted Therapy of Prostate Cancer					

Our product development efforts were initiated by discoveries related to apoptosis, a tightly regulated form of cell death that can occur in response to internal stresses or external events such as exposure to radiation or toxic chemicals. Apoptosis is a major determinant of the tissue damage that occurs in a variety of medical conditions involving ischemia, or temporary loss of blood flow, such as cerebral stroke, heart attack and acute renal failure. In addition, apoptotic loss of cells of the hematopoietic system and gastrointestinal tract is largely responsible for the acute lethality of high-dose radiation exposure. On the other hand, apoptosis is also an important protective mechanism that allows the body to eliminate defective cells such as those with cancer-forming potential.

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We have developed novel strategies to target the molecular mechanisms controlling apoptotic cell death for therapeutic benefit. These strategies take advantage of the fact that tumor and normal cells respond to apoptosis-inducing stresses differently due to tumor-specific defects in cellular signaling pathways such as inactivation of p53 (a pro-apoptosis regulator) and constitutive activation of Nuclear Factor kappa-B ("NF-kB"), (a pro-survival regulator).

Thus, we designed two oppositely-directed general therapeutic concepts:

(a) temporary and reversible suppression of apoptosis in normal cells to protect healthy tissues from stress-induced damage using compounds we categorize as Protectans, which include entolimod, Mobilan, and CBLB612; and,

(b) reactivation of apoptosis in tumor cells to eliminate cancer using compounds we categorize as Curaxins, which includes CBL0137, currently being developed by our former subsidiary, Incuron.

In recent years, our understanding of the mechanisms of actions underlying the activity of these compounds has grown substantially beyond the initial founding concepts around modulation of apoptosis.

Entolimod Biodefense Indication

Our most advanced Protectan product candidate is entolimod, an engineered derivative of the Salmonella flagellin protein that was designed to retain its specific TLR5-activating capacity while increasing its stability, reducing its immunogenicity and enabling high-yield production. We are developing entolimod as a medical radiation countermeasure for reducing the risk of death from ARS, which we refer to as a Biodefense Indication.

The market for medical radiation countermeasures grew dramatically following the September 11, 2001 terrorist attacks and the subsequent use of anthrax in a biological attack in the U.S. Terrorist activities worldwide have continued in the intervening years and the possibility of chemical, biological, radiation and nuclear attacks continues to represent a perceived threat for governments world-wide. In addition to the U.S. government, which maintains a national stockpile of products for emergency use (the "National Stockpile"), we believe the potential markets for the sale of radiation countermeasures include U.S. federal, state and local governments, including defense and public health agencies; foreign governments; non-governmental organizations; multinational corporations; transportation and security companies; healthcare providers; and, nuclear power facilities.

Acute high-dose whole body or significant partial body radiation exposure induces massive apoptosis of cells of the hematopoietic system and gastrointestinal tract, which leads to ARS, a potentially fatal condition. The threat of ARS is primarily limited to emergency/defense scenarios and is significant given the possibility of nuclear/radiological accidents, warfare or terrorist incidents. The scale of possible exposure (number of people affected) has been estimated by the U.S. government to be in the range of 500,000 based on a modeled 10-kiloton device detonation in New York City. We believe the significant limitations of the two currently approved treatments to deal with such an event make entolimod a compelling product candidate. It is not feasible or ethical to test the efficacy of entolimod as a radiation countermeasure in humans. Therefore, we are developing entolimod under the FDA’s Animal Rule guidance (see "– Government Regulation – Animal Rule"). The Animal Rule authorizes the FDA to rely on data from animal studies to provide evidence of a product’s effectiveness under circumstances where there is a reasonably well-understood mechanism for the activity of the product. Under these requirements, and with the FDA’s prior agreement, medical countermeasures, like entolimod, may be approved for use in humans based on evidence of effectiveness derived from appropriate animal studies, evidence of safety derived from studies in humans and any additional supporting data.

Our pivotal efficacy study conducted in 179 non-human primates demonstrated with a high degree of statistical significance that injection of a single dose of entolimod given to rhesus macaques 25 hours after exposure to a 70% lethal dose of total body irradiation improved animal survival by nearly three-fold compared to the control group. Dose-dependence of entolimod’s efficacy was demonstrated with doses above the minimal efficacious dose establishing a plateau at approximately 75% survival at 60 days after irradiation, as compared to 27.5% survival in the placebo-treated group.

Our pivotal study conducted in 160 non-irradiated non-human primates established the dose-dependent effect of entolimod on biomarkers for animal-to-human dose conversion.

Our clinical studies of entolimod in 150 healthy human subjects demonstrated the safety profile of entolimod and established the dose-dependent effect of entolimod on efficacy biomarkers in humans. In these studies, and in the oncology studies in which 63 cancer patients have been administered to date, transient decrease in blood pressure and elevation of liver enzymes were observed along with transient mild to moderate flu-like syndrome. Such effects are the most common adverse events and they are linked to up-regulation of cytokines that are also biomarkers for efficacy.

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As discussed above, we are seeking pre-EUA authorization from the FDA for entolimod, for which we submitted an application in 2015 and have had subsequent discussions with the FDA. Also, as noted above, we have submitted a MAA to the EMA for entolimod as a MRC in Europe. The MAA was evaluated in the end of the fourth quarter of 2017 and is currently under review by the EMA.

The FDA has granted Fast Track status to entolimod (see "– Government Regulation – Fast Track Designation") and Orphan Drug status for prevention of death following a potentially lethal dose of total body irradiation during or after a radiation disaster (see "– Government Regulation – Orphan Drug Designation"). In January 2016, the EMA granted entolimod Orphan Drug Designation for treatment of ARS (see "– Government Regulation – Orphan Drug Designation") and has validated the Pediatric Investigational Plan ("PIP") that is required prior to an MAA approval.

Entolimod Oncology Indication

In addition to developing entolimod as a MRC for reducing the risk of death from ARS, we have initiated an evaluation of entolimod's potential to treat cancer by activating the innate and adaptive immune response in patients. In preclinical studies, entolimod produced tissue-specific activation of innate immune responses via interaction with its receptor, TLR5, and the liver was identified as a primary mediator of entolimod activity. Entolimod has also been shown to have a direct cytotoxic effect on tumors expressing TLR5 in animal models. Evaluations of local administration of entolimod in organs expressing TLR5, such as the bladder, have also been performed in animal models.

We completed a Phase 1 open-label, dose-escalation trial of entolimod in 26 patients with advanced cancer in the U.S. in 2015 and an extension study in additional patients in Russia receiving the entolimod drug product formulation proposed for commercialization is ongoing. The data for the U.S. study were presented at the 2015 annual meeting of ASCO. Twenty-six patients with previously treated metastatic cancers, including colorectal, non-small cell lung, anal and urothelial bladder tumors were enrolled in the study. Stable disease for more than 6 weeks was observed in 8 patients with various cancer types; among these, 3 patients (with anal, colorectal and urothelial cancers) had maintenance of stable disease for more than 12 weeks. Patients exhibited $CD8^+$ T-cell activation with stable or decreased levels of myeloid-derived suppressive cells, accompanied by increased immunostimulatory cytokines (G-CSF, IL-6, and IL-8). The tolerability profile in patients with advanced cancer was similar to that observed in two previously conducted studies in 150 healthy subjects receiving entolimod. As expected with activation of innate immune pathways, common adverse events were flu-like symptoms and fever, with some patients having transient, spontaneously resolving tachycardia, hypotension and hyperglycemia. Overall, treatment with entolimod was well tolerated.

In addition, we have conducted a clinical study of the safety and tolerability of entolimod as a neo-adjuvant therapy before cancer surgery in treatment-naïve patients with primary colorectal cancer. Because the study included older patients (up to 84 years) and those with other health conditions, the trial further extended an understanding of entolimod effects in a broader population of study patients. The safety profile of the drug appeared generally similar to the profiles previously identified in healthy subjects and patients with cancer who participated in prior studies. Increases in plasma cytokines and alterations of blood cells were observed that appeared consistent with TLR5-mediated mobilization and trafficking of immunocytes to peripheral tissues, although changes in tumor immune cell infiltration appeared to be independent of treatment group in this exploratory study. This study was partially funded by the MPT development contract.

In February 2016, we announced the publication of studies elucidating immunotherapeutic mechanisms through which entolimod suppresses metastasis in Proceedings of the National Academy of Sciences of the United States of America ("PNAS"). The studies presented in the PNAS publication decipher the cascade of cell-signaling events that are triggered by entolimod activation of the TLR5 pathway in the liver. The data also define the functional roles of natural killer ("NK"), dendritic, and CD8+ T-cells in the drug’s activity as a suppressor of metastasis. The studies demonstrate that entolimod administration induces chemokines that attract NK cells to the liver via a CXCR3-dependent mechanism. CXCR3 is a chemokine receptor that is highly expressed on both NK and effector T cells and plays an important role in cell trafficking to tissues. Once in the liver, NK cells, which are components of the innate immune system, engage an adaptive antitumor immune response through dendritic cell activation. This NK-to-dendritic cell

interaction generates CD8+ T-cell-dependent antitumor memory that results in tumor rejection upon animal re-challenge with tumor. Importantly, localized antitumor effects in the liver combine with systemic responses that enable suppression of metastasis to the lung.

We have exclusive worldwide development and commercialization rights to entolimod.

CBLB612

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CBLB612 is a proprietary compound based upon a natural activator of another tissue-specific component of the innate immune system, the TLR2/TLR6 heterodimeric receptor. CBLB612 is a pharmacologically optimized synthetic molecule that structurally mimics naturally occurring lipopeptides of Mycoplasma (a genus of parasitic bacteria) and activates NF-kB pro-survival and immunoregulatory signaling pathways via specific binding to TLR2 on a subset of body tissues and cell types that express this receptor. Preclinical studies have shown that CBLB612 stimulates white blood cell regeneration.

In July 2015, we reported the results of a Phase 1, single-center, blind, placebo-controlled, single ascending dose study in Russia evaluating the safety and tolerability of CBLB612 in healthy volunteers and measuring response of various hematopoietic stem and progenitor cell types in order to gain a preliminary estimate of the drug's hematopoietic stem cell stimulatory efficacy. Analysis of data from the 56 healthy volunteers enrolled in the study indicates that single subcutaneous injections of CBLB612 in doses ranging from 0.5 to 4 micrograms were generally well-tolerated, with the 4 microgram dose identified as the maximum tolerated dose. Observed adverse events were typically mild or moderate in severity, transient, and related to the drug's mechanism of action. Single injections of CBLB612 induced dose-dependent increases in absolute neutrophil counts lasting approximately 20 hours. Administrations of CBLB612 also resulted in rapid, dose-dependent increases of plasma levels of the specified cytokines. Cytokine levels returned to baseline levels several hours after administration of the drug.

Recently we have completed dosing in a Phase 2, randomized, placebo-controlled clinical study of CBLB612 as myelosuppressive prophylaxis in patients with breast cancer receiving doxorubicin-cyclophosphamide chemotherapy. Objectives of the study included evaluation of the depth and duration of chemotherapy-induced neutropenia and thrombocytopenia, progenitor cell and reticulocyte mobilization, changes in plasma cytokines, and safety. While the efficacy hypothesis of the study was not confirmed, the CBLB612 appeared to be generally well tolerated at the doses used in this clinical trial.

These two clinical studies were supported by a 139 million ruble matching funds development contract that we received in July 2012 from MPT (see Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations"). We currently have no active clinical studies ongoing with CBLB612.

We licensed CBLB612 to Zhejiang Hisun Pharmaceutical Co., Ltd. for the territories of China, Taiwan, Hong Kong, and Macau. We have rest-of-world development and commercialization rights to CBLB612.

Mobilan

Mobilan is the lead product candidate of Panacela. Mobilan is a recombinant non-replicating adenovirus that directs expression of TLR5 and its agonistic ligand, a secretory non-glycosylated version of entolimod. In preclinical studies, delivery of Mobilan to tumor cells results in constitutive autocrine TLR5 signaling and strong activation of the innate immune system with subsequent development of adaptive anti-tumor immune responses.

Panacela has completed enrollment of patients in a Phase 1 multicenter, randomized, placebo-controlled, single-blinded study in Russia evaluating single injections of ascending doses of Mobilan administered directly into the prostate of patients with prostate cancer. In addition, in July 2016, recruitment of prostate cancer patients was opened in another multicenter, randomized, double-blind study in Russia evaluating the safety, pharmacodynamics, and efficacy of different treatment regiments of Mobilan.

These studies were partially funded under a 149 million ruble matching funds development contract that Panacela received in October 2013 from MPT which concluded as of December 31, 2016.

Panacela holds exclusive worldwide development and commercialization rights to Mobilan.

As of December 31, 2017, we owned 67.57% of Panacela.

CBL0137

CBL0137 is a small molecule with a multi-targeted mechanism of action that may be broadly useful for the treatment of many different types of cancer and is being developed by Incuron. During 2015 we sold our remaining equity interest in Incuron but retain a 2% royalty on (a) product sales of CBL0137, (b) consideration received by Incuron from a licensee or sublicensee, and (c) consideration received in connection with the first change of control of Incuron. Incuron's royalty obligations continue until April 29, 2025.

CBL0137 may offer greater efficacy and substantially lower risk for the development of drug resistance than conventional chemotherapeutic agents. CBL0137 inhibits MYC protein, NF-kB, Heat Shock Factor Protein-1

("HSF-1"), and Hypoxia-inducible factor 1-alpha; these are transcription factors that are important for the viability of many types of tumors. The drug also activates tumor suppressor protein p53 by modulating intracellular localization and activity of chromatin remodeling complex Facilitates Chromatin Transcription ("FACT"). CBL0137 has been shown to be efficacious in animal models of colon, lung, breast, renal,

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pancreatic, head and neck and prostate cancers; melanoma; glioblastoma; and neuroblastoma. It has also been shown to be efficacious in animal models of hematological cancers, including lymphoma, leukemia and multiple myeloma. Incuron is currently enrolling patients with advanced, solid tumors into two Phase 1 studies, one in Russia evaluating the oral administration of CBL0137 and one in the U.S. evaluating the intravenous administration of CBL0137. These studies are designed to investigate the safety, pharmacokinetics, pharmacodynamics, and antitumor activity of CBL0137. Incuron is conducting these parallel evaluations of oral and intravenous routes of administration and continuous low-dose versus interrupted high-dose schedules to reduce the company's developmental risk by fully characterizing the clinical pharmacology of CBL0137.

In addition, Incuron is recruiting patients into a Phase 1 dose escalation and cohort-expansion study of intravenous formulation of CBL0137 in previously treated patients with hematological cancers in the U.S.

Incuron holds worldwide development and commercialization rights to CBL0137.

STRATEGIC PARTNERSHIPS

Since our inception, strategic alliances and collaborations have been integral to our business. We have exclusively licensed rights in each of our technologies from The Cleveland Clinic and RPCI and maintain innovative partnerships with each. We have also leveraged the experience, contacts and knowledge of our founders to engage financial partners in Russia. Through these partnerships we have collaborated with world-class scientists to develop our novel technologies and accessed non-traditional funding sources, including U.S. federal and foreign government contracts and project-oriented funding. We have received project-oriented funding from Rusnano through the formation of Panacela.

Both Panacela, as well as our wholly owned subsidiary BioLab 612, maintain operations in Russia and benefit from programs supporting domestic pharmaceutical industry development in Russia.

The Cleveland Clinic

In July 2004, CBLI entered into an exclusive license agreement with The Cleveland Clinic ("The Cleveland Clinic License"), pursuant to which CBLI was granted an exclusive license to The Cleveland Clinic's research base underlying our therapeutic platform. We amended The Cleveland Clinic License effective as of September 22, 2011, pursuant to which we were granted an exclusive license to The Cleveland Clinic's research base underlying certain product candidates in development by Panacela ("Panacela Products"), including Mobilan and several earlier-stage compounds that are not currently material to our business. In consideration for The Cleveland Clinic License, we agreed to issue The Cleveland Clinic common stock and make certain milestone, royalty, and sublicense royalty payments as described below.

The Cleveland Clinic License requires milestone payments, which may be credited against future royalties owed to The Cleveland Clinic, as described in the table below.

Milestone Description	For Products Limited to Biodefense Uses	For All Other Products (Maximum amount)*
For any IND filing for a product	$ 50,000	$ 50,000
For any product entering Phase II clinical trials or similar registration	100,000	250,000
For any product entering Phase III clinical trials	—	700,000
For any product license application, BLA or NDA Filing for	350,000	1,500,000

a product**		
Upon regulatory approval permitting any product to be sold to the commercial market	1,000,000	4,000,000

Maximum amounts listed for achievement of milestone in U.S. If milestones are reached in another country first, * milestone payments will be prorated for certain products under the license based on the market size for the product in such country as that market relates to the then current U.S. market.

** New Drug Application ("NDA")

We have also agreed to make milestone payments of up to approximately $6.5 million for each Panacela Product that achieves certain developmental and regulatory milestones, provided that if CBLI or an affiliate of CBLI and The Cleveland Clinic jointly own the Panacela Product, the milestone amounts will be reduced by 50%.

The Cleveland Clinic License requires royalty payments of (a) 2% of net sales of any product candidate under a licensed patent solely owned by The Cleveland Clinic; and (b) 1% of net sales of any product candidate under a licensed patent that is jointly

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owned by The Cleveland Clinic and CBLI or an affiliate of CBLI. Further, if CBLI receives upfront sublicense fees or sublicense royalty payments for sublicenses granted by CBLI to third parties for any licensed patents solely owned by The Cleveland Clinic, CBLI will pay The Cleveland Clinic (i) 35% of such fees if the sublicense is granted prior to filing an IND application, (ii) 20% of such fees if the sublicense is granted after an IND filing but prior to final approval of the Product License Application or NDA, or (iii) 10% of such fees if the sublicense is granted after final approval of the relevant Product License Application or NDA, provided that such sublicense fees shall not be less than 1% of net sales. The above sublicense fees and sublicense royalty payments are reduced by 50% if The Cleveland Clinic and CBLI or an affiliate of CBLI jointly own the licensed patent.

Through December 31, 2017, CBLI had paid The Cleveland Clinic $150,000 for milestone payments on products limited to biodefense uses, and $400,000 for all other products.

As each patent covered by The Cleveland Clinic License expires, the license agreement will terminate as to such patent. The Cleveland Clinic may terminate The Cleveland Clinic License upon a material breach by us, as specified in the agreement. However, we may avoid such termination if we cure the breach within 90 days of receipt of a termination notice. CBLI may terminate The Cleveland Clinic License in its entirety or any specific patent licensed under the agreement by giving at least 90 days written notice of such termination to The Cleveland Clinic. The agreement will, subject to certain exceptions, automatically terminate with respect to a licensed product if The Cleveland Clinic does not receive a royalty payment for more than 1-year after the payment of royalties has begun.

Roswell Park Cancer Institute

We have entered into a number of agreements with RPCI relating to the licensure and development of our product candidates including:

- Two exclusive license and option agreements effective December 2007 and September 2011;
- Various sponsored research agreements entered into between January 2007 to present; and
- Clinical trial agreements for the conduct of our Phase 1 entolimod oncology study and Incuron’s Phase 1 CBL0137 intravenous administration study.

In December 2007, CBLI entered into an agreement with RPCI pursuant to which CBLI has an option to exclusively license any technological improvements to our foundational technology developed by RPCI for the term of the agreement. We believe our option to license additional technology under the agreement potentially provides us with access to technology that may supplement our product pipeline in the future. In consideration for this option and exclusive license, we agreed to make certain milestone, royalty and sublicense royalty payments. Additionally, RPCI may terminate the license upon a material breach by us. However, we may avoid such termination if we cure the breach within 90 days of receipt of a termination notice. The license does not have a specified term; however, as each patent covered by this license agreement expires, the royalties to be paid on each product relating to the licensed patent shall cease.

In September 2011, Panacela entered into an agreement with RPCI (the "Panacela-RPCI License") to exclusively license from RPCI certain rights to the Panacela Products, including Mobilan and several earlier-stage compounds that are not currently material to our business, and to non-exclusively license from RPCI certain know-how relating to the aforementioned product candidates for the limited purposes of research and development and regulatory, export and other government filings. Additionally, under the Panacela-RPCI License, Panacela has a right to exclusively license from RPCI (i) any technological improvements to the Panacela Products developed by RPCI before September 2016, and (ii) any technology jointly developed by Panacela and RPCI. In consideration for the Panacela-RPCI License, Panacela agreed to issue RPCI common stock and to make certain milestone, royalty and sublicense royalty payments as described below.

The Panacela-RPCI License requires milestone payments for developmental and regulatory milestones reached in the U.S. of up to approximately $2.5 million for each Panacela Product that achieves certain developmental and regulatory milestones. Additionally, Panacela will owe additional payments of up to approximately $275,000 for each other country where a licensed Panacela Product achieves similar milestones.

The Panacela-RPCI License requires royalty payments on net sales based on percentages in the low single digits. In addition, if Panacela sublicenses any of the licensed Panacela Products, Panacela will owe sublicensing fees ranging

from 5% to 15% of any fees received from the sublicensee by Panacela or an affiliate depending upon whether or not an IND has been filed or final approval of the relevant NDA has been obtained for such licensed product.

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As each patent covered by the Panacela-RPCI License expires, the license agreement will terminate as to such patent. In addition, the license agreement will terminate with respect to the licensed know-how after 20 years. RPCI may terminate the license upon a material breach by us, as specified in the agreement. However, we may avoid such termination if we cure the breach within 90 days of receipt of a termination notice (or 30 days if notice relates to non-payment of amounts due to RPCI). Panacela may terminate the license agreement in whole or as to any specific patent licensed under the agreement by giving at least 60 days written notice of such termination to RPCI. The agreement will, subject to certain exceptions, automatically terminate with respect to a licensed Panacela Product if Panacela fails to market, promote and otherwise exploit the licensed technology so that RPCI does not receive a royalty payment during any 12-month period after the first commercial sale of such licensed product.

We have also entered into a number of sponsored research agreements with RPCI pursuant to which both parties have sponsored research to be conducted by the other party. Under our sponsored research agreement with RPCI, title to any inventions under the agreement is determined in a manner substantially similar to U.S. patent law, and we have the option to license from RPCI, on an exclusive basis, the right to develop any inventions of RPCI (whether solely or jointly developed) under the agreement for commercial purposes. In addition, the sponsored research agreement may be terminated by one party if the other party becomes subject to bankruptcy or insolvency, the other party is debarred by the U.S. government or the other party breaches a material provision of the agreement and fails to cure such breach within 20 days of receiving written notice.

Under the sponsored research agreements with RPCI, we own any invention that is described in our research plan, co-own any inventions not described in our research plan that are made by Dr. Andrei Gudkov, our Chief Scientific Officer, and RPCI owns any other inventions not described in our research plan. We further have a right to exclusively license from RPCI any invention developed under such sponsored research agreements that are owned by RPCI. Such sponsored research agreements with RPCI expire in 2018, although we expect to enter into similar future arrangements.

We entered into an asset transfer and clinical trial agreement with RPCI for the conduct, by RPCI, of our Phase 1 clinical trial to evaluate the safety and pharmacokinetic profile of entolimod in patients with advanced cancers, which has now been largely completed.

Rusnano

In 2011, we formed Panacela with Rusnano to carry out a complete cycle of development and commercialization in Russia for the treatment of oncological, infectious or other diseases. We invested $3.0 million in Panacela preferred shares and warrants, and, together with certain third-party owners, assigned and/or exclusively licensed, as applicable, to Panacela worldwide development and commercialization rights to five preclinical product candidates in exchange for Panacela common shares. Rusnano invested $9.0 million in Panacela preferred shares and warrants. In 2013, Rusnano loaned Panacela $1.5 million through a convertible term loan (the "Panacela Loan"). In December of 2015, together with Rusnano, we recapitalized Panacela to fully retire the Panacela Loan and certain other trade payables. Rusnano maintained its ownership percentage in Panacela, while CBLI's ownership stake grew to 66.77%. As of December 31, 2017, we had an ownership stake of approximately 67.57%.

INTELLECTUAL PROPERTY

Our intellectual property consists of patents, trademarks, trade secrets, and know-how. Our ability to compete effectively depends in large part on our ability to obtain patents for our technologies and products, maintain trade secrets, operate without infringing the rights of others, and prevent others from infringing our proprietary rights. We will be able to protect our proprietary technologies from unauthorized use by third parties only to the extent that they are covered by valid and enforceable patents, or are effectively maintained as trade secrets. As a result, patents or other proprietary rights are an essential element of our business. Our patent portfolio includes patents and patent applications with claims directed to compositions of matter, pharmaceutical formulations, and methods of use. Some of our issued patents, and the patents that may be issued based on our patent applications, may be eligible for patent life extension under the Drug Price Competition and Patent Term Restoration Act of 1984 in the U.S., supplementary protection certificates in the European Union ("E.U.") or similar mechanisms in other countries or territories. The following are the patent positions relating to our product candidates as of December 31, 2017.

In the U.S., we have 22 issued patents or allowed patent applications relating to our clinical-stage programs expiring on various dates between 2024 and 2032 as well as numerous pending patent applications and foreign counterpart patent filings which relate to our proprietary technologies. These patents and patent applications include claims directed to compositions of matter and methods of use.

We have 17 issued or allowed U.S. patents covering entolimod, which expire between 2024 and 2032. These patents include composition of matter claims, as well as method of use claims relating to our biodefense and oncology indications, reducing effects of chemotherapy, and treatment of reperfusion injuries. In addition, we have pending U.S. patent applications related to compositions of matter, oncology methods of use, and others biodefense methods, which, if issued, will expire between 2025 and 2035.

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We have 4 issued or allowed U.S. patents covering CBLB612 and related agents, which expire between 2026 and 2027. These patents include composition of matter and methods of use claims.

We have one issued U.S. patent covering compositions of matter for various vectors, including Mobilan, which expires in 2032. We also have issued or allowed patents covering Mobilan and related agents, which expire in 2030 that cover a broad list of international territories including the E.U., Australia, Japan and Russia. These patents include composition of matter and methods of use claims.

In addition, as of December 31, 2017, we had more than a hundred additional patents and patent applications filed worldwide. Any patents that may issue from our pending patent applications would expire between 2024 and 2035, excluding patent term extensions. These patents and patent applications disclose compositions of matter and methods of use.

Our policy is to seek patent protection for the inventions that we consider important to the development of our business. We intend to continue to file patent applications to protect technology and compounds that are commercially important to our business, and to do so in countries where we believe it is commercially reasonable and advantageous to do so. We also rely on trade secrets to protect our technology where patent protection is deemed inappropriate or unobtainable. We protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, collaborators, and contractors.

RESEARCH AND DEVELOPMENT

As of December 31, 2017, our research and development group, including Russian-based personnel, consisted of 10 individuals. Our research and development focuses on management of outsourced preclinical research, clinical trials, and manufacturing technologies. We invested $5.0 million and $6.5 million in research and development in the years ended December 31, 2017 and 2016, respectively.

SALES AND MARKETING

We currently do not have marketing, sales, or distribution capabilities. We do, however, currently have worldwide development and commercialization rights for products arising out of substantially all of our programs, as discussed above. In order to commercialize any of these drugs, if and when they are approved for sale, we will need to enter into partnerships for the commercialization of the approved product(s) or develop the necessary marketing, sales, and distribution capabilities.

COMPETITION

The biotechnology and biopharmaceutical industries are characterized by rapid technological developments and intense competition. This competition comes from both biotechnology and major pharmaceutical companies. Many of these companies have substantially greater financial, marketing, and human resources than we do, including, in some cases, considerably more experience in clinical testing, manufacturing, and marketing of pharmaceutical products. There are also academic institutions, governmental agencies, and other research organizations that are conducting research in areas in which we are working. They may also develop products that may be competitive with our product candidates, either on their own or through collaborative efforts. We expect to encounter significant competition for any products we develop. Our product candidates' competitive position among other biotechnology and biopharmaceutical companies will be based on, among other things, time to market, patent position, efficacy, safety, reliability, availability, patient convenience, ease of delivery, manufacturing cost, and price. In these cases, we may not be able to commercialize our product candidates or achieve a competitive position in the market. This would adversely affect our business.

Specifically, the competition for entolimod and our other clinical-stage product candidates includes the following:

Entolimod Biodefense Indication

Product candidates for treatment of the ARS face significant competition for U.S. government funding for both development and procurement of medical countermeasures and must satisfy government procurement requirements for biodefense products. Currently the only FDA-approved drugs for the treatment of ARS are filgrastim (Neupogen™) and peg-filgrastim (Neulasta™). Filgrastim (granulocyte colony-stimulating factor ("GCS-F") and peg-filgrastim (PEGylated form of GCS-F) stimulate neutrophils and may reduce infection related to ARS. Unlike entolimod, these drugs do not improve platelet counts or lessen bleeding, and do not ameliorate gastrointestinal dysfunction due to ARS. In label-supporting survival studies, filgrastim and peg-filgrastim were administered repeatedly and treatment

was accompanied by laboratory monitoring and required intensive supportive care (including platelet transfusions). By contrast, entolimod survival studies included only a single injection, without any intensive medical support, which we believe makes it significantly more suitable for use in a mass-casualty situation.

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The U.S. government has purchased several colony stimulating factors to treat injuries to bone marrow in victims of radiological or nuclear accidents or acts of terrorism for the National Stockpile. In 2013 it obligated $157 million to Amgen USA, Inc., for 541,000 doses of Neupogen® and $37 million to Sanofi-Aventis U.S., LLC for 66,000 doses of Leukine® (granulocyte-macrophage colony-stimulating factor). In October 2016, the U.S. government purchased an additional $37.6 million worth of Leukine® and peg-filgrastim, Neulasta®, from Amgen USA, Inc., for another $37.7 million. The U.S government also announced that it continues to work with Sanofi-Aventis to support the studies needed to request FDA approval of Leukine®. These purchases were made using funding and authority provided through the Project BioShield Act of 2004. Under the Project BioShield Act, the U.S. government supports the advanced development and procurement of new medical countermeasures - drugs, vaccines, diagnostics, and medical supplies - to protect health against chemical, biological, radiological and nuclear threats.

In addition to the colony-stimulating factors, we are aware of a number of companies also developing radiation countermeasures to treat the effects of ARS including: Aeolus Pharmaceuticals, Araim Pharmaceuticals, Inc., Cellerant Therapeutics, Inc., Humanetics Corporation, Neumedicines, Inc., Pluristem Therapeutics, Inc, RxBio, Inc., and Soligenix, Inc. Although their approaches to treatment of ARS are different, we compete with these companies for U.S. government development funding and may ultimately compete with them for U.S. and foreign government purchase and stockpiling of radiation countermeasures.

Additionally, our ability to sell to the government also can be influenced by competition from the products, such as Neupogen®, Neulasta®, and Leukine®, which were previously purchased by the U.S. government for the National Stockpile.

Entolimod Immuno-Oncology Program and Mobilan

Immunotherapies are major drivers of commercial growth in cancer therapy and constitute the primary competition for a potential immunotherapeutic agent like entolimod or Mobilan. Examples of marketed drugs in these categories include: pembrolizumab (Keytruda®) (Merck) indicated for advanced melanoma, metastatic non-small cell lung cancer ("NSCLC"), recurrent or metastatic head and neck squamous cell carcinoma, refractory classical Hodgkin lymphoma, and urothelial carcinoma; nivolumab (Opdivo®) (Bristol-Myers Squibb Company) for advanced melanoma and metastatic squamous NSCLC, hepatocellular carcinoma, head and neck squamous cell carcinoma , renal cell carcinoma, classical Hodgkin lymphoma, urothelial carcinoma, and high or mismatch repair deficient metastatic colorectal cancer; ipilimumab (Yervoy®) (Bristol-Myers Squibb) of unresectable or metastatic melanoma, and for non-muscle-invasive bladder cancer. These drugs may be appropriate combination partners for entolimod or Mobilan in the appropriate treatment settings. However, these drugs may also be competitors for the market share in the treatment of various tumor types.

CBLB612

Mitigation of chemotherapy-induced myelosuppression is a multi-billion-dollar commercial category within oncology. Filgrastim, (Neupogen®) (Amgen), and peg-filgrastim (Neulasta®) (Amgen), or various biosimilar versions of these drugs, are the current standards for treatment of this condition. Filgrastim and pegfilgrastim are well established as neutrophil support factors in patients with cancer undergoing myelosuppressive chemotherapy.

MANUFACTURING

Our product candidates are biologics and small molecules that can be readily synthesized by processes that we have developed. We do not own or operate manufacturing facilities for the production of our product candidates for preclinical, clinical or commercial quantities. We rely on third-party manufacturers, and in most cases only one third party, SynCo Bio Partners B.V., to manufacture critical raw materials, drug substance and final drug product for our research, preclinical development and clinical trial activities. Commercial quantities of any drugs we seek to develop will have to be manufactured in facilities and by processes that comply with the FDA and other regulations, and we plan to rely on third parties to manufacture commercial quantities of products we successfully develop.

GOVERNMENT REGULATION

Government authorities in the U.S. and in other countries regulate the research, development, testing, manufacture, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, quality control, labeling, and export and import of pharmaceutical products such as those that we are developing. We cannot provide assurance that

any of our product candidates will prove to be safe or effective, will receive regulatory approvals, or will be successfully commercialized.

U.S. Drug Development Process

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In the U.S., the FDA regulates drugs and drug testing under the Federal Food, Drug, and Cosmetic Act and in the case of biologics, also under the Public Health Service Act. Our product candidates must follow processes consistent with these legislations before they may be marketed in the U.S.:

- preclinical laboratory and animal tests performed in compliance with current GLPs;
- development of manufacturing processes which conform to current Good Manufacturing Practices ("GMPs");
- submission and acceptance of an Investigational New Drug ("IND") application which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in compliance with current Good Clinical Practices ("GCPs") to establish the safety and efficacy of the proposed drug for its intended use; or in the case of entolimod, for reducing the risk of death following exposure to potentially lethal radiation, we are required to perform pivotal animal studies in compliance with GLP and some aspects of GCP to establish efficacy; and
- submission to and review and approval by the FDA of a NDA or BLA prior to any commercial sale or shipment of a product; or in the case of entolimod a pre-EUA prior to sales to the National Stockpile.

Nonclinical testing. Nonclinical testing includes laboratory evaluation of a product candidate, its chemistry, formulation, safety and stability, as well as animal studies to assess the potential safety and efficacy of the product candidate. The conduct of the nonclinical tests must comply with federal regulations and requirements including cGMP and GLP. Prior to the initiation of GLP animal studies, including our pivotal studies for development of entolimod under the Animal Rule, an Institutional Animal Care and Use Committee ("IACUC") at each testing site must review and approve each study protocol and any amendments thereto.

We must submit to the FDA the results of nonclinical studies, which may include laboratory evaluations and animal studies, together with manufacturing information and analytical data, and the proposed clinical protocol for the first clinical trial of the drug as part of an IND. An IND is a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to the interstate shipment and administration of any new drug that is not the subject of an approved pre-EUA, NDA, or BLA. Nonclinical tests and studies can take several years to complete, and despite completion of those tests and studies, the FDA may not permit clinical testing to begin.

The IND process. The FDA requires a 30-day waiting period after the submission of an IND application before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period or at any time thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a "clinical hold" that may affect one or more specific studies or all studies conducted under the IND. In the case of a clinical hold, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials placed on hold can begin or continue. The IND application process may be extremely costly and could substantially delay development of our products. Moreover, positive results of preclinical animal tests do not necessarily indicate positive results in clinical trials.

Prior to the initiation of each clinical study, the corresponding clinical protocol must be submitted to the IND and to an independent Institutional Review Board ("IRB") at each medical site proposing to conduct the clinical trial. The IRB must review and approve each study protocol, and any amendments thereto, and study subjects must sign an informed consent. Protocols include, among other things, the objectives of the study, dosing procedures, subject selection, and exclusion criteria and the parameters to be used to monitor patient safety. Progress reports of work performed in support of IND studies must be submitted at least annually to the FDA. Reports of serious, unexpected, and related adverse events must be submitted to the FDA and the investigators in a timely manner.

Clinical trials. Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The drug is introduced into healthy human subjects or patients with advanced disease (in the case of certain inherently toxic products for severe or life-threatening diseases such as cancer) and tested for safety, dosage tolerance, absorption, distribution, metabolism, and excretion;
-

Phase 2: Involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage; and

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- Phase 3: Clinical trials are undertaken to further evaluate dosage, clinical efficacy, and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide, if appropriate, an adequate basis for product labeling.

We cannot be certain that we will successfully complete any phase of clinical testing of our product candidates within any specific time period, if at all. Clinical testing must meet the requirements of IRB oversight, informed consent and GCP. The FDA, the sponsor, or the IRB at each institution at which a clinical trial is being performed may suspend a clinical trial at any time for various reasons, including a belief that the participants are being exposed to an unacceptable health risk.

During the development of a new drug, sponsors are given an opportunity to meet with the FDA at certain points. These meetings typically occur prior to submission of an IND, at the end of Phases 1 and 2 and before NDA or BLA submission. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end-of-Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug.

The NDA or BLA process. If clinical trials are successful, the next step in the drug regulatory approval process is the preparation and submission to the FDA of an NDA or BLA, as applicable. The NDA or BLA, as applicable, is a vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for marketing and sale in the U.S. The NDA or BLA, as applicable, must contain a description of the manufacturing process and quality control methods, as well as results of preclinical tests, toxicology studies, clinical trials and proposed labeling, among other things. A substantial user fee must also be paid with the application, unless an exemption applies. Every newly marketed pharmaceutical must be the subject of an approved NDA or BLA.

Upon submission of an NDA or BLA, the FDA will make a threshold determination of whether the application is sufficiently complete to permit review, and, if not, will issue a refuse-to-file letter. If the application is accepted for filing, the FDA will attempt to review and take action on the application in accordance with performance goal commitments the FDA has made in connection with the prescription drug user fee law in effect at that time. Current timing commitments under the user fee law vary depending on whether an NDA or BLA is for a priority drug or not, and in any event are not a guarantee that an application will be approved or even acted upon by any specific deadline. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the NDA or BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by the recommendation of an advisory committee. The FDA may deny or delay approval of applications that do not meet applicable regulatory criteria or if the FDA determines that the data do not adequately establish the safety and efficacy of the drug. In addition, the FDA may approve a product candidate subject to the completion of post-marketing studies, commonly referred to as Phase 4 trials, to monitor the effect of the approved product. The FDA may also grant approval with restrictive product labeling, or may impose other restrictions on marketing or distribution such as the adoption of a Risk Evaluation and Mitigation Strategies ("REMS").

Manufacturing and post-marketing requirements. If approved, a pharmaceutical may only be marketed in the dosage forms and for the indications approved in the NDA or BLA, as applicable. Special requirements also apply to any samples that are distributed in accordance with the Prescription Drug Marketing Act. The manufacturers of approved products and their manufacturing facilities are subject to continual review and periodic inspections by the FDA and other authorities where applicable, and must comply with ongoing requirements, including the FDA’s GMP requirements. Once the FDA approves a product, a manufacturer must provide certain updated safety and efficacy information, submit copies of promotional materials to the FDA, and make certain other required reports. Product and labeling changes, as well as certain changes in a manufacturing process or facility or other post-approval changes, may necessitate additional FDA review and approval. Failure to comply with the statutory and regulatory requirements subjects the manufacturer to possible legal or regulatory action, such as untitled letters, warning letters, suspension of manufacturing, seizure of product, voluntary recall of a product, injunctive action or possible criminal or civil penalties. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval. Because we intend to contract

with third parties for manufacturing of our products, our ability to control third party compliance with FDA requirements will be limited to contractual remedies and rights of inspection. Failure of third party manufacturers to comply with GMP or other FDA requirements applicable to our products may result in, among other things, total or partial suspension of production, failure of the government to grant approval for marketing, and withdrawal, suspension, or revocation of marketing approvals. With respect to post-market product advertising and promotion, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among others, standards for direct-to-consumer advertising, promoting drugs for uses or in patient populations that are not described in the drug’s approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the Internet. Failure to comply with FDA requirements can have negative consequences, including adverse

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publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

The FDA's policies may change, and additional government regulations may be enacted which could prevent or delay regulatory approval of our potential products. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the U.S. or abroad.

Animal Rule

In 2002, the FDA amended its requirements applicable to BLAs/NDAs to permit the approval of certain drugs and biologics that are intended to reduce or prevent serious or life-threatening conditions based on evidence of safety from clinical trial(s) in healthy subjects and effectiveness from appropriate animal studies when human efficacy studies are not ethical or feasible. These regulations, which are known as the "Animal Rule", authorize the FDA to rely on animal studies to provide evidence of a product's effectiveness under circumstances where there is a reasonably well-understood mechanism for the activity of the agent. Under these requirements, and with the FDA's prior agreement, drugs used to reduce or prevent the toxicity of chemical, biological, radiological, or nuclear substances may be approved for use in humans based on evidence of effectiveness derived from appropriate animal studies and any additional supporting data. Products evaluated under this rule must demonstrate effectiveness through pivotal animal studies, which are generally equivalent in design and robustness to Phase 3 clinical studies. The animal study endpoint must be clearly related to the desired benefit in humans and the information obtained from animal studies must allow for selection of an effective dose in humans. Safety under this rule is established under preexisting requirements, including safety studies in both animals (toxicology) and humans. Products approved under the Animal Rule are subject to additional requirements including post-marketing study requirements, restrictions imposed on marketing or distribution and requirements to provide information to patients.

We intend to utilize the Animal Rule in seeking marketing approval for entolimod as a medical radiation countermeasure because we cannot ethically expose humans to lethal doses of radiation. Other countries may not at this time have established criteria for review and approval of these types of products outside their normal review process, i.e. there is no "Animal Rule" equivalent in countries other than the U.S., but some may have similar policy objectives in place for these product candidates. Given the nature of nuclear and radiological threats, we do not believe that the lack of established criteria for review and approval of these types of products in other countries will significantly inhibit us from pursuing sales of entolimod to foreign countries.

All data obtained from the preclinical studies and clinical trials of entolimod, in addition to detailed information on the manufacture and composition of the product, would be submitted in a BLA to the FDA for review and approval for the manufacture, marketing and commercial shipment of entolimod.

Emergency Use Authorization

The Commissioner of the FDA, under delegated authority from the Secretary of the U.S. Department of Health and Human Services ("DHHS"), may, under certain circumstances, issue an Emergency Use Authorization ("EUA"), that would permit the use of an unapproved drug product or unapproved use of an approved drug product. Before an EUA may be issued, the Secretary must declare an emergency based on one of the following grounds:

- a determination by the Secretary of Department of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a specified biological, chemical, radiological, or nuclear agent or agents;
- a determination by the Secretary of the DoD that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to U.S. military forces of attack with a specified biological, chemical, radiological, or nuclear agent or agents; or
- a determination by the Secretary of DHHS of a public health emergency that effects, or has the significant potential to effect, national security and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agent.

In order to be the subject of an EUA, the FDA Commissioner must conclude that, based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating or preventing a

disease attributable to the agents described above, that the product's potential benefits outweigh its potential risks and that there is no adequate approved alternative to the product.

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Although an EUA cannot be issued until after an emergency has been declared by the Secretary of DHHS, the FDA strongly encourages an entity with a possible candidate product, particularly one at an advanced stage of development, to contact the FDA center responsible for the candidate product before a determination of actual or potential emergency. Such an entity may submit a request for consideration that includes data to demonstrate that, based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition. This is called a pre-EUA submission and its purpose is to allow FDA review considering that during an emergency, the time available for the submission and review of an EUA request may be severely limited.

We submitted a pre-EUA in 2015 in order to inform and expedite the FDA's issuance of an EUA, should one become necessary in the event of an emergency. The FDA does not have review deadlines with respect to pre-EUA submissions. Additionally, there is no guarantee that the FDA will agree that entolimod meets the criteria for EUA, or, if they do agree, that such agreement by the FDA will lead to procurement by the U.S. or other governments or further development funding.

Public Readiness and Emergency Preparedness Act

The Public Readiness and Emergency Preparedness Act (the "PREP Act"), provides immunity for manufacturers from all claims under state or federal law for "loss" arising out of the administration or use of a "covered countermeasure." However, injured persons may still bring a suit for "willful misconduct" against the manufacturer under some circumstances. "Covered countermeasures" include security countermeasures and "qualified pandemic or epidemic products", including products intended to diagnose or treat pandemic or epidemic disease, such as pandemic vaccines, as well as treatments intended to address conditions caused by such products. For these immunities to apply, the Secretary of DHHS must issue a declaration in cases of public health emergency or "credible risk" of a future public health emergency. Since 2007, the Secretary of DHHS has issued nine declarations under the PREP Act to protect countermeasures that are necessary to prepare the nation for potential pandemics or epidemics from liability. We believe, in the event of an emergency, were the FDA to issue an EUA for entolimod, it would receive protection under the terms of the PREP Act.

Fast Track Designation

Entolimod has been granted Fast Track designation by the FDA for reducing the risk of death following total body irradiation. The FDA's Fast Track designation program is designed to facilitate the development and review of new drugs, including biological products that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs for the conditions. Fast Track designation applies to a combination of the product and the specific indication for which it is being studied. Thus, it is the development program for a specific drug for a specific indication that receives Fast Track designation. The sponsor of a product designated as being in a Fast Track drug development program may engage in early communication with the FDA, including timely meetings and early feedback on clinical trials and may submit portions of an NDA or BLA on a rolling basis rather than waiting to submit a complete application. Products in Fast Track drug development programs also may receive priority review or accelerated approval, under which an application may be reviewed within six months after a complete NDA or BLA is accepted for filing or sponsors may rely on a surrogate endpoint for approval, respectively. The FDA may notify a sponsor that its program is no longer classified as a Fast Track development program if the Fast Track designation is no longer supported by emerging data or the designated drug development program is no longer being pursued. Receipt of Fast Track designation does not guarantee that we will experience a faster development process, review or approval as compared to conventional FDA procedures or that we will qualify or be able to take advantage of the FDA's expedited review procedures.

Orphan Drug Designation

Entolimod has been granted Orphan Drug designation by the FDA for prevention of death following a potentially lethal dose of total body irradiation. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition which is defined as one affecting fewer than 200,000 individuals in the U.S. or more than 200,000 individuals where there is no reasonable expectation that the product development cost will be recovered from product sales in the U.S. Orphan Drug designation must be requested before submitting an NDA or BLA and does not convey any advantage in, or shorten the duration of, the regulatory review and approval

process.

If an Orphan Drug-designated product subsequently receives the first FDA approval for the disease for which it has such designation, the product will be entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances for seven years as compared to five years for a standard new drug approval. As referenced above, we have received Orphan Drug designation for entolimod. We intend to seek Orphan Drug designation for our other products as appropriate, but an Orphan Drug designation may not provide us with a material commercial advantage.

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Entolimod has also been granted Orphan Drug Designation in the E.U. As in the U.S., the E.U. may grant orphan drug status for specific indications if the request is made before an application for marketing authorization is made. The E.U. considers an orphan medicinal product to be one that affects less than five of every 10,000 people in the E.U. A company whose application for orphan drug designation in the E.U. is approved is eligible to receive, among other benefits, regulatory assistance in preparing the marketing application, protocol assistance and reduced application fees. Orphan drugs in the E.U. also enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication, unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan designated product.

Foreign Drug Development and Approval Regulation

In addition to regulations in the U.S., we are and will be subject to a variety of foreign regulations governing clinical trials and will be subject to a variety of foreign regulation governing commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from country to country. Other countries, at this time, do not have an equivalent to the Animal Rule and, as a result, do not have established criteria for review and approval of these types of products outside their normal review process, but some countries may have similar policy objectives in place for these product candidates.

European Drug Development and Approval Regulations. The EMA is an E.U. agency responsible for the evaluation of medical products. Like the FDA, the EMA mandates preclinical testing, three phases of clinical trials, and a final approval procedure as part of the drug development process. In the U.S., however, clinical trials and market approval are conducted under the FDA supervision and no authorizations can be obtained at the state level. In the E.U., clinical trials are initiated on a member state level and market authorization may follow a centralized, decentralized, or a mutual recognition pathway. The centralized pathway allows a candidate drug to be reviewed by the EMA and recommended to the European Commission for final approval. This pathway is mandatory for therapeutics treating specific conditions, such as cancer, HIV/ AIDS, diabetes, and rare diseases. In the decentralized procedure, applications for market authorization by the European Commission can be simultaneously requested from each member state. In the mutual recognition procedure, a drug is first evaluated by a single member state and the assessment may be used to obtain market authorization in another member state. This process is common for the approval of generic pharmaceuticals.

Another difference in drug evaluation process is the metrics adopted for measuring drug efficacy. While both the FDA and the EMA recognize the importance of patient-reported outcomes, the EMA focuses on global assessments of patient-reported quality of life, whereas the FDA focuses on symptom-specific measures and requires early planning and cooperation with patient groups to determine the most important symptom concerns.

Market approval in the E.U. is further complicated by additional regulations adopted by some of the member states that ultimately determine which drug can actually be marketed in that specific state. For example, a drug approved by the EMA also needs approval from the Medicines and Healthcare Products Regulatory Agency in order to be marketed in the United Kingdom. In addition, the National Institute for Health and Care Excellence has to assess potential cost concerns to determine whether the same drug can be purchased by the National Health Service for patient use. Finally, the individual E.U. member states control sales and promotional activities of all pharmaceuticals. Consequently, the national regulatory authorities are responsible for regulating pharmaceutical advertising, which is instead less restrictive in the United States.

Despite the submission of identical clinical data supporting the same drug, the EMA and FDA can come to different evaluations and conclusions. Between 1995 and 2008, 20% of oncological pharmaceuticals were approved by either the FDA or the EMA, but not both, and 28% of approved drugs had significant variations in the label wording.

Russian Drug Development and Approval Regulations. Our Russian activities are regulated by the Ministry of Health of the Russian Federation ("Minzdrav"). This federal executive authority is responsible for developing state policies as well as normative and legal regulations in the healthcare and pharmaceutical industries, including policies and

regulations regarding the quality, efficacy and safety of pharmaceutical products.

In addition, the Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation, known as Roszdravnadzor, is the executive authority subordinated to Minzdrav, which, among other things, (i) performs control and surveillance of certain activities, including preclinical and clinical trials, and monitors compliance with the state standards for medical products and pharmaceutical activities; (ii) issues licenses for the manufacture of drug products and pharmaceutical activities; (iii) grants allowance for clinical trials, use of new medical technologies and import and export of medical products, including import of products for use in clinical trials; and (iv) reviews and grants or denies registrations of medical products for sale in Russia.

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The principal statute that governs our activities in Russia is the Federal Law No. 61-FZ "On Medicine Circulation" of April 12, 2010 (as amended). This law regulates the research, development, testing, preclinical and clinical studies, state registration, quality control, manufacture, storage, transporting, export and import, licensing, advertisement, sale, transfer, utilization and destruction of medical products within Russia, among other things. All medical products must be registered in Russia and comply with stringent safety and quality controls and testing.

In addition, our activities are subject to a number of other Russian laws, regulations and orders relating to the drug development activities, taxation, corporate governance, employment and other areas. In particular, the incorporation, corporate governance, shareholders' rights, and contractual matters related to our Russian subsidiaries and joint ventures are governed by the Civil Code of the Russian Federation and the Federal Law No. 14-FZ "On Limited Liability Companies" of February 8, 1998 (as amended). In accordance with this legislation we must comply with certain shareholders’ and board of directors’ approval requirements, including those applicable to major and interested party transactions.

Also, pursuant to the Russian Labor Code, our Russian subsidiaries and joint ventures must enter into employment contracts with each employee, afford them at least 28 days paid vacation period, limit the working week to 40 hours per week and follow the code’s specific procedures in case of employment termination.

EMPLOYEES

As of February 12, 2018, CBLI and its consolidated subsidiaries had 19 employees, 13 of whom are located in the U.S. and 6 of whom are located outside of the U.S. Of these employees, 12 were employed on a full-time basis and 7 were employed on a part-time basis.

ENVIRONMENT

We have made, and will continue to make, expenditures for environmental compliance and protection. Expenditures for compliance with environmental laws and regulations have not had, and are not expected to have, a material effect on our capital expenditures, results of operations, or competitive position.

Item 1A. Risk Factors

Risks Relating to our Financial Position and Need for Additional Financing

We will require substantial additional financing in order to meet our business objectives.

Since our inception, most of our resources have been dedicated to preclinical and clinical research and development ("xR&D") of our product candidates. In particular, we are currently developing several product candidates, each of which will require substantial funds to complete. We believe that we will continue to expend substantial resources for the foreseeable future in the development of these product candidates. These expenditures will include costs associated with preclinical and clinical R&D, obtaining regulatory approvals, product manufacturing, corporate administration, business development, and marketing and selling for approved products. In addition, other unanticipated costs may arise. As of December 31, 2017, our cash, cash equivalents, and short-term investments amounted to $8.8 million. We believe that our existing cash, cash equivalents, and marketable securities will allow us to fund our operating plan for at least 12 months beyond the filing date of this Annual Report on Form 10-K. Because the outcome and timing of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts of capital necessary to successfully complete the development and commercialization of our product candidates. Our future capital requirements depend on many factors, including:

- the number and characteristics of the product candidates we pursue;
- the scope, progress, results, and costs of researching and developing our product candidates, and conducting pre-clinical and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the cost of commercialization activities for any of our product candidates that are approved for sale, including marketing, sales, and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize;

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- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the success of the pre-EUA submission we made with the FDA, the success of the MAA we made with the EMA, and any future submissions in the U.S., E.U., and other countries that we may make; and
- the timing, receipt, and amount of sales of, or royalties on, our future products, if any.

When our available cash and cash equivalents become insufficient to satisfy our liquidity requirements, or if and when we identify addit