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