

BRAINSTORM CELL THERAPEUTICS INC.  
Form 424B3  
May 10, 2016

**Filed Pursuant to Rule 424(b)(3)**

**Registration Statement No. 333-186516**

**Prospectus Supplement No. 12**

**(to Prospectus dated August 13, 2013, as supplemented by Prospectus Supplement No. 1 dated August 16, 2013, Prospectus Supplement No. 2 dated November 14, 2013, Prospectus Supplement No. 3 dated March 27, 2014, Prospectus Supplement No. 4 dated May 13, 2014, Prospectus Supplement No. 5 dated August 12, 2014, Prospectus Supplement No. 6 dated August 27, 2014, Prospectus Supplement No. 7 dated November 13, 2014, Prospectus Supplement No. 8 dated March 26, 2015, Prospectus Supplement No. 9 dated May 18, 2015, Prospectus Supplement No. 10 dated August 13, 2015 and Prospectus Supplement No. 11 dated November 17, 2015)**

**BRAINSTORM CELL THERAPEUTICS INC.**

**23,529,411 Units**

**Each Unit Consisting of One Share of Common Stock**

**and**

**0.75 of a Warrant to Purchase One Share of Common Stock**

This prospectus supplement, together with the prospectus listed above, is to be used by certain holders of the above-referenced securities or by their pledgees, donees, transferees or other successors-in-interest in connection with the offer and sale of such securities.

This prospectus supplement updates and should be read in conjunction with the prospectus dated August 13, 2013 (as supplemented to date), which is to be delivered with this prospectus supplement. Such documents contain information that should be considered when making your investment decision. To the extent there is a discrepancy between the information contained herein and the information in the prospectus, the information contained herein supersedes and replaces such conflicting information.

This prospectus supplement consists of Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 9, 2016.

Our common stock is traded on the Nasdaq Capital Market, under the symbol “BCLI”. On May 9, 2016, the last reported sales price for our common stock was \$2.11 per share. We do not intend to list the warrants on any securities exchange or other trading market and we do not expect that a public trading market will develop for the warrants.

**Investing in the Company’s securities involves risks. See “Risk Factors” beginning on page 5 of the Prospectus, as supplemented or amended by the prospectus supplements filed to date, to read about factors you should consider.**

**NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.**

The date of this Prospectus Supplement No. 12 is May 10, 2016

**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

WASHINGTON, D.C. 20549

**FORM 10-K**

**x ANNUAL REPORT UNDER SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

**FOR THE FISCAL YEAR ENDED DECEMBER 31, 2015**

**“ TRANSITION REPORT UNDER SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

**FOR THE TRANSITION PERIOD FROM \_\_\_\_\_ TO \_\_\_\_\_**

*COMMISSION FILE NUMBER 001-36641*

**BRAINSTORM CELL  
THERAPEUTICS INC.**

(Exact Name of Registrant as specified in its charter)

Delaware 20-7273918  
(State or other jurisdiction of (I.R.S. Employer  
incorporation or organization) Identification No.)

3 University Plaza Drive, Suite 320  
Hackensack, NJ 07601  
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (201) 488-0460

Securities registered under Section 12(b) of the Act:

<b>Title of each class</b>	<b>Name of each exchange on which registered</b>
Common Stock, \$0.00005 par value	NASDAQ Stock Market LLC

Securities registered under Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.  
Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act.

Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes  No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes  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 the 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. "

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

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller reporting company   
(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act).

Yes  No

The approximate aggregate market value of the voting and non-voting common equity held by non-affiliates of the issuer as of June 30, 2015 (the last business day of the registrant's most recently completed second fiscal quarter), was \$57,972,791.

As of March 4, 2016, the number of shares outstanding of the registrant's Common Stock, \$0.00005 par value per share, was 18,654,040.

**BRAINSTORM CELL THERAPEUTICS INC.**

**ANNUAL REPORT ON FORM 10-K**

**YEAR ENDED DECEMBER 31, 2015**

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## **PART I**

### **SPECIAL NOTE**

*Unless otherwise specified in this Annual Report on Form 10-K, all references to currency, monetary values and dollars set forth herein shall mean United States (U.S.) dollars.*

### **SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

*This Annual Report contains numerous statements, descriptions, forecasts and projections, regarding Brainstorm Cell Therapeutics Inc. and its potential future business operations and performance, including statements regarding the market potential for treatment of neurodegenerative disorders such as ALS, the sufficiency of our existing capital resources for continuing operations in 2016, the safety and clinical effectiveness of our NurOwn® technology, our clinical trials of NurOwn® and its related clinical development, and our ability to develop collaborations and partnerships to support our business plan. These statements, descriptions, forecasts and projections constitute “forward-looking statements,” and as such involve known and unknown risks, uncertainties, and other factors that may cause our actual results, levels of activity, performance and achievements to be materially different from any results, levels of activity, performance and achievements expressed or implied by any such “forward-looking statements.” Some of these are described under “Risk Factors” in this Annual Report. In some cases you can identify such “forward-looking statements” by the use of words like “may,” “will,” “should,” “could,” “expects,” “hopes,” “anticipates,” “believes,” “intends,” “plans,” “estimates,” “predicts,” “likely,” “potential,” or “continue” or the negative of any of these terms or similar words. These “forward-looking statements” are based on certain assumptions that we have made as of the date hereof. To the extent these assumptions are not valid, the associated “forward-looking statements” and projections will not be correct. Although we believe that the expectations reflected in these “forward-looking statements” are reasonable, we cannot guarantee any future results, levels of activity, performance or achievements. It is routine for our internal projections and expectations to change as the year or each quarter in the year progresses, and therefore it should be clearly understood that the internal projections and beliefs upon which we base our expectations may change prior to the end of each quarter or the year. Although these expectations may change, we may not inform you if they do and we undertake no obligation to do so, except as required by applicable securities laws and regulations. We caution investors that our business and financial performance are subject to substantial risks and uncertainties. In evaluating our business, prospective investors should carefully consider the information set forth under the caption “Risk Factors” in addition to the other information set forth herein and elsewhere in our other public filings with the Securities and Exchange Commission (“SEC”).*

### **Item 1. BUSINESS.**

#### **Company Overview**



We are a biotechnology company developing novel adult stem cell therapies for debilitating neurodegenerative disorders such as Amyotrophic Lateral Sclerosis (“ALS”, also known as Lou Gehrig’s disease), Multiple Sclerosis (“MS”), and Parkinson’s disease (“PD”) among others. These diseases for the most part have no or limited treatment options and as such represent unmet medical needs. We believe that NurOwn®, our proprietary process for the propagation of Mesenchymal Stem Cells (“MSC”) and their differentiation into neurotrophic factor- (“NTF”) secreting cells (“MSC-NTF”), and their transplantation at, or near, the site of damage, offers the hope of more effectively treating neurodegenerative diseases. Our core technology was developed in collaboration with Prof. Daniel Offen of the Felsenstein Medical Research Center of Tel Aviv University and the late Prof. Eldad Melamed, who passed away in October 2015, and was former head of Neurology of the Rabin Medical Center and former member of the Scientific Committee of the Michael J. Fox Foundation for Parkinson's Research . Our wholly-owned Israeli subsidiary, Brainstorm Cell Therapeutics Ltd. (the “Israeli Subsidiary”), holds rights to commercialize the technology, through a licensing agreement with Ramot at Tel Aviv University Ltd. (“Ramot”), the technology transfer company of Tel Aviv University, Israel. We currently employ 17 employees in Israel and 3 in the United States.

### **Our Proprietary Technology**

Our NurOwn® technology is based on a novel differentiation protocol which induces differentiation of the bone marrow-derived mesenchymal stem cells into neuron-supporting cells, MSC-NTF cells, capable of releasing several neurotrophic factors, including Glial-derived neurotrophic factor (“GDNF”), Brain-derived neurotrophic factor (“BDNF”), Vascular endothelial growth factor (“VEGF”) and Hepatocyte growth factor (“HGF”) which are critical for the growth, survival and differentiation of developing neurons. GDNF is one of the most potent survival factors known for peripheral neurons. VEGF and HGF have been reported to have important neuro-protective effects in ALS.

Our approach to treatment of neurodegenerative diseases with autologous adult stem cells includes a multi-step process beginning with harvesting of undifferentiated stem cells from the patient's own bone marrow, and concluding with transplantation of differentiated, neurotrophic factor-secreting mesenchymal stem cells (MSC-NTF) into the same patient – intrathecally and/or intramuscularly. Intrathecal (injection into the cerebrospinal fluid) transplantation consists of injection by a standard lumbar puncture; there is no need for a laminectomy, which is an invasive, orthopedic spine operation to remove a portion of the vertebral bone, as required by technologies in which cells are implanted directly into the spinal cord. Intramuscular (injection directly into muscle) transplantation is performed via a standard injection procedure as well.

Our proprietary, production process for induction of differentiation of human bone marrow derived mesenchymal stem cells into differentiated cells that produce NTF (MSC-NTF) for clinical use is conducted in full compliance with current Good Manufacturing Practice (“cGMP”).

Our proprietary technology is licensed to and developed by our Israeli Subsidiary.

### ***The NurOwn® Transplantation Process***

- Bone marrow aspiration from patient;
- Isolation and propagation of the mesenchymal stem cells;
- Differentiation of the mesenchymal stem cells into neurotrophic-factor secreting (MSC-NTF) cells; and
- Autologous transplantation into the patient’s spinal cord and/or muscle tissue.

### ***Differentiation before Transplantation***

The ability to induce differentiation of autologous adult mesenchymal stem cells into MSC-NTF cells *before* transplantation is unique to NurOwn®, making it the first-of-its-kind for treating neurodegenerative diseases.

The specialized cells secrete neurotrophic factors that may lead to:

- Protection of existing motor neurons;
- Promotion of motor neuron growth; and
- Re-establishment of nerve-muscle interaction.

### ***Autologous (Self-transplantation)***

The NurOwn® approach is autologous, or self-transplanted, using the patient’s own stem cells. In autologous transplantation there is no risk of rejection and no need for treatment with immunosuppressive agents, which can cause severe and/or long-term side effects. In addition, the use of adult stem cells is free of controversy associated with the use of embryonic stem cells in some countries.

## The ALS Program

NurOwn® is in clinical development for the treatment of ALS. It has been granted Fast Track designation by the U.S. Food and Drug Administration (the “FDA”) for this indication, and has been granted Orphan Status in both the United States and in Europe. We have completed two clinical trials of NurOwn® in patients with ALS at Hadassah Medical Center (“Hadassah”) in collaboration with Professor Dimitrios Karussis, who served as the principal investigator on these studies. We also have an agreement with Hadasit Medical Research Services and Development Ltd., a subsidiary of the Hadassah Medical Organization, pursuant to which Hadassah provides the Israeli Subsidiary with lab services relating to studies of NurOwn®. The first study, a Phase 1/2 safety and efficacy study of NurOwn® in ALS patients administered either intramuscularly or intrathecally, was initiated in June 2011 after receiving approval from the Israeli Ministry of Health (“MoH”). In March 2013, Professor Karussis presented some of the data from this trial at the American Academy of Neurology Annual Meeting. The trial results demonstrated the safety of NurOwn® as well as signs of efficacy on both the ALS Functional Rating Score (“ALSFRRS-R”) and Forced Vital Capacity (“FVC”).

In January 2013, the Israeli MoH approved the second study, a Phase 2a combined (intramuscular and intrathecal) treatment, dose-escalating trial, which we also conducted at Hadassah in collaboration with Prof. Karussis. On September 27, 2013, we announced that we had completed treatment of 12 patients in our ALS Phase 2a NurOwn® dose-escalating clinical trial. An interim safety summary for the first 12 patients in the study was submitted to the Hadassah Medical Center Ethical Committee about two month after transplantation of the 12th patient. On December 10, 2013, we announced that Prof. Karussis presented some of his preliminary findings from this trial at the 24<sup>th</sup> International Symposium on ALS/MND in Milan, Italy. In June 2014, Professor Karussis presented interim data from this study at the Joint Congress of European Neurology in Istanbul, Turkey. The last follow-up visits in this study occurred in September 2014. On January 5, 2015, the Company presented final top line data from this study in a press release and investor conference call. The results of this study confirmed the safety profile observed in the earlier Phase 1/2 trial, with the vast majority of adverse events being low-grade. There were two deaths and two serious adverse events, all of which were deemed by the investigators to be unrelated to treatment. Subjects in this study showed a meaningful reduction in the rate of disease progression for the three and six months after treatment, compared to the three months prior to treatment.

In January 2016, the Company announced that the results of the two completed studies were published in the Journal of the American Medical Association (JAMA) Neurology medical journal. The results of these studies show that NurOwn® can slow disease progression in ALS

In December 2013, the Company submitted an Investigational New Drug (“IND”) application to the FDA for NurOwn® in ALS, and on April 28, 2014, the FDA approved commencement of the Company’s randomized, double-blind, placebo controlled multi-center Phase 2 clinical trial of NurOwn® in ALS patients. On June 6, 2014, the Company announced that this clinical trial began, with the enrollment of the first patient at Massachusetts General Hospital in Boston, Massachusetts. The trial is also being conducted at the University of Massachusetts Memorial Hospital in Worcester, Massachusetts and the Mayo Clinic in Rochester, Minnesota. For this study, NurOwn® production occurs at the Connell and O’Reilly Cell Manipulation Core Facility at the Dana Farber Cancer Institute in Boston, Massachusetts and at the Human Cellular Therapy Lab at the Mayo Clinic. This study is designed to enroll 48 patients randomized in a 3:1 ratio to receive NurOwn® or placebo.

In February 2015, the Company announced that the Data Safety Monitoring Board (“DSMB”) for the multi-center U.S. Phase 2 clinical trial reviewed the safety data collected through a cutoff date in January 2015, and did not find any lab abnormalities, adverse events or significant protocol deviations that would be cause for concern and therefore approved continuation of the trial as planned.

On August 11, 2015, the Company announced that it had completed enrollment achieving the target of 48 subjects to be enrolled in its ongoing randomized, double-blind placebo-controlled Phase 2 clinical trial of NurOwn® in ALS. In November 2015, the Company announced that the DSMB for the multi-center U.S. Phase 2 clinical trial reviewed the safety data collected through a cutoff date in October 2015, which included 47 of the 48 patients enrolled in the study. No treatment-related serious adverse events (SAEs) were reported for the study. Furthermore, the DSMB did not identify any adverse events, lab abnormalities or significant protocol deviations that would be cause for concern.

Results from this trial are not expected until the middle of 2016.

In January 2016, the Company entered into a collaborative agreement with Hadassah Medical Center in Jerusalem, Israel, to conduct the planned multi dose Phase 2 trial with NurOwn® in ALS.

This Phase 2 multi dose study will be BrainStorm's third clinical trial conducted at Hadassah and is designed to provide guidance in preparing a Phase 3 program for NurOwn® stem cell based therapy in ALS. The trial is expected to enroll up to 24 patients who will receive three consecutive stem cell transplantations in order to explore the safety and efficacy of a multi dose treatment. The trial has been approved by the Hadassah's Helsinki Committee and is now awaiting the approval of the Israeli MoH.

The agreement was signed with Hadassah, through its technology transfer company Hadasit Medical Research Services and Development Co. Ltd. The Principal Investigator will be Professor Dimitrios Karussis, MD, PhD, head of the Unit of Neuroimmunology and Cell Therapies at Hadassah's Department of Neurology, who served as Principal Investigator in Brainstorm’s prior ALS studies.

Future development of NurOwn® in ALS will require additional clinical trials, including a Phase 3 FDA-approved multi dose trial.

### **Future Development Plans**

In addition to its active clinical program in ALS, the Company is reviewing the potential clinical development of NurOwn® in other neurodegenerative disorders, such as Parkinson's disease, Huntington's disease, and multiple sclerosis. The Company has conducted preclinical research in additional neurologic disease areas, including autism. In January 2015, the Company announced positive results from preclinical studies of NurOwn™ in the BTBR mouse model of autism. The BTBR mouse exhibits several stereotypical behavioral characteristics that resemble behaviors seen in autism spectrum disorders, including repetitive behaviors, altered social interactions, cognitive rigidity and impaired adaption to environment. The Company is planning a possible Phase 1 study for autism in 2016.

In addition, the Company is engaged in a number of research initiatives to improve the scale and efficiency of NurOwn® production and to improve the stability of NurOwn®, which is currently produced in clean room facilities close to the clinical trial sites, where the cells are administered to patients. In January 2013, we announced the development of a proprietary method for cryopreservation, or freezing, of cells, which will enable long-term storage, and production of repeat patient doses of NurOwn® without the need for additional bone marrow aspirations. We believe that cryopreservation will enable us to create a personalized NurOwn® stem cell bank for each patient, for ongoing, repeated treatments. We are planning to use cryopreserved cells in the upcoming Phase 2 clinical trial that will involve administration of multiple doses of NurOwn®.

We are also engaged in collaboration with Octane Biotech Inc. ("Octane"), a Canadian firm that focuses on culture systems for cell and tissue therapy, to develop a NurOwn® bioreactor. On June 27, 2014, the Company announced that this collaboration has successfully developed a sophisticated Alpha prototype of the NurOwn® Bioreactor, utilizing a customized disposable cartridge that is dedicated to the intricacies of the Company's NurOwn® process. Based on this first working prototype, the Company and Octane are advancing to the next stage of development with a goal of eventually qualifying a bioreactor for full clinical use. In December 2015, the Company and Octane announced that they have made significant progress toward the development of a novel bioreactor for industrial-scale manufacture of NurOwn® and had completed key development activities related to the customization of specific features of Octane's Cocoon™ instrumentation platform to enable efficient delivery of NurOwn® stem cell therapy.

## Corporate Information

We are incorporated under the laws of the State of Delaware. Our principal executive offices are located at 3 University Plaza Drive, Suite 320, Hackensack, NJ 07601, and our telephone number is (201) 488-0460. We maintain an Internet website at <http://www.brainstorm-cell.com>. The information on our website is not incorporated into this Annual Report on Form 10-K.

## History

The Company was incorporated under the laws of the State of Washington on September 22, 2000, under the name Wizbang Technologies, Inc. and acquired the right to market and sell a digital data recorder product line in certain states in the U.S. Subsequently, the Company changed its name to Golden Hand Resources Inc. On July 12, 2004, the Company entered into a research and license agreement with Ramot to acquire certain stem cell technology and decided to discontinue all activities related to the sales of the digital data recorder product. In November 2004, the Company changed its name from Golden Hand Resources Inc. to Brainstorm Cell Therapeutics Inc. to better reflect its new line of business in development of novel cell therapies for neurodegenerative diseases. In October 2004, the Company formed its wholly-owned subsidiary, Brainstorm Cell Therapeutics Ltd. in Israel. On December 18, 2006, the stockholders of the Company approved a proposal to change the state of incorporation of the Company from the State of Washington to the State of Delaware. The reincorporation was completed on December 21, 2006 through the merger of the Company into a newly formed, wholly-owned Delaware subsidiary of Brainstorm, also named Brainstorm Cell Therapeutics Inc. On February 19, 2013, the Israeli Subsidiary formed its wholly-owned subsidiary, Brainstorm Cell Therapeutics UK Ltd. in the United Kingdom (the "UK Subsidiary"). A reverse stock split of the Company's shares of Common Stock by a ratio of 1-for-15 was effected on September 15, 2014 at 11:59 p.m. pursuant to an amendment to the Company's Certificate of Incorporation approved by the stockholders of the Company on August 14, 2014. Unless otherwise indicated, all share numbers and exercise prices in this Annual Report on Form 10-K are split-adjusted.

The Company's shares of Common Stock were approved for uplisting to the NASDAQ Capital Market, and commenced trading on the NASDAQ Capital Market when trading began on September 30, 2014. The Company's Common Stock trades under the ticker symbol "BCLI."

## Recent Developments

### *Securities Offerings*

On June 19, 2014, the Company, pursuant to a June 13, 2014 securities purchase agreement entered into with a group of investors, including several healthcare-focused funds (the “Investors”), effected a private placement of Common Stock and warrants to purchase Common Stock. The Company received gross proceeds of \$10.5 million, resulting from the issuance and sale of 2.8 million shares of Common Stock at a price per share of \$3.75. The Investors received warrants to purchase up to 2.8 million shares of Common Stock at an exercise price of \$5.22 per share (the “2014 Warrants”). The shares of Common Stock issued in the private placement and underlying the 2014 Warrants were registered with the SEC effective July 24, 2014.

On January 8, 2015, holders of 2014 Warrants to purchase an aggregate of approximately 2.5 million shares of our Common Stock exercised their warrants which resulted in approximately \$13 million in proceeds to the Company. As part of this exercise of warrants, we issued new warrants to the holders to purchase up to an aggregate of 3.8 million shares of Common Stock at an exercise price of \$6.50.

#### *Amendment to Certificate of Incorporation to Decrease Authorized Shares*

On August 31, 2015, the Company filed a Certificate of Amendment of Certificate of Incorporation (the “Certificate of Amendment”) with the Secretary of State of the State of Delaware to reduce the number of authorized shares of the Company’s Common Stock from 800,000,000 to 100,000,000. The Certificate of Amendment had been approved by the Board of Directors on August 28, 2015 and by the Company’s stockholders at the Company’s 2015 Annual Meeting of Stockholders on August 26, 2015.

#### *Governmental Grants*

In February 2015, we received non-dilutive grants amounting to approximately \$1.76 million, from the Israeli Office of the Chief Scientist (“OCS”) bringing the cumulative amount of grants received as of December 31, 2015 to approximately \$5.82 million. As of December 31, 2015, we recorded an additional grants receivable of \$418,000 relating to expenses incurred by us as of that date and, in December 2015 we submitted a request for additional grants relating to our expected 2016 expenses amounting to approximately \$1.8 million. This request is now under consideration of the OCS and we expect to obtain approval of our request before June 30, 2016.

With regards to any funding received from the OCS, we are obligated to pay royalties to the OCS, amounting to 3% to 3.5% of revenues (subject to the relevant regulations, as amended from time to time) derived from sales of the products funded with the OCS grant, depending on the origin of the products’ production. Such royalty payments shall be up to an amount equal to 100% of the grant received. The grant is linked to the exchange rate of the U.S. dollar and bears interest of Libor per annum.

Any plan approved by the OCS research committee for grant funding is subject to Israel's Encouragement of Industrial Research and Development Law, 5744 – 1984 (“R&D Law”), which, among others, restricts the transfer of any know-how (as further defined therein) and the transfer of the manufacture of the outcome product of such Approved Plan outside of Israel.

The OCS research committee may, in special cases, approve the transfer abroad of know-how or any right thereof, derived from research and development conducted under the Approved Plan in Israel, in exchange for receiving know-how from the party abroad; provided, however, that such exchange is towards joint and new research and development.

The OCS research committee may, in special cases and on grounds to be recorded, approve a request to transfer outside of Israel, the manufacturing or the rights to manufacture a product developed within the framework of the Approved Plan; provided, however, that in exchange for such approval, the OCS shall be entitled to, *inter alia*, payment of increased royalties due to the transfer of such manufacturing rights

#### *Chief Financial Officer and Controller*

On May 13, 2015, the Company entered into a Separation Agreement (the “Separation Agreement”) with Liat Sossover, the Company's Chief Financial Officer pursuant to which Ms. Sossover's employment with the Company ended June 30, 2015, and all Company stock options previously issued to Ms. Sossover and outstanding ceased to further vest after June 30, 2015 but such options, to the extent already vested on June 30, 2015, continued to be outstanding and exercisable until December 31, 2015. Ms. Sossover's role as Chief Financial Officer and Treasurer and all other officer positions with the Company and its affiliates was terminated effective upon execution of the Separation Agreement. Ms. Sossover's departure was not the result of any disagreement with the Company regarding its operations, policies, practices or related matters.

On May 13, 2015, the Company appointed its Controller, Alla Patlis, as its Interim Chief Financial Officer, which she served as until July 30, 2015. In connection with her appointment as Interim Chief Financial Officer of the Company, Ms. Patlis' employment agreement was amended to increase her salary to NIS 20,000 (approximately U.S. \$5,100) per month, effective March 1, 2015.

The Company appointed Yoram Bibring as its Chief Financial Officer and Treasurer, effective July 30, 2015. On July 30, 2015, the Company and Yoram Bibring entered into an employment agreement which sets forth the terms of Mr. Bibring's employment (the “Bibring Employment Agreement”). Pursuant to the Bibring Employment Agreement, Yoram Bibring was paid a salary at the annual rate of \$225,000. Mr. Bibring also receives other benefits that are generally



made available to the Company's employees. The Employment Agreement provides that if within twelve months after a Change of Control (as defined in the Bibring Employment Agreement), Mr. Bibring's employment is terminated for any reason other than for cause, disability or death, or by Mr. Bibring due to a Change of Control Termination (as defined in the Bibring Employment Agreement), the Company shall pay Mr. Bibring a payment equal to his target bonus compensation for the year in which the Change of Control occurs, and his base salary for twelve months following the date of such termination.

Mr. Bibring also was granted a stock option (the "Bibring Grant") on July 30, 2015 for the purchase of 165,000 shares of the Company's Common Stock at an exercise price equal to \$3.17 per share. Subject to Mr. Bibring's continued service with the Company through the applicable vesting dates, the Initial Grant will vest and become exercisable as to 25% of the Shares on the first anniversary of the Grant Date (the "Initial Vesting Date") and the remainder of the Shares will vest and become exercisable in equal monthly installments on each of the 36 monthly anniversaries following the Initial Vesting Date, and shall vest and become exercisable in full immediately prior to a Change of Control (as defined in the Bibring Employment Agreement). The Bibring Grant was issued outside of the Company's 2014 Stock Incentive Plan as an employment inducement grant.

On November 16, 2015, the Company and Yoram Bibring entered into a First Amendment to Employment Agreement with effect from December 1, 2015 (the "Bibring Amendment"), amending the Bibring Employment Agreement. Pursuant to the Bibring Amendment, Mr. Bibring serves as the Company's Chief Financial Officer on a half-time basis beginning on December 1, 2015. Starting December 1, 2015, the Company pays Mr. Bibring an amount equal to 50% of his previous base salary. As of December 1, 2015, the Bibring Grant was amended such that 82,500 shares were cancelled. The 82,500 remaining shares continue to vest and become exercisable in accordance with the terms of the Bibring Grant: 20,625 shares vest and become exercisable on July 30, 2016 and 2.08333% of the 82,500 shares vest and become exercisable on each monthly anniversary date starting on August 30, 2016 through the fourth anniversary of the grant, so that the 82,500 shares will become fully vested and exercisable on July 30, 2019. Mr. Bibring's vacation was amended to 80 hours per year.

*Chief Executive Officer and Chief Medical Advisor*

On September 22, 2015, the Company appointed Chaim Lebovits as its Chief Executive Officer. On September 22, 2015 Anthony Fiorino, MD, PhD ceased to serve as Chief Executive Officer of the Company. Dr. Fiorino had served as the Company Chief Executive Officer since June 9, 2014.

Effective November 1, 2015, the Company appointed Anthony Fiorino, M.D., Ph.D. as its Chief Medical Advisor. In connection with the appointment, on November 10, 2015 the Company and Dr. Fiorino entered into a First Amendment to Employment Agreement with effect from October 30, 2015 (the "Fiorino Amendment"), amending the Employment Agreement dated as of June 9, 2014 between the Company and Dr. Fiorino (the "Fiorino Employment Agreement").

Pursuant to the Fiorino Amendment, Dr. Fiorino will serve as the Company's Chief Medical Advisor beginning on November 1, 2015. From November 1, 2015 through April 30, 2016, the Company shall continue to pay Dr. Fiorino an amount equal to his current base salary. Any Company stock options issued to Dr. Fiorino that were unvested as of October 30, 2015 were terminated. All stock options that were unvested as of October 30, 2015 shall remain exercisable through and including September 30, 2016. For Chief Medical Advisor services in excess of twenty (20) hours per week during the period from October 31, 2015 to April 30, 2016, the Company shall additionally compensate Dr. Fiorino at the rate of \$150.00 per hour. For Chief Medical Advisor services after April 30, 2016, the Company shall compensate Dr. Fiorino at the rate of \$250.00 per hour. In addition the Company agreed to reimburse Dr. Fiorino's reasonable expenses relating to Company services. Payments and continued exercisability of options are subject to the execution and delivery to the Company of a release of claims by Dr. Fiorino. No additional severance or termination payment will be owed by the Company upon termination of the Fiorino Employment Agreement as modified by the Fiorino Amendment.

On September 28, 2015, the Company's wholly owned subsidiary Brainstorm Cell Therapeutics Ltd. (the "Subsidiary") and Chaim Lebovits entered into an employment agreement which sets forth the terms of Mr. Lebovits' employment (the "Lebovits Employment Agreement"). Pursuant to the Lebovits Employment Agreement, Chaim Lebovits will be paid a salary at the annual rate of \$282,500. Mr. Lebovits will also receive other benefits that are generally made available to the Subsidiary's employees. In addition, he will be provided with a cellular phone and a company car, with all costs including taxes borne by the Subsidiary.

Mr. Lebovits also was granted a stock option (the "Grant") on September 28, 2015 (the "Grant Date") for the purchase of up to 369,619 shares of the Company's Common Stock at a per share exercise price equal to the closing price of the Company's Common Stock (during normal trading hours) on the date of grant. Subject to Mr. Lebovits' continued service with the Company through the applicable vesting dates, the Grant will vest and become exercisable in 12 consecutive equal monthly installments starting with the Grant Date, shall be exercisable for a period of two years

after termination of employment, and shall vest and become exercisable in full 10 days prior to a change of control of the Company if the Grant is not assumed by the acquirer. The Grant was issued under the Company's 2014 Global Share Option Plan.

In addition, a portion of this option representing 83,781 shares of Common Stock may not be exercised until the stockholders of the Company approve a further increase in the number of Common Stock that are reserved for issuance under the Company's 2014 Global Share Option Plan. This portion of the option will be accounted for as granted if and when the approval is obtained.

## **Company Business Strategy**

Our business strategy is to develop and commercialize NurOwn® as a treatment for one or more neurodegenerative diseases. To this end, our efforts are currently directed to several areas in research, development and manufacturing. The ALS program represents our lead indication and is the most advanced in development, hence much of the Company's focus is on this program. Important tasks include the continued execution of the US randomized, double-blind, placebo controlled Phase 2 study, for which we completed enrollment in 2015. In January 2016, we published the results of our Phase 1/2 and Phase 2a studies in the Journal of the American Medical Association (JAMA) Neurology medical journal. Finally, we are making preparations to begin a multi-dose study in ALS patients in Israel in 2016. Beyond ALS, we are seeking to move additional programs into clinical development. To that end, we are reviewing our existing preclinical data, initiating research in new areas like autism, and engaging with regulatory and scientific experts to determine the most attractive clinical opportunities. With regard to manufacturing, as noted above, several ongoing research projects and our collaboration with Octane have a goal of increasing the scale and efficiency of NurOwn® production. Our current strategy is designed to allow the Company to be in a position to run larger, registration studies in the most efficient time frame possible. We may choose to seek a strategic partnership with a pharmaceutical or biotechnology company to support the execution of a registration clinical program.

Our business model calls for significant investments in research and development. Our research and development expenditures (i) in 2015 (before participation by the OCS) were \$6,335,000 which included \$130,000 in stock-based compensation and (ii) in 2014 (before participation by the OCS) were \$6,116,000 which included \$176,000 in stock-based compensation.

## **Stem Cell Therapy**

Our activities are within the stem cell therapy field. Stem cells are non-specialized cells with a potential for both self-renewal and differentiation into cell types with a specialized function, such as muscle, blood or brain cells. The cells have the ability to undergo asymmetric division such that one of the two daughter cells retains the properties of the stem cell, while the other begins to differentiate into a more specialized cell type. Stem cells are therefore central to normal human growth and development, and also are a potential source of new cells for the regeneration of diseased and damaged tissue. Stem cell therapy aims to restore diseased tissue function by the replacement and/or addition of healthy cells by stem cell transplants.

Mesenchymal stem cells ("MSCs") are a type of stem cell that can be obtained easily from adults and used for both autologous (cells administered back to the same person from whom they were harvested) and allogeneic (cells administered to a person different than the person from whom the cells were harvested) approaches. MSCs are "multipotent" cells that can produce more than one type of specialized cell of the body, such as bone, fat, cartilage, and

other types of cells. They secrete factors that promote tissue repair, and decrease inflammatory and immune reactions. The bone marrow is an invaluable source of MSCs and can be accessed through a simple procedure of aspiration. We believe that human MSCs, which are capable of *in vitro* growth and expansion and multipotent differentiation, are a preferable source of therapeutic stem cells.

## **Neurodegenerative Diseases**

Studies of neurodegenerative diseases suggest that symptoms that arise in afflicted individuals are secondary to defects in neuron cell function and neural circuitry. To date, systemic drug delivery approaches have not been effective in the treatment of these diseases possibly due to the blood-brain-barrier. Consequently, alternative approaches for treating neurodegenerative diseases have been attempted, such as transplantation of cells capable of replacing or supplementing the function of damaged neurons at the site of damage. For such cell replacement therapy to work, implanted cells must survive and integrate, both functionally and structurally, within the damaged tissue.

### **Amyotrophic Lateral Sclerosis (ALS)**

ALS, often referred to as “Lou Gehrig's disease,” is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. Motor neurons reach from the brain to the spinal cord and from the spinal cord to the muscles throughout the body. The progressive degeneration of the motor neurons in ALS leads to progressive weakness, respiratory failure and eventually, to death, with a median survival for ALS patients is just 3-4 years from the onset of symptoms. Across the world, the prevalence of ALS is approximately 4-7 per 100,000. It is estimated that as many as 30,000 Americans have the disease at any given time, with a similar number afflicted in Europe. Estimated annual treatment costs for advanced stage patients can be as high as \$200,000 (Source: Alliance for Regenerative Medicine).

Treatment decisions are typically determined by the patient's symptoms and the stage of the disease. Some medications used for ALS patients include:

Riluzole – the only medication approved by the FDA to treat ALS. Riluzole extends the time to death or ventilation by several months; however it has not been shown to improve the daily functioning of ALS patients;

Neurodex – approved by the FDA for the treatment of pseudo-bulbar affect, a type of emotional lability that sometimes develops in ALS patients, as well as in patients with other neurological diseases.

Baclofen or diazepam – not FDA-approved for ALS but sometimes used to control muscle spasms, stiffness or tightening (spasticity) that interfere with daily activities; and

Trihexyphenidyl or amitriptyline – not FDA-approved for ALS but sometimes used to treat patients who have excess saliva or secretions, and emotional changes.

Other medications may be prescribed to help reduce such symptoms as fatigue, pain, sleep disturbances, constipation, and excess saliva and phlegm.

### **Multiple Sclerosis (MS)**

MS is a chronic neurodegenerative disorder that affects the brain and spinal cord. Nerve cells are normally insulated with a protective layer called myelin, which allows nerve signals to travel properly. In MS, the myelin is destroyed (demyelination), causing loss of function of the nerve cells and disrupting transmission of brain messages to various parts of the body. While generally thought to be an autoimmune disease, the exact cause of MS is unknown.

MS can cause blurred vision, slurred speech, tremors, numbness, extreme fatigue, and problems with memory and concentration. Most MS patients experience muscle weakness in their extremities and difficulty with coordination and balance. These symptoms may be severe enough to impair walking or even standing. In the worst cases, MS can produce partial or complete paralysis. Most commonly, the course of MS is waxes and wanes (“relapsing-remitting MS”), with progressive forms of the disease somewhat less common.

There are currently over 2.5 million people with MS worldwide, with roughly 800,000 of these in the U.S. and Europe. Over 10,000 new cases are diagnosed annually in the U.S., with the majority of these in women between the ages of 20 and 50. Annual treatment costs for MS can be as much as \$34,000 a year per patient.

Treatment of MS focuses on symptom management, treatment of attacks, and reduction of disease progression. There are a variety of disease-modifying treatments FDA-approved for relapsing-remitting MS; however, patients with progressive forms of MS have limited treatment options.

### **Parkinson’s Disease (PD)**

PD is a chronic, progressive disorder in which dopamine-producing neurons residing in the Substantia Nigra region of the brain undergo degeneration and eventually die, resulting in progressive impairment in movement and gait and eventually, leading to dementia. The cause of the disease is unknown.

Over 6.3 million people worldwide suffer from PD, of whom about one million are in the United States. Most people are diagnosed with the disease between the ages of 55 and 65 and about 85% of people with PD are over the age of 65. Prevalence of PD is increasing in line with the general aging of the population. The total economic burden of the disease has been estimated by the National Parkinson Foundation to exceed \$14 billion annually in the U.S. alone.

Treatment of PD primarily comprises dopamine replacement, either directly (levodopa), with dopamine mimetics or by inhibition of its breakdown. These treatments focus on treating the symptoms of the disease and are not a cure for PD. Levodopa has a propensity to cause serious motor response complications with long-term use. Moreover, effective drug dosage often requires gradual increase, leading to more adverse side effects and eventual resistance to its therapeutic action. This greatly limits patient benefit. Therefore, physicians and researchers have sought levodopa-sparing strategies in patients with early-stage disease to delay the need for levodopa.

PD is also treated by Deep Brain Stimulation (“DBS”), which consists of implanting electrodes deep into the brain to provide permanent electrical stimulation to specific areas of the brain and to cause a delay in the activity in those areas. However, DBS is problematic as it can cause uncontrollable and severe side effects such as bleeding in the brain, infection and depression. In addition, like drug therapy, DBS focuses on treating the symptoms of PD and does not provide a cure.

There is a greatly unsatisfied need for novel approaches towards management of PD, primarily to control levodopa-induced adverse side effects and motor dysfunction, as well as to delay the onset of disease-related dementia.

In addition to the symptomatic drug development approaches, there is an intense effort to develop cell and gene therapeutic “curative” approaches to restore the neural function in patients with PD, by (i) replacing the dysfunctional cells with dopamine producing cell transplant, or by (ii) providing growth factors and proteins, such as GDNF, that can maintain or preserve the patient’s remaining dopaminergic cells, protecting them from further degeneration.

## **Autism Spectrum Disorder**

Autism spectrum disorder is a complicated and poorly understood disorder of brain development characterized by difficulties in social interaction, verbal and nonverbal communication and repetitive behaviors. Approximately 1% of the world population falls on the spectrum and while behavioral therapy can produce meaningful benefits in autism patients, there are no drugs approved to treat the disorder. We have studied MSC-NTF cells in the BTBR mouse strain, which exhibits several behaviors that resemble behaviors seen in autism spectrum disorders, including repetitive behaviors, altered social interactions, cognitive rigidity and impaired adaption to environment. Across a variety of measures, including assessments of repeated self-grooming, social interaction and cognitive rigidity, MSC-NTF cells caused behavioral and cognitive benefits in BTBR mice after a single treatment compared to control mice.

## **Intellectual Property**

### *Patents:*

On March 4, 2014, we were granted a U.S. Patent (No. 8,663,987) for our “Mesenchymal Stem Cells for the Treatment of CNS Diseases” (serial number 12/994,761) patent application. This patent relates to our proprietary stem cells induced to secrete large quantities of neurotrophic factors for the treatment of neurodegenerative diseases. A divisional patent application therefrom was issued as US Patent 8,900,574 on December 2, 2014.

On February 11, 2014, the U.S. Patent and Trademark Office (“USPTO”) granted US patent, 8,647,874 for the patent application entitled "Isolated Cells and Populations Comprising Same for the Treatment of CNS Diseases." This patent relates to the production method of the Company's proprietary stem cells induced to secrete large quantities of neurotrophic factors for the treatment of neurodegenerative diseases. On September 3, 2014, the European Patent Office (“EPO”) issued corresponding patent 1893747, which is currently validated in: CH, CZ, DE, DK, ES, FR, GB, IE, IT and NL.

On January 22, 2015, we received a Notice of Allowance from Israel’s Patent Office for our patent application No. 209604 titled “Isolated Population of Cells, Methods of Generating Same, and Uses Thereof in the Treatment of CNS Diseases.” The patent was issued on September 1, 2015.

We have pending patent applications as follows:



A. The Israeli Subsidiary is the sole owner of United States Provisional patent application Serial No. 61/679,822, filed August 6, 2012, entitled "Methods of Generating Mesenchymal Stem Cells Which Secrete Neurotrophic Factors." This application has now been filed as International Application No.: PCT IL2013/050660 and is currently pending as National Phase in the US, EU, Israel, Canada, Brazil and Japan.

This invention is directed to a method of generating MSCs which secrete neurotrophic factors ("NTFs") comprising incubating a population of undifferentiated MSCs in a differentiating medium comprising basic fibroblast growth factor ("bFGF"), platelet derived growth factor ("PDGF"), heregulin and cAMP. The application also covers a method of treating a disease for which administration of neurotrophic factors is beneficial in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of isolated population of MSCs which secretes neurotrophic factors made according to the above method. Also taught is a method of selecting MSCs which secrete NTFs from a mixed population of MSCs, comprising (a) analyzing the cells of said mixed population of cells for at least one of the following parameters: (i) cells which express CD44 below a predetermined threshold, or (ii) cells which express CD73 above a predetermined threshold; and (b) selecting cells which are positive for at least one of said parameters, thereby selecting the MSCs which secrete neurotrophic factors. The application teaches a pharmaceutical composition comprising the isolated population of MSCs as an active agent and a pharmaceutically acceptable carrier.

The Israeli Subsidiary is the sole owner of United States Provisional patent application Serial No. 61/938,172, filed February 11, 2014, entitled "Methods Qualifying Cells." This application has now been filed as International Application No.: PCT/IL2015/050159

B. The Israeli Subsidiary is co-owner, with Ramot, in the invention entitled "Mesenchymal Stem Cells for the Treatment of CNS Diseases", filed as a PCT application on May 26, 2009, currently pending as National Phase patent applications in the following countries:

- Europe: Serial No. 09754337.5
- Europe: Serial No. 13164650.7
- Hong Kong: Serial No. 11107062.5
- Hong Kong: Serial No. 13109415.3

This invention is directed to an isolated human cell comprising at least one mesenchymal stem cell phenotype and secreting brain-derived neurotrophic factor (“BDNF”), wherein a basal secretion of the BDNF is at least five times greater than a basal secretion of the BDNF in a mesenchymal stem cell. Also disclosed in this application is an isolated cell population comprising human mesenchymal stem cells, wherein at least 50% of the cells express glial fibrillary acidic protein (“GFAP”) and secrete at least one neurotrophic factor. Also taught is an isolated cell population comprising human cells wherein (i) at least N% of said human cells secreting BDNF, wherein a basal secretion of said BDNF is at least five times greater than a basal secretion of the BDNF in a mesenchymal stem cell; (ii) at least M% of said human cells comprise at least one mesenchymal stem cell phenotype; and (iii) at least one of the human cells secretes the BDNF and the mesenchymal stem cell phenotype; where M and N are each independently selected between 1 and 99. Methods of generating same and uses of same are also disclosed. The method of generating cells useful for treating a CNS disease or disorder comprises (a) incubating mesenchymal stem cells in a culture medium comprising platelet lysate to generate propagated mesenchymal stem cells; and (b) incubating said propagated mesenchymal stem cells in a differentiating medium, thereby generating cells useful for treating the CNS disease or disorder. Another method taught is that of generating cells secreting neurotrophic factors, comprising (i) incubating mesenchymal stem cells in a serum free medium comprising platelet lysate to generate propagated mesenchymal stem cells; and (ii) incubating the propagated mesenchymal stem cells in a differentiating medium comprising at least one differentiating agent, said at least one differentiating agent being selected from the group consisting of platelet derived growth factor (“PDGF”), human neuregulin 1-b1, FGF2, EGF, N2, IBMX and cAMP, thereby generating cells secreting neurotrophic factors. The European applications claim an isolated human cell comprising a cell being non-genetically manipulated, and characterized by: a) expressing tyrosine hydroxylase, nestin and H-NF and b) secreting BDNF, and c) not secreting nerve growth factor (“NGF”) wherein a basal secretion of said BDNF is at least five times greater than a basal secretion of said BDNF in a mesenchymal stem cell; an isolated cell population comprising cells generated from human bone marrow derived cells expressing CD73, CD90 and CD105 and not expressing CD14, CD19, CD34, CD45 and HLA-DR, wherein at least 50% of the cells of the cell population express GFAP and secrete BDNF; and a method of generating cells useful for treating a CNS disease or disorder, the method comprising: (1) incubating bone marrow derived cells expressing CD73, CD90 and CD105 and not expressing CD14, CD19, CD34, CD45 and HLA-DR in a culture medium comprising human platelet lysate to generate propagated cells; and (2) incubating said propagated cells in a medium comprising a differentiating agent, thereby generating cells useful for treating the CNS disease or disorder, wherein said differentiating agent is selected from the group consisting of PDGF, human neuregulin 1- 1, FGF2, EGF, N2, IBMX and cAMP.

C. The Israeli Subsidiary is the licensee of the following patent applications owned by Ramot under terms set forth in the Second Ramot Agreement and the Assignment Agreement, as follows:

1. Invention entitled “Isolated Cells and Populations Comprising Same for the Treatment of CNS Diseases”, filed as a PCT application on June 18, 2006, currently pending as National Phase patent application in the US, Serial No.14/173,846.

This invention is directed to an isolated human cell and populations thereof comprising at least one astrocytic phenotype and at least one mesenchymal stem cell phenotype, wherein the mesenchymal stem cell phenotype is not an astrocytic phenotype; an isolated human cell comprising at least one mesenchymal stem cell phenotype and at least

one astrocytic structural phenotype, wherein the mesenchymal stem cell phenotype is not an astrocytic structural phenotype; or an isolated human cell comprising at least one mesenchymal stem cell phenotype and at least one astrocytic functional phenotype, wherein the mesenchymal stem cell phenotype is not an astrocytic functional phenotype. Also taught is a method of generating astrocyte-like cells expressing S100 beta, glial fibrillary acidic protein (GFAP), glutamine synthetase, GLAST, GLTI and glial derived neurotrophic factor (GDNF) comprising (a) culturing mesenchymal stem cells in a medium comprising human epidermal growth factor (hEGF) and human basic fibroblast growth factor (hbFGF); and (b) incubating the mesenchymal stem cells in a differentiating medium comprising platelet derived growth factor (PDGF) and human neuregulin 1-b1, thereby generating astrocyte-like cells. Another disclosed method of generating astrocyte-like cells teaches (i) incubating mesenchymal stem cells in a medium comprising hEGF and hbFGF to generate cells predisposed to generate into astrocyte-like cells; and (ii) incubating the predisposed cells in a differentiating medium comprising PDGF and human neuregulin 1-b1, thereby generating astrocyte-like cells.

2. Invention entitled “Methods, nucleic acid constructs and cells for treating neurodegenerative disorders”, filed on May 17, 2005 as United States patent application Serial No. 13/783,607. This invention is directed to a method of treating a neurodegenerative disorder by administering to an individual in need thereof cells capable of exogenously regulatable neurotransmitter synthesis. The cells are produced by incubating bone marrow stromal cells in a differentiating medium comprising docosahexaenoic acid or arachidonic acid and at least one differentiating agent.

*Trademarks:*

We have registered the trademark NUROWN (application no. 85154891, filed October 18, 2010) for use in connection with “compositions of cells derived from stem cells for medical purposes; stem cells for medical purposes.” US Trademark No. 4641441 for NUROWN was registered on November 18, 2014.

The patent applications, as well as relevant know-how and research results are licensed from Ramot. We intend to work with Ramot to protect and enhance our mutual intellectual property rights by filing continuations and divisional patent applications. New discoveries arising in the course of research and development within the Company were and will be patented by us independently.

*Research and License Agreement with Ramot*

On July 12, 2004, we entered into a Research and License Agreement (the “Original Ramot Agreement”) with Ramot, the technology licensing company of Tel Aviv University, which agreement was amended on March 30, 2006 by the Amended Research and License Agreement (described below). Under the terms of the Original Ramot Agreement, Ramot granted to us a license to (i) the inventions, know-how and results made with respect to the above-mentioned stem cell technology developed by the team led by Prof. Melamed and Prof. Offen in the course of the performance of the research, and the patents and pending patent applications owned by Ramot, and (ii) the results of further research to be performed by the same team on the development of the stem cell technology. Simultaneously with the execution of the Original Ramot Agreement, we entered into individual consulting agreements with Prof. Melamed and Prof. Offen pursuant to which all intellectual property developed by Prof. Melamed or Prof. Offen in the performance of services thereunder will be owned by Ramot and licensed to us under the Original Ramot Agreement.

Under the Original Ramot Agreement, we agreed to fund further research relating to the licensed technology in an amount of \$570,000 per year for an initial period of two years, and for an additional two-year period if certain research milestones were met.

In consideration for the license, we originally agreed to pay Ramot:

- An up-front license fee payment of \$100,000;
- An amount equal to 5% of all net sales of products; and
- An amount equal to 30% of all sublicense receipts.

On March 30, 2006 and on May 23, 2006, we entered into an Amended Research and License Agreement and an Amendment Agreement to the Amended Research and License Agreement, respectively (collectively, the “Amended Research and License Agreement”) with Ramot. Under the Amended Research and License Agreement, the funding of further research relating to the licensed technology in an amount of \$570,000 per year was reduced to \$380,000 per year. Moreover, under the Amended Research and License Agreement, the initial period of time that we agreed to fund the research was extended from an initial period of two (2) years to an initial period of three (3) years. The Amended Research and License Agreement also extended the additional two-year period in the Original Ramot Agreement to an additional three-year period, if certain research milestones were met.

We entered into a Second Amended and Restated Research and License Agreement with Ramot on July 26, 2007, effective July 12, 2004 (the “Second Ramot Agreement”), which amended and replaced the Amended Research and License Agreement. The Second Ramot Agreement imposed on us development and commercialization obligations, milestone and other obligations. The license was granted in consideration for (i) royalty payments ranging from three

percent (3%) to five percent (5%) of all net sales and (ii) potential payments concerning sublicenses ranging from twenty percent (20%) to twenty-five percent (25%) of sublicense receipts. In addition, in the event that the research period was extended for an additional three year period in accordance with the terms of the Second Ramot Agreement, then we had to make payments to Ramot for each year of the extended research period in the amount of \$380,000. As of June 30, 2007, we owed Ramot an aggregate amount of \$513,249 in overdue payments and patent fees under the Amended Research and License Agreement.

On August 1, 2007, we obtained a waiver and release from Ramot pursuant to which Ramot agreed to an amended payment schedule regarding our payment obligations under the Second Ramot Agreement and waived all claims against us resulting from our previous breaches, defaults and non-payment under the Amended Research and License Agreement.

After our failure to meet the amended payment schedule and subsequent negotiations, on December 24, 2009, we entered into a Letter Agreement and an amended agreement to the Second Ramot Agreement (collectively, the "Letter Agreement") with Ramot, pursuant to which, among other things, Ramot agreed to: (i) release us from our obligation to fund three years of additional research (which would have totaled \$1,140,000) and (ii) accept conversion of certain research payments due in the amount of \$272,000 into 74,666 shares of our Common Stock. Pursuant to the Letter Agreement, we agreed, among other things, to: (i) reimburse Ramot for outstanding patent-related expenses; and (ii) abandon our rights in certain joint patent rights and patents of Ramot in certain countries.

As of February 2011, Ramot had sold the 74,666 shares of Common Stock of the Company for approximately \$235,000 and we paid the remaining \$5,000 due to Ramot. To date there is no additional debt to Ramot.

On December 20, 2011, we entered into an Assignment Agreement with our Israeli Subsidiary (the "Assignment Agreement"), with the consent of Ramot. Under the Assignment Agreement, we assigned and transferred all of our rights, interests, titles, liabilities and obligations (the "Rights") under the Second Ramot Agreement to our Israeli Subsidiary, effective as of January 1, 2007 and our Israeli Subsidiary agreed to assume all such Rights. We agreed to be a guarantor of all obligations of our Israeli Subsidiary under the Second Ramot Agreement and Ramot can look to us to demand compliance with the Second Ramot Agreement.

In May 2012, we, the Israeli Subsidiary and Prof. Offen entered into a Consulting Agreement, effective as of January 1, 2012, which replaced the previous consulting agreement, dated July 31, 2004, pursuant to which all work product resulting from the provision of services will vest solely with the Israeli Subsidiary and if any work product resulting from the provision of services results in the creation or development of intellectual property it will be deemed a joint invention, and will be jointly owned by Ramot and the Israeli Subsidiary.

On April 30, 2014 our Israeli Subsidiary and Ramot entered into Amendment No. 2 to the Second Ramot Agreement, pursuant to which a new research period from April 30, 2014 to October 30, 2014 was created.



On March 1, 2016, our Israeli Subsidiary and Ramot entered into Amendment No. 3 to the Second Ramot Agreement, pursuant to which Ramot agreed to assign to the Israeli Subsidiary, effective February 18, 2016, all of its worldwide right, title and interest in and to the results of the research conducted under the Agreement and performed during the research period from April 30, 2014 to October 30, 2014. This change of status from exclusive licensee of these patents, to owner these patents, did not materially change the ability of the Company to exclude others from practicing the invention claimed therein.

## **Government Regulations and Supervision**

### **Government Regulation and Product Approval**

Once fully developed, we intend to market our bone marrow derived differentiated neurotrophic-factor secreting cell products, NurOwn®, for autologous transplantation in patients by neurosurgeons in medical facilities in the U.S., Europe, Japan and the Pacific Rim. We plan to submit a biologics license application (“BLA”) in the United States from the development of NurOwn® for the treatment of ALS patients. We initiated the regulatory process with a Pre-IND meeting with the FDA in September 2012, and submitted our IND application in December 2013. We have retained expert regulatory consultants to assist us in our approaches to the FDA.

In January 2013, the EMA Committee for Advanced Therapies classified NurOwn® as an Advanced Therapy Medicinal Product.

Government authorities in the United States at the federal, state and local level extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of products such as those we are developing. Our product candidates must receive final approval from the FDA before they may legally be marketed in the United States or by the appropriate foreign regulatory agency before it may be legally marketed in foreign countries.

### ***U.S. Drug Development Process***

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. Biologics are subject to regulation by the FDA under the FDCA, the Public Health Service Act, or the PHSA, and related

regulations and other federal, state and local laws and regulations. Biological products are therapies used to treat disease and health conditions. They include a wide variety of products including vaccines, blood and blood components, gene therapies, tissue and proteins. Unlike most prescription products made through chemical processes, biological products generally are made from human and/or animal materials. To be lawfully marketed in interstate commerce, a biologic product must be the subject of a BLA, issued by the FDA on the basis of a demonstration that the product is safe, pure and potent, and that the facility in which the product is manufactured meets standards to assure that it continues to be safe, pure and potent. The FDA has developed and is continuously updating the requirements with respect to cell and gene therapy products and has issued documents concerning the regulation of cellular and tissue-based products. Manufacturers of cell and tissue-based products must comply with the FDA's current good tissue practices, or cGTP, which are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of such products. The primary intent of the cGTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease.

The process of obtaining regulatory approvals and ensuring compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, product detention, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a biological product or drug may be marketed in the United States generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices or other regulations;
- Submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- Performance of adequate and well-controlled clinical trials according to Good Clinical Practices, or GCP, to establish the safety and efficacy of the proposed biological product or drug for its intended use;
- Submission to the FDA of a new drug application, or NDA, for a new drug; or a biologic license application for a new biological product;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with Good Manufacturing Practices, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the drug's or biologic's identity, strength, quality and purity; and
- FDA review and approval of the BLA or NDA.



The testing and approval process require substantial time, effort and financial resources and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Once a pharmaceutical product candidate is identified for development, it enters the preclinical testing phase. Preclinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor must also include a protocol detailing, among other things, the objectives of the initial clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical trial lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance. Accordingly, we cannot assure you that submission of an IND will result in the FDA allowing clinical trials to begin or, once begun, issues will not arise that result in the suspension or termination of such trial.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent. Further, an institutional review board, or IRB, must review and approve the plan for any clinical trial before it commences at any institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical trial and the consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Once an IND is in effect, each new clinical protocol and any amendments to the protocol must be submitted to the IND for FDA review, and to the IRBs for approval.

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

*Phase 1.* The product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients having the specific disease.

*Phase 2.* Phase 2 trials involve investigations 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 the optimal dosage and schedule.

*Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for regulatory approval and product labeling.

Post-approval studies, also called Phase 4 trials, may be conducted after initial marketing approvals. These studies are used to obtain additional experience from the treatment of patients in the intended therapeutic indication and may be required by the FDA as part of the approval process.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected side effects. Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients.

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

During the development of a new drug or biologic, a sponsor may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim. An SPA is intended to provide assurance that if the agreed upon clinical trial protocol is followed, the clinical trial endpoints are achieved, and there is a favorable risk-benefit profile, the data may serve as the primary basis for an efficacy claim in support of a BLA or an NDA. However, an SPA is not a guarantee of an approval of a product candidate or any permissible claims about the product candidate. In particular, SPAs are not binding on the FDA if previously unrecognized public health concerns arise during the performance of the clinical trial, other new scientific concerns regarding the product candidate's safety or efficacy arise, or if the sponsoring company fails to comply with the agreed upon clinical trial protocol.

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the biologic or drug, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA or BLA, requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of substantial user fees which may be waived under certain limited circumstances.

### ***FDA Review of Biologics License Applications and New Drug Applications***

The FDA reviews all BLAs and NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept a BLA or an NDA for filing. In this event, the BLA or NDA must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has ten months in which to complete the initial review of a standard BLA or NDA and respond to the applicant and six months for a priority BLA or NDA. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs or NDAs. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things, whether the product is safe, pure, and potent and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, purity and potency. Before approving an NDA or BLA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements, and additionally, in the case of biologics in accordance with cGTP guidelines, and adequate to assure consistent production of the product within required specifications. 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 and under what conditions. An advisory committee is a panel of independent experts who provide advice and recommendations when requested by the FDA on matters of importance that come before the agency. The FDA is not bound by the recommendation of an advisory committee.

The approval process is lengthy and difficult and the FDA may refuse to approve a BLA or NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information.

Even if such data and information is submitted, the FDA may ultimately decide that the BLA or NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the BLA or NDA in its present form. The complete response letter usually describes all of the specific deficiencies that the FDA identified in the BLA or NDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to conform the application to a

condition suitable for approval. If a complete response letter is issued, the applicant may either resubmit the BLA or NDA, addressing all of the deficiencies identified in the letter, withdraw the application, or request an opportunity for a hearing.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug's or biologic's safety and effectiveness after BLA or NDA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

### *Orphan Drug Designation*

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA or BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. However, orphan product designation does provide the potential for a period of exclusivity and we may be eligible for grant funding of up to \$400,000 per year for four years to defray costs of clinical trial expenses, tax credits for clinical research expenses and potential exemption from the FDA application user fee.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as (i) the drug's orphan designation is revoked; (ii) its marketing approval is withdrawn; (iii) the orphan exclusivity holder consents to the approval of another applicant's product; (iv) the orphan exclusivity holder is unable to assure the availability of a sufficient quantity of drug; or (v) a showing of clinical superiority to the product with orphan exclusivity by a competitor product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our drug or biological candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar but not identical benefits in the European Union.



In February 2011, we received Orphan Drug Designation for NurOwn® for the treatment of ALS in the United States. In July 2013, we received Orphan Medicinal Product Designation for NurOwn® for the treatment of ALS from the European Commission. Orphan designation grants a 10-year marketing exclusivity in the EU for the designated indication, as well as several other regulatory incentives.

### ***Patent Term Restoration and Marketing Exclusivity***

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between (a) the effective date of an IND and the submission date of a BLA or an NDA plus (b) the time between the submission date of a BLA or an NDA and the approval of that application. Only one patent applicable to an approved drug or biologic is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of approval of the drug or biologic. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

### ***Biologics Price Competition and Innovation Act of 2009***

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, amended the PHSA to create a new licensure framework for biosimilar products, which could ultimately subject our biological product candidates to competition. Under the BPCIA, a manufacturer may submit an application for licensure of a biological product that is "biosimilar to" or "interchangeable with" a referenced, branded biologic product. Previously, there had been no licensure pathway for such biosimilar or interchangeable products. For purposes of the BPCIA, a reference product is defined as the single biological product licensed under a full BLA against which a biological product is evaluated in an application submitted under a follow-on BLA.

The BPCIA also created a 12-year period of reference product exclusivity, which can be extended to 12.5 years with pediatric exclusivity. The 12-year exclusivity period begins on the date of first licensure of the reference product under the PHSA and during which the licensure of a follow-on application for a biosimilar or interchangeable product cannot be made effective. During the first four years (or four and one-half years with pediatric exclusivity) of the 12-year period, an application for a biosimilar or interchangeable version of the reference product cannot be submitted to the FDA. Under budget proposals submitted by President Obama, the Administration has requested that reference product exclusivity would decrease from twelve to seven years. Congress has not yet enacted such a change in the

BPCIA, but could move to enact such a decrease in the reference product exclusivity period.

The BPCIA includes limits on obtaining 12-year reference product exclusivity for certain changes or modifications to the reference product. A separate 12-year reference product exclusivity period does not apply to:

- a BLA supplement for the product that is the reference product;  
a subsequent BLA filed by the same reference product sponsor or manufacturer (or a licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or
- a modification to the structure of the biological product that does not result in a change in safety, purity or potency.

In February 2012, the FDA issued three draft guidance documents on biosimilar product development. The FDA is soliciting comments on the draft guidance documents which are described by the FDA as follows: (1) Scientific Considerations in Demonstrating Biosimilarity to a Reference Product, which is intended to assist companies in demonstrating that a proposed therapeutic protein product is biosimilar to a reference product for the purpose of submitting an application, called a "351(k)" application, to the FDA. This draft guidance describes a risk-based "totality-of-the-evidence" approach that the FDA intends to use to evaluate the data and information submitted in support of a determination of biosimilarity of the proposed product to the reference product; (2) Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product, which provides an overview of analytical factors to consider when assessing biosimilarity between a proposed therapeutic protein product and a reference product for the purpose of submitting a 351(k) application; and (3) Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009, which provides answers to common questions from people interested in developing biosimilar products. We cannot predict when or whether these draft guidance documents will ever be finalized or what changes the agency may make in its approach to implementation of the BPCIA.

In addition to creating a 12-year period of reference product exclusivity, the BPCIA clarifies the interaction of that exclusivity with orphan drug exclusivity, such that, if a reference product has been designated for a rare disease or condition the licensure of a biosimilar or interchangeable version of a reference product for such disease or condition may only occur after the later of the expiration of any applicable seven-year orphan drug exclusivity or the 12-year reference product exclusivity (or seven and one-half years and 12.5 years with pediatric exclusivity).

Our biological product candidates, if approved, could be considered reference products entitled to 12-year exclusivity. Even if our products are considered to be reference products eligible for exclusivity, another company could market a competing version of any of our biological products if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

The BPCIA also sets forth a complex mechanism for resolving patent disputes that involves a step-wise exchange of information prior to the initiation of a patent infringement lawsuit against a biosimilar or interchangeable product sponsor. Unlike the Hatch-Waxman Act, the BPCIA provides no automatic stay on approval of a biosimilar product application, except an interchangeable product receives the lesser of one year of exclusivity after the date of first commercial marketing or 18 months of exclusivity after a final court decision or dismissal of a patent challenge or, if the applicant has not been sued, after approval. The BPCIA does not prevent a competitor from conducting its own clinical trials and submitting a full BLA on the same or similar product.

### ***Post-Approval Requirements***

Any drugs for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse effects with the product, reporting of changes in distributed products which would require field alert reports (FARs) for drugs and biological product deviation reports (BPDRs), providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. In September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-marketing authority, including the authority to require postmarketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluations and mitigation strategies, or REMS, approved by the FDA. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers of drugs and biologics must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.



Drug and biologic manufacturers and other entities involved in the manufacturing and distribution of approved drugs and biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, GTP applicable to biologics, and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the drug. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release.

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Discovery of previously unknown problems with a product subsequent to its approval may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, the FDA regulations and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our product candidates. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

### ***Foreign Regulation***

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our product candidates to the extent we choose to clinically evaluate or sell any products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product 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. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved outside the United States.

### *Third Party Payor Coverage and Reimbursement*

Significant uncertainty exists as to the coverage and reimbursement status of any of our biologic or drug candidates for which we obtain regulatory approval. In both the United States and foreign markets, our ability to commercialize our product candidates successfully, and to attract commercialization partners for our product candidates, depends in significant part on the availability of adequate financial coverage and reimbursement from third party payors, including, in the United States, governmental payors such as the Medicare and Medicaid programs, managed care organizations, and private health insurers. Medicare is a federally funded program managed by the Centers for Medicare and Medicaid Services, or CMS, through local fiscal intermediaries and carriers that administer coverage and reimbursement for certain healthcare items and services furnished to the elderly and disabled. Medicaid is an insurance program for certain categories of patients whose income and assets fall below state defined levels and who are otherwise uninsured that is both federally and state funded and managed by each state. The federal government sets general guidelines for Medicaid and each state creates specific regulations that govern its individual program. Each payor has its own process and standards for determining whether it will cover and reimburse a procedure or particular product. Private payors often rely on the lead of the governmental payors in rendering coverage and reimbursement determinations. Therefore, achieving favorable CMS coverage and reimbursement is usually a significant gating issue for successful introduction of a new product. The competitive position of some of our products will depend, in part, upon the extent of coverage and adequate reimbursement for such products and for the procedures in which such products are used. Prices at which we or our customers seek reimbursement for our product candidates can be subject to challenge, reduction or denial by the government and other payors.

The U.S. Congress and state legislatures may, from time to time, propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our product candidates profitably. For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act and the associated reconciliation bill, which we refer to collectively as the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Health Care Reform Law revises the definition of “average manufacturer price” for reporting purposes, which could increase the amount of Medicaid drug rebates to states once the provision is effective. Further, the law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law.

Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our product candidates.

The cost of pharmaceuticals continues to generate substantial governmental and third party payor interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Our results of operations could be adversely affected by current and future healthcare reforms.

Some third party payors also require pre-approval of coverage for new or innovative devices, biologics or drug therapies before they will reimburse healthcare providers that use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and operate profitably.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug or biological candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs and biologics, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

### *Other Healthcare Laws and Compliance Requirements*

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the United States Department of Justice and individual United States Attorney offices within the Department of Justice, and state and local governments. These regulations include:

the federal healthcare program anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other government reimbursement programs that are false or fraudulent;

the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

the federal transparency requirements under the Health Care Reform Law requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests;

the FDCA, which among other things, strictly regulates drug and biologic product marketing, prohibits manufacturers from marketing drug or biologic products for off-label use and regulates the distribution of drug samples; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

### **Compliance with Environmental, Health and Safety Laws**

In addition to FDA regulations, we are also subject to evolving federal, state and local environmental, health and safety laws and regulations. In the past, compliance with environmental, health and safety laws and regulations has not had a material effect on our capital expenditures. We believe that we comply in all material respects with existing environmental, health and safety laws and regulations applicable to us. Compliance with environmental, health and safety laws and regulations in the future may require additional capital expenditures.

## **Sales and Marketing**

We intend to establish and maintain fully-equipped cGMP-certified Cell-Processing Centers in strategic locations to conduct NurOwn® production and distribution over the broadest geographic area. Each Cell-Processing Center would receive an initial bone marrow sample of the patient, harvested at a medical center. The patient's MSC cells would be isolated and expanded, in order to produce an initial dose of NurOwn® cells. A master cell bank for each individual patient would be cryopreserved and maintained for production of subsequent, future NurOwn® doses on a long-term basis for future treatments. These doses would be produced as needed and transported to the medical centers, where they would then be transplanted back into the patient.

We intend to seek partnering opportunities with a strategic partner as we progress towards advanced clinical development and commercialization.

## **Competition**

There are a number of clinical trials underway for potential treatments for ALS, of which only two are stem cell-based trials being conducted by other commercial entities: (i) US-based Neuralstem (CUR) is currently conducting a Phase 2 trial for its allogeneic, human (fetal) spinal cord derived neural stem cells; and (ii) Q Therapeutics has gained FDA approval for a Phase 1/2 study with its Q-Cells®, purified human glial progenitor cells isolated from brain tissue. Corestem, a Korean company, recently completed a Phase 1 trial in ALS showing that repeated intrathecal administration of autologous, bone marrow-derived mesenchymal stem cells was safe. No significant clinical benefit was reported. There is little public information available about Corestem. Five non-stem cell-based companies are undergoing Phase 1/2, Phase 2 or Phase 3 clinical trials for ALS. Cytokinetics is a late stage biopharmaceutical company running a Phase 3 clinical trial with Tirasemtiv, a chemical compound developed to enhance the signals between motor neurons and neuromuscular junctions (NMJ). A number of academic institutions are also developing treatment candidates for ALS.

## **Employees**

We currently have 20 employees, 17 of whom are full-time. None of our employees is represented by a labor union.

## **Additional Information**

We maintain a website at [www.brainstorm-cell.com](http://www.brainstorm-cell.com). We make available through our website, free of charge, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as soon as reasonably practicable after we electronically file those reports with, or furnish them to, the SEC. We also similarly make available, free of charge through our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act. We are not including the information contained at [www.brainstorm-cell.com](http://www.brainstorm-cell.com) or at any other Internet address as part of, or incorporating it by reference into, this Annual Report on Form 10-K.

## **Item 1A. RISK FACTORS**

*We operate in a rapidly changing environment that involves a number of risks, some of which are beyond our control. Forward-looking statements in this report and those made from time to time by us through our senior management are made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements concerning the expected future revenues, earnings or financial results or concerning project plans, performance, or development of products and services, as well as other estimates related to future operations are necessarily only estimates of future results and there can be no assurance that actual results will not materially differ from expectations. Forward-looking statements represent management's current expectations and are inherently uncertain. We do not undertake any obligation to update forward-looking statements, except as required by applicable securities laws and regulations. If any of the following risks actually occurs, our financial condition and operating results could be materially adversely affected.*

### **Risks related to our business**

*We need to raise additional capital. If we are unable to raise additional capital on favorable terms and in a timely manner, we will not be able to execute our business plan and we could be forced to restrict or cease our operations.*

We will need to raise additional funds to meet our anticipated expenses so that we can execute our business plan. We expect to incur substantial and increasing net losses for the foreseeable future as we increase our spending to execute our development programs. Our auditors have expressed in their audit report that there is substantial doubt regarding our ability to continue as a going concern.

The amount of financing required will depend on many factors including our financial requirements to fund our research and clinical trials, and our ability to secure partnerships and achieve partnership milestones as well as to fund other working capital requirements. Our ability to access the capital markets or to enlist partners is mainly dependent on the progress of our research and development and regulatory approval of our products.

We expect that the net proceeds from the June 2014 private placement and the exercise of certain June 2014 warrants pursuant to a January 8, 2015 Warrant Exercise Agreement will be sufficient to meet our obligations through the completion of our Phase 2 clinical trial in the United States. However, additional capital may be required or the Company will need to reduce its operating costs in order to finance the Company's operations beyond the current plans or if there are unanticipated significant increases in costs over the next 12 months.

Should we raise additional funds through the issuance of equity, equity-related or debt securities, these securities may have rights, preferences or privileges (including registrations rights) senior to those of the rights of our Common Stock and our stockholders will experience additional dilution.

***Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.***

As described in Note 1 of our 2014 financial statements incorporated herein by reference, our auditors in their audit opinion have expressed concern with respect to our ability to continue as a going concern. Our financial statements do not include any adjustments that may result from the outcome of this uncertainty. If we cannot continue as a viable entity, our stockholders may lose some or all of their investment in us.

***If our NurOwn® treatment candidate does not demonstrate safety and efficacy sufficient to obtain regulatory approval, it will not receive regulatory approval and we will be unable to market it.***

The therapeutic treatment development and regulatory approval process is expensive, uncertain and time-consuming. The timing of any future regulatory approval, if any, for our NurOwn® treatment candidate cannot be accurately predicted. We do not expect to receive regulatory approval for any of our product candidates until at least 2018, if ever. If we fail to obtain regulatory approval for our NurOwn® treatment candidate, we will be unable to market and sell it and we may never be profitable.

As part of the regulatory process, we must conduct clinical trials, including Phase 2 and Phase 3 clinical trials, for our NurOwn® treatment candidate to demonstrate safety and efficacy in humans to the satisfaction of the FDA and regulatory authorities in other countries.





A failure of one or more of our clinical trials can occur at any stage of testing. Previous results obtained in uncontrolled clinical trials may not be predictive of future results obtained in controlled clinical trials. Interim results obtained in clinical trials may not be confirmed upon full analysis of the results of a clinical trial. Results of later stage clinical trials may fail to show the desired safety and efficacy despite acceptable results in earlier clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that have believed their product candidates performed satisfactorily in preclinical and clinical trials have nonetheless failed to obtain marketing approval of their treatments.

Specifically, we are currently comparing our NurOwn® treatment candidate against placebo. There is no other active therapy for ALS. While comparisons of outcomes to results from other reported clinical trials can provide some insight into the efficacy of our NurOwn® treatment candidate, there are many factors that affect the outcome of clinical trials, some of which are not apparent in published reports, and results from two different trials cannot always be reliably compared.

***Part of our business in the foreseeable future will be based on technology licensed from Ramot and if this license were to be terminated upon failure to make required royalty payments in the future, we would need to change our business strategy and we may be forced to cease our operations.***

Agreements we and our Israeli Subsidiary have with Ramot impose on us royalty payment obligations. If we fail to comply with these obligations, Ramot may have the right to terminate the license under certain circumstances. If Ramot elects to terminate our license, we would need to change our business strategy and we may be forced to cease our operations. We currently do not owe Ramot any overdue payments. Royalties are due upon commencement of revenues by the Company.

***Our Company has a history of losses and we expect to incur losses for the foreseeable future.***

As a development stage company, we are in the early stages of executing our business plan. We had no operational revenues for the fiscal years ended December 31, 2015 or December 31, 2014. Our ability to operate successfully is materially uncertain and our operations are subject to significant risks inherent in a developing business enterprise. We are currently in the process of introducing the Company to strategic partners. In the upcoming three years, the Company will focus on clinical trials. We are unable at this time to foresee when we will generate operational revenues from strategic partnerships or otherwise. Furthermore, we expect to incur substantial and increasing operating losses for the next several years as we increase our spending to execute our development programs. These losses are expected to have an adverse impact on our working capital, total assets and stockholders' equity, and we may never achieve profitability.

***Our product development programs are based on novel technologies and are inherently risky.***

We are subject to the risks of failure inherent in the development of products based on new technologies. The novel nature of our stem cell therapy creates significant challenges with regard to product development and optimization, manufacturing, government regulations, and market acceptance. For example, the FDA has relatively limited experience with stem cell therapies. None have been approved by them for commercial sale, and the pathway to regulatory approval for our cell therapy product candidates may accordingly be more complex and lengthy. As a result, the development and commercialization pathway for our therapies may be subject to increased uncertainty, as compared to the pathway for new conventional drugs.

***We are faced with uncertainties related to our research.***

Our research programs are based on scientific hypotheses and experimental approaches that may not lead to desired results. In addition, the timeframe for obtaining proof of principle and other results may be considerably longer than originally anticipated, or may not be possible given time, resource, financial, strategic and collaborator scientific constraints. Success in one stage of testing is not necessarily an indication that the particular program will succeed in later stages of testing and development. It is not possible to predict, based upon studies in in-vitro models and in animals, whether any of the therapies designed for these programs will prove to be safe, effective, and suitable for human use. Each therapy will require additional research and development, scale-up, formulation and extensive clinical testing in humans. Unsatisfactory results obtained from a particular study relating to a program may cause the Company to abandon its commitment to that program or to the lead therapy or product candidate being tested. The discovery of unexpected toxicities, lack of sufficient efficacy, unacceptable pharmacology, inability to increase scale of manufacture, market attractiveness, regulatory hurdles, competition, as well as other factors, may make our targets, lead therapies or product candidates unattractive or unsuitable for human use, and we may abandon our commitment to that program, target, lead therapy or product candidate. In addition, preliminary results seen in animal and/or limited human testing may not be substantiated in larger controlled clinical trials.

***If serious or unexpected adverse side effects are identified during the development of our NurOwn® treatment candidate, we may need to abandon or limit its development.***

If patients treated with our NurOwn® treatment candidate suffer serious or unexpected adverse effects, we may need to abandon its development or limit development to certain uses or subpopulations in which these effects are less prevalent, less severe or more acceptable from a risk-benefit perspective.

***The field of stem cell therapy is relatively new and our development efforts may not yield an effective treatment of human diseases.***

Our intended cell therapeutic treatment methods for ALS involve a new approach that has not yet been proven to work in humans. We are currently conducting a Phase 2 placebo-controlled clinical trial for ALS, which, together with other stem cell therapies, may ultimately prove ineffective in treatment of human diseases. If we cannot successfully implement our NurOwn® stem cell therapy in human testing, we would need to change our business strategy and we may be forced to cease our operations.

***Our NurOwn® treatment candidate is based on a novel technology, which may raise development issues that we may not be able to resolve, regulatory issues that could delay or prevent approval or personnel issues that may keep us from being able to develop our treatments.***

Regulatory approval of treatment candidates that utilize novel technology such as ours can be more expensive and take longer than for other treatments that are based on more well-known or more extensively studied technology, due to our and the regulatory agencies' lack of experience with them. This may lengthen the regulatory review process, require us to perform additional studies, including clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. For example, the differentiated cell component of our NurOwn® treatment candidate is a complex biologic product that is manufactured from the patient's own bone marrow that must be appropriately harvested, isolated, expanded and differentiated so that its identity, strength, quality, purity and potency may be characterized prior to release for treatment. No differentiated cell treatment for ALS has yet been approved for marketing by the FDA or any other regulatory agency. The tests that we use to make identity, strength, quality, purity and potency determinations on our NurOwn® treatment candidate may not be sufficient to satisfy the FDA's expectations regarding the criteria required for release of products for patient treatment and the regulatory agency may require us to employ additional testing measures for this purpose, which could require us to undertake additional testing and/or additional clinical trials.

The novel nature of our NurOwn® treatment candidate also means that fewer people are trained in or experienced with treatments of this type, which may make it difficult to recruit, hire and retain capable personnel for the research, development and manufacturing positions that will be required to continue our development and commercialization efforts.

*A significant global market for our services has yet to emerge.*

Very few companies have been successful in their efforts to develop and commercialize a stem cell product. Some stem cell products in general may be susceptible to various risks, including undesirable and unintended side effects, unintended immune system responses, inadequate therapeutic efficacy, or other characteristics that may prevent or limit their approval or commercial use. The demand for stem cell processing and the number of people who may use cell or tissue-based therapies is difficult to forecast. Physicians, patients, formularies, third party payers or the medical community in general may not accept or utilize any products that the Company or its collaborative partners may develop. Our success is dependent on the establishment of a large global market for our products and services and our ability to capture a share of this market.

*We have limited experience in conducting and managing clinical trials and the application process necessary to obtain regulatory approvals.*

Our limited experience in conducting and managing clinical trials and the application process necessary to obtain regulatory approvals might prevent us from successfully designing or implementing a preclinical study or clinical trial. Many companies in the industry have suffered significant setbacks in advanced clinical trials, despite promising results in earlier trials. If our clinical trials are unsuccessful, or if we do not complete our clinical trials, we may not receive regulatory approval for or be able to commercialize our product candidates.

If we do not succeed in conducting and managing our preclinical development activities or clinical trials, or in obtaining regulatory approvals, we might not be able to commercialize our product candidates, or might be significantly delayed in doing so, which will materially harm our business.

Our ability to generate revenues from any of our product candidates will depend on a number of factors, including our ability to successfully complete clinical trials, obtain necessary regulatory approvals and implement our commercialization strategy. We may, and anticipate that we will need to, transition from a company with a research and development focus to a company capable of supporting commercial activities and we may not succeed in such a transition.

***We may not be able to secure and maintain research institutions to conduct our clinical trials.***

We rely on research institutions to conduct our clinical trials. Our reliance upon research institutions, including hospitals and clinics, provides us with less control over the timing and cost of clinical trials and the ability to recruit subjects. If we are unable to reach agreements with suitable research institutions on acceptable terms, or if any resulting agreement is terminated, we may be unable to quickly replace the research institution with another qualified institution on acceptable terms. Furthermore, we may not be able to secure and maintain suitable research institutions to conduct our clinical trials.

***We are subject to a strict regulatory environment. If we fail to obtain and maintain required regulatory approvals for our potential cell therapy products, our ability to commercialize our potential cell therapy products will be severely limited.***

None of our product candidates have received regulatory approval for commercial sale yet. We do not expect to receive regulatory approval for any of our product candidates until at least 2018, if ever.

Numerous statutes and regulations govern human testing and the manufacture and sale of human therapeutic products in the United States and other countries where we intend to market our products. Such legislation and regulation bears upon, among other things, the approval of protocols and human testing, the approval of manufacturing facilities, testing procedures and controlled research, review and approval of manufacturing, preclinical and clinical data prior to marketing approval including adherence to GMP during production and storage as well as regulation of marketing activities including advertising and labeling.

The completion of the clinical testing of our product candidates and the obtaining of required approvals are expected to take several years and require the expenditure of substantial resources. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent regulatory approval and/or commercialization of our product candidates, including the following:

The FDA or similar foreign regulatory authorities may find that our product candidates are not sufficiently safe or effective or may find our processes or facilities unsatisfactory;

Officials at the Israeli MoH, the FDA or similar foreign regulatory authorities may interpret data from preclinical studies and clinical trials differently than we do;

Our clinical trials may produce negative or inconclusive results or may not meet the level of statistical significance required by the Israeli MoH, the FDA or other regulatory authorities, and we may decide, or regulators may require us, to conduct additional preclinical studies and/or clinical trials or to abandon one or more of our development programs;

The Israeli MoH, the FDA or similar foreign regulatory authorities may change their approval policies or adopt new regulations;

There may be delays or failure in obtaining approval of our clinical trial protocols from the Israeli MoH, the FDA or other regulatory authorities or obtaining institutional review board approvals or government approvals to conduct clinical trials at prospective sites;

We, or regulators, may suspend or terminate our clinical trials because the participating patients are being exposed to unacceptable health risks or undesirable side effects;

We may experience difficulties in managing multiple clinical sites;

Enrollment in our clinical trials for our product candidates may occur more slowly than we anticipate, or we may experience high drop-out rates of subjects in our clinical trials, resulting in significant delays; and

We may be unable to manufacture or obtain from third party manufacturers sufficient quantities of our product candidates for use in clinical trials.

Investors should be aware of the risks, problems, delays, expenses and difficulties which may be encountered by us in light of the extensive regulatory environment in which our business operates. In particular, our development costs will increase if we have material delays in our clinical trials, or if we are required to modify, suspend, terminate or repeat a clinical trial. If we are unable to conduct our clinical trials properly and on schedule, marketing approval may be delayed or denied by the Israeli MoH or the FDA.

Even if a product candidate is approved by the Israeli MoH, the FDA or any other regulatory authority, we may not obtain approval for an indication whose market is large enough to recoup our investment in that product candidate. We may never obtain the required regulatory approvals for any of our product candidates. Later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on the product or manufacturer, including a withdrawal of the product from the market.

***Even if regulatory approvals are obtained for our product candidates, we will be subject to ongoing government regulation. If we or one or more of our partners or collaborators fail to comply with applicable current and future laws and government regulations, our business and financial results could be adversely affected.***

The healthcare industry is one of the most highly regulated industries in the United States. The federal government, individual state and local governments and private accreditation organizations all oversee and monitor the activities of individuals and businesses engaged in the delivery of health care products and services. Even if regulatory authorities approve any of our human therapeutic product candidates, current laws, rules and regulations that could directly or indirectly affect our ability and the ability of our strategic partners and customers to operate each of their businesses could include, without limitation, the following:

- State and local licensing, registration and regulation of laboratories, the collection, processing and storage of human cells and tissue, and the development and manufacture of pharmaceuticals and biologics;
- The federal Clinical Laboratory Improvement Act and amendments of 1988;
- Laws and regulations administered by the FDA, including the Federal Food Drug and Cosmetic Act and related laws and regulations;
- The Public Health Service Act and related laws and regulations;
- Laws and regulations administered by the United States Department of Health and Human Services, including the Office for Human Research Protections;
- State laws and regulations governing human subject research;
- Occupational Safety and Health requirements; and
- State and local laws and regulations dealing with the handling and disposal of medical waste.

Compliance with such regulation may be expensive and consume substantial financial and management resources. If we, or any future marketing collaborators or contract manufacturers, fail to comply with applicable regulatory requirements, we may be subject to sanctions including fines, product recalls or seizures, injunctions, total or partial suspension of production, civil penalties, withdrawal of regulatory approvals and criminal prosecution. Any of these sanctions could delay or prevent the promotion, marketing or sale of our products.

***Our NurOwn® treatment candidate, even if approved, may not be accepted in the marketplace; therefore, we may not be able to generate significant revenue, if any.***

Even if our NurOwn® treatment candidate is approved for sale, physicians and the medical community may not ultimately use it or may use it only in applications more restricted than we anticipate. Our NurOwn® treatment candidate, if successfully developed, will compete with a number of traditional products manufactured and marketed by major pharmaceutical and biotechnology companies. Our NurOwn® treatment candidate may also compete with new products currently under development by such companies and others. Physicians will prescribe a treatment only if they determine, based on experience, clinical data, side effect profiles and other factors, that it is beneficial as

compared to other products currently available and in use. Physicians also will prescribe a product based on their traditional preferences. Many other factors influence the adoption of new products, including patient perceptions and preferences, marketing and distribution restrictions, adverse publicity, product pricing, views of thought leaders in the medical community and reimbursement by government and private payers. Any of these factors could have a material adverse effect on our business, financial condition, and results of operations.

***Adoption of our NurOwn® treatment candidate for the treatment of patients with ALS, or other neurodegenerative diseases, even if approved, may be slow or limited. If our NurOwn® treatment candidate does not achieve broad acceptance as a treatment option for ALS, or other neurodegenerative diseases, our business would be harmed.***

If approved, the rate of adoption of our NurOwn® treatment candidate as a treatment for ALS, or other neurodegenerative diseases, and the ultimate sales volume for our treatment, will depend on several factors, including educating treating physicians on how to use our NurOwn® treatment candidate. Our NurOwn® treatment candidate utilizes individualized stem cell therapy, which is significantly different from the pharmacological approach currently used to treat neurodegenerative diseases. Acceptance of our NurOwn® treatment candidate by treating physicians may require us to provide them with extensive education regarding the mechanism of action of our treatment, the method of delivery of the treatment, expected side effects and the method of monitoring patients for efficacy and follow-up. In addition, the manufacturing and delivery processes associated with our treatment will require treating physicians to adjust their current treatment of patients, which may delay or prevent market adoption of our NurOwn® treatment candidate as a preferred therapy, even if approved.

***We are subject to environmental, health and safety laws.***

We are subject to various laws and regulations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals and humans, emissions and wastewater discharges, and the use and disposal of hazardous or potentially hazardous substances used in connection with our research. We also cannot accurately predict the extent of regulations that might result from any future legislative or administrative action. Any of these laws or regulations could cause us to incur additional expense or restrict our operations.



Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development or production efforts.

***Our success will depend in part on establishing and maintaining effective strategic partnerships and collaborations, which may impose restrictions on our business and subject us to additional regulation.***

A key aspect of our business strategy is to establish strategic relationships in order to expand or complement our research and development or commercialization capabilities, and to reduce the cost of research and development. There can be no assurance that we will enter into such relationships, that the arrangements will be on favorable terms or that such relationships will be successful. If we are ultimately successful in executing our strategy of securing collaborations with companies that would undertake advanced clinical development and commercialization of our products, we may not have day-to-day control over their activities. Any such collaborator may adhere to criteria for determining whether to proceed with a clinical development program under circumstances where we might have continued such a program. Potential collaborators may have significant discretion in determining the efforts and amount of resources that they dedicate to our collaborations or may be unwilling or unable to fulfill their obligations to us, including their development and commercialization. Potential collaborators may underfund or not commit sufficient resources to the testing, marketing, distribution or other development of our products. They may also not properly maintain or defend our intellectual property rights or they may utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability. Potential collaboration partners may have the right to terminate the collaboration on relatively short notice and if they do so or if they fail to perform or satisfy their obligations to us, the development or commercialization of products would be delayed and our ability to realize any potential milestone payments and royalty revenue would be adversely affected.

***We will need to develop or acquire additional capabilities in order to commercialize our NurOwn® treatment candidate, if approved for sale, and we may encounter unexpected costs or difficulties in doing so.***

We will need to acquire additional capabilities and effectively manage our operations and facilities to successfully pursue and complete future research, development and, if our NurOwn® treatment candidate receives regulatory approval, commercialization efforts. Currently, we have no experience in preparing applications for marketing approval, commercial-scale manufacturing, managing of large-scale information technology systems or managing a large-scale distribution system. We will need to add personnel and expand our capabilities, which may strain our existing managerial, operational, regulatory compliance, financial and other resources. To do this effectively, we must:

- train, manage and motivate a growing employee base;
- accurately forecast demand for our treatment; and

expand existing operational, financial and management information systems.

We will need to increase our manufacturing capacity prior to seeking approval for the sale of our products. If we are not successful in establishing a regulatory compliant manufacturing process, we may not obtain approval of products or our ability to obtain regulatory approval for sale could be delayed, which would further delay the period of time when we would be able to generate revenues from the sale of such products, if we are even able to generate revenues at all.

***We expect to expand our development, regulatory, manufacturing and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product development, regulatory affairs, manufacturing and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

***We have never manufactured our NurOwn® treatment candidate at commercial scale and there can be no assurance that it can be manufactured in compliance with regulations at a cost or in quantities necessary to make it commercially viable.***

We have no experience in commercial-scale manufacturing, the management of large-scale information technology systems or the management of a large-scale distribution system. We may develop our manufacturing capacity in part by expanding our current facilities and/or by setting up additional facilities in other regions of the country. These activities would require substantial additional funds and we would need to hire and train significant numbers of qualified employees to staff these facilities. We may not be able to develop commercial-scale facilities that are sufficient to produce the treatment candidates or their components for later-stage clinical trials or commercial use.

Furthermore, we must supply all necessary documentation, including product characterization and process validation, to regulatory authorities in support of our BLA on a timely basis and must adhere to cGMP regulations and current Good Tissue Practices (“GTP”) enforced by the regulatory authority through its facilities inspection program. We have not fully characterized our NurOwn® treatment candidate and have not validated our manufacturing process. If the FDA determines that the products used in our clinical trials are not sufficiently characterized, we may be required to repeat all or a portion of our clinical trials. If our facilities cannot pass a pre-approval plant inspection, the regulatory approval of the treatment candidates will not be granted.

***We are subject to significant regulation with respect to manufacturing of our NurOwn® treatment candidate.***

All entities involved in the preparation of a therapeutic biological for clinical trials or commercial sale are subject to extensive regulation. Our NurOwn® treatment candidate must be manufactured in accordance with cGMP and GTP before it can be used in our clinical trials or approved for commercial sale. These regulations govern manufacturing processes and procedures and the implementation and operation of quality systems to control and assure the quality of investigational treatment candidates and treatments, including treatment component characterization and process validation, approved for sale. Our facilities and quality systems and the facilities and quality systems of some or all of our third party suppliers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our NurOwn® treatment candidate. If any inspection or audit of our manufacturing facilities identifies a failure to comply with applicable regulations, or if a violation of applicable regulations occurs independent of an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed on us or third parties with whom we contract could materially harm our business.

***Lack of coordination internally among our employees and externally with physicians, hospitals and third-party suppliers and carriers, could cause manufacturing difficulties, disruptions or delays and cause us to not meet our expected clinical trial requirements or potential commercial requirements.***

Manufacturing our NurOwn® treatment candidate requires coordination internally among our employees and externally with physicians, hospitals and third-party suppliers and carriers. For example, a patient’s physician or clinical site will need to coordinate with us for the shipping of a patient’s bone marrow to our manufacturing facility, and we will need to coordinate with them for the shipping of the treatment components to them. Such coordination involves a number of risks that may lead to failures or delays in manufacturing our NurOwn® treatment candidate, including:

- failure to obtain a sufficient supply of key raw materials of suitable quality;

- difficulties in manufacturing our treatment candidates for multiple patients simultaneously;
- difficulties in obtaining adequate patient-specific material, such as bone marrow samples, from physicians;
- difficulties in completing the development and validation of the harvested cells required to ensure the consistency of our NurOwn® treatment candidate;
- failure to ensure adequate quality control and assurances in the manufacturing process as we increase production quantities;
- difficulties in the timely shipping of patient-specific materials to us or in the shipping of the treatment candidates to the treating physicians due to errors by third-party carriers, transportation restrictions or other reasons;
- loss or destruction of, or damage to, patient-specific materials or our NurOwn® treatment candidate during the shipping process due to improper handling by third-party carriers, hospitals, physicians or us;
- loss or destruction of, or damage to, patient-specific materials or our NurOwn® treatment candidate during storage at our facilities; and
- loss or destruction of, or damage to, patient-specific materials or our NurOwn® treatment candidate stored at clinical and future commercial sites due to improper handling or holding by clinicians, hospitals or physicians.

If we are unable to coordinate appropriately, we may encounter delays or additional costs in achieving our clinical and commercialization objectives, including in obtaining regulatory approvals of our treatment candidates and supplying products, which could materially damage our business and financial position.

***We face competition in our efforts to develop cell therapies for ALS and other neurodegenerative diseases.***

We face competition in our efforts to develop cell therapies and other treatment or procedures to cure or slow the effects of ALS and other neurodegenerative diseases. Among our competitors are companies that are involved in the fetal-derived cell transplants or embryonic stem cell derived cell therapy and companies developing adult stem cells. Other companies are developing traditional chemical compounds, new biological drugs, cloned human proteins and other treatments, which are likely to impact the markets that we intend to target. Some of our competitors possess longer operating histories and greater financial, managerial, scientific and technical resources than we do and some possess greater name recognition and established customer bases. Some also have significantly more experience in preclinical testing, human clinical trials, product manufacturing, the regulatory approval process and marketing and distribution than we do.

***The trend towards consolidation in the pharmaceutical and biotechnology industries may adversely affect us.***

There is a trend towards consolidation in the pharmaceutical and biotechnology industries. This consolidation trend may result in the remaining companies having greater financial resources and discovery technological capabilities, thus intensifying competition in these industries. This trend may also result in fewer potential collaborators or licensees for our therapeutic product candidates. Also, if a consolidating company is already doing business with our competitors, we may lose existing licensees or collaborators as a result of such consolidation.

***There is a scarcity of experienced professionals in the field of cell therapy and we may not be able to retain key personnel or hire new key personnel needed to implement our business strategy and develop our products and businesses. If we are unable to retain or hire key personnel, we may be unable to continue to grow our business or to implement our business strategy, and our business may be materially and adversely affected.***

Given the specialized nature of cell therapy and the fact that it is a young field, there is an inherent scarcity of experienced personnel in the field. Our success depends on a significant extent to the continued services of certain highly qualified scientific and management personnel. We face competition for qualified personnel from numerous industry sources, and there can be no assurance that we will be able to attract and retain qualified personnel on acceptable terms. The loss of service of any of our key personnel could have a material adverse effect on our operations or financial condition. In the event of the loss of services of such personnel, no assurance can be given that we will be able to obtain the services of adequate replacement personnel. We do not have key person life insurance on our key personnel. The future success of the Company also depends upon our ability to attract and retain additional qualified personnel (including medical, scientific, technical, commercial, business and administrative personnel) necessary to support our anticipated growth, develop our business, and maintain appropriate licensure, on acceptable terms. There can be no assurance that we will be successful in attracting or retaining personnel required by us to continue and grow our operations. The loss of a key employee, the failure of a key employee to perform in his or her current position or our inability to attract and retain skilled employees, as needed, could result in our inability to continue to grow our business or to implement our business strategy, or may have a material adverse effect on our business, financial condition and results of operations.

***Technological and medical developments or improvements in conventional therapies could render the use of stem cells and our services and planned products obsolete.***

The pharmaceutical industry is characterized by rapidly changing markets, technology, emerging industry standards and frequent introduction of new products. The introduction of new products embodying new technologies, including new manufacturing processes, and the emergence of new industry standards may render our technologies obsolete, less competitive or less marketable. Advances in other treatment methods or in disease prevention techniques could significantly reduce or entirely eliminate the need for our stem cell services, planned products and therapeutic efforts.

Additionally, technological or medical developments may materially alter the commercial viability of our technology or services, and require us to incur significant costs to replace or modify equipment in which we have a substantial investment. In either event, we may experience a material adverse effect on our business, results of operations and financial condition.

*We may expend our limited resources to pursue our NurOwn® treatment candidate or a specific indication for its use and fail to capitalize on treatment candidates or indications that may be more profitable or for which there is a greater likelihood of success.*

Because we have limited financial and managerial resources, we have focused development of our NurOwn® treatment candidate for use in patients with ALS. As a result, we may forego or delay pursuit of opportunities with other treatment candidates or for other indications that later prove to have greater commercial potential. Our spending on current and future research and development efforts on our NurOwn® treatment candidate for this indication may not yield a commercially viable treatment. Our resource allocation decisions also may cause us to fail to capitalize on a viable commercial treatment, a more viable indication or profitable market opportunities.

We have based our research and development efforts on our NurOwn® treatment candidate. Notwithstanding our large investment to date and anticipated future expenditures in our NurOwn® treatment candidate, we have not yet developed, and may never successfully develop, any marketed treatments using this approach. As a result of pursuing the development of our NurOwn® treatment candidate, we may fail to develop treatment candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success.

Our long-term business plan is to develop our NurOwn® treatment candidate for the treatment of neurodegenerative diseases, such as ALS, MS and PD. Even if we successfully develop our NurOwn® treatment candidate for use in one indication, we may not be successful in our efforts to identify or discover additional indications for it. Clinical programs to develop new indications for our NurOwn® treatment candidate will require substantial technical, financial and human resources. These development programs may initially show promise in identifying potential treatment indications, yet fail to obtain regulatory approval for commercial sale.

If we do not accurately evaluate the commercial potential or target market for our NurOwn® treatment candidate, we may relinquish valuable rights to that treatment through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

***If Ramot is unable to obtain patents on the patent applications and technology licensed to our Israeli Subsidiary or if patents are obtained but do not provide meaningful protection, we may not be able to successfully market our proposed products.***

We rely upon the patent applications filed by Ramot, the technology licensing company of Tel Aviv University, and the license granted to us by Ramot, all in accordance with the Second Ramot Agreement dated as of July 26, 2007. We further agreed under the Second Ramot Agreement that Ramot, in consultation with us, is responsible for obtaining patent protection for technology owned by Ramot and licensed to us. No assurance can be given that any of our pending or future patent applications will be approved, that the scope of any patent protection granted will exclude competitors or provide us with competitive advantages, that any of the patents that may be issued to us will be held valid if subsequently challenged, or that other parties will not claim rights to or ownership of our patents or other proprietary rights that we hold license to. Furthermore, there can be no assurance that others have not developed or will not develop similar products, duplicate any of our technology or products or design around any patents that have been or may be issued to us or any future licensors. Since patent applications in the United States and in Europe are not disclosed until applications are published, there can be no assurance that others did not first file applications for products covered by our pending patent applications, nor can we be certain that we will not infringe any patents that may be issued to others. Also, we have abandoned our rights to certain patents of Ramot in certain countries in connection with the Letter Agreement by and between us and Ramot dated December 24, 2009, which may limit our ability to fully market our proposed products.

We also rely upon unpatented proprietary technology, know-how and trade secrets and seek to protect them through confidentiality agreements with employees, consultants and advisors. If these confidentiality agreements are breached, we may not have adequate remedies for the breach. In addition, others may independently develop or otherwise acquire substantially the same proprietary technology as our technology and trade secrets.

***We may be unable to protect our intellectual property from infringement by third parties.***

Despite our efforts to protect our intellectual property, third parties may infringe or misappropriate our intellectual property. Our competitors may also independently develop similar technology, duplicate our processes or services or design around our intellectual property rights. We may have to litigate to enforce and protect our intellectual property rights to determine their scope, validity or enforceability. Intellectual property litigation is costly, time-consuming, diverts the attention of management and technical personnel and could result in substantial uncertainty regarding our future viability. The loss of intellectual property protection or the inability to secure or enforce intellectual property protection would limit our ability to develop or market our services in the future. This would also likely have an adverse effect on the revenues generated by any sale or license of such intellectual property. Furthermore, any public announcements related to such litigation or regulatory proceedings could adversely affect the price of our Common Stock.

***Third parties may claim that we infringe on their intellectual property.***

We may be subject to costly litigation in the event our technology is claimed to infringe upon the proprietary rights of others. Third parties may have, or may eventually be issued, patents that would be infringed by our technology. Any of these third parties could make a claim of infringement against us with respect to our technology. We may also be subject to claims by third parties for breach of copyright, trademark or license usage rights. Litigation and patent interference proceedings could result in substantial expense to us and significant diversion of efforts by our technical and management personnel. An adverse determination in any such proceeding or in patent litigation could subject us to significant liabilities to third parties or require us to seek licenses from third parties. Such licenses may not be available on acceptable terms or at all. Adverse determinations in a judicial or administrative proceeding or failure to obtain necessary licenses could prevent us from commercializing our products, which would have a material adverse effect on our business, results of operations and financial condition.

***As a result of our reliance on consultants, we may not be able to protect the confidentiality of our technology, which, if disseminated, could negatively impact our plan of operations.***

We currently have relationships with academic and industry consultants and subcontractors who are not directly employed by us, and we may enter into additional relationships of such nature in the future. We have limited control over the activities of these consultants and can expect only limited amounts of their time to be dedicated to our activities. These persons may have consulting, employment or advisory arrangements with other entities that may conflict with or compete with their obligations to us. Our consultants typically sign agreements that provide for confidentiality of our proprietary information and results of studies. However, in connection with every relationship, we may not be able to maintain the confidentiality of our technology, the dissemination of which could hurt our competitive position and results of operations. To the extent that our scientific consultants develop inventions or processes independently that may be applicable to our proposed products, disputes may arise as to the ownership of the proprietary rights to such information, we may expend significant resources in such disputes and we may not win those disputes.

***It is uncertain to what extent the government, private health insurers and third-party payers will approve coverage or provide reimbursement for the therapies and products to which our services relate. Availability for such reimbursement may be further limited by an increasing uninsured population and reductions in Medicare and Medicaid funding in the United States.***

Our ability to successfully commercialize our human therapeutic products will depend significantly on our ability to obtain acceptable prices and the availability of reimbursement to the patient from third-party payers, such as government and private insurance plans. While we have not commenced discussions with any such parties, these third-party payers frequently require companies to provide predetermined discounts from list prices, and they are increasingly challenging the prices charged for pharmaceuticals and other medical products. Our human therapeutic products may not be considered cost-effective, and reimbursement to the patient may not be available or sufficient to allow us to sell our products on a competitive basis. Further, as cost containment pressures are increasing in the health care industry, government and private payers adopt strategies designed to limit the amount of reimbursement paid to



health care providers. Such cost containment measures may include:

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- Reducing reimbursement rates;
- Challenging the prices charged for medical products and services;
- Limiting services covered;
- Decreasing utilization of services;
- Negotiating prospective or discounted contract pricing;
- Adopting capitation strategies; and
- Seeking competitive bids.

Similarly, the trend toward managed health care and bundled pricing for health care services in the United States could significantly influence the purchase of healthcare services and products, resulting in lower prices and reduced demand for our therapies.

We may not be able to negotiate favorable reimbursement rates for our human therapeutic products. If we fail to obtain acceptable prices or an adequate level of reimbursement for our products, the sales of our products would be adversely affected or there may be no commercially viable market for our products.

***Unintended consequences of recently adopted health reform legislation in the U.S. may adversely affect our business.***

The healthcare industry is undergoing fundamental changes resulting from political, economic and regulatory influences. In the U.S., comprehensive programs are under consideration that seek to, among other things, increase access to healthcare for the uninsured and control the escalation of healthcare expenditures within the economy. On March 23, 2010, health reform legislation was approved by Congress and has been signed into law. While we do not believe this legislation will have a direct impact on our business, the legislation has only recently been enacted and requires the adoption of implementing regulations, which may have unintended consequences or indirectly impact our business. For instance, the scope and implications of the recent amendments pursuant to the Fraud Enforcement and Recovery Act of 2009 have yet to be fully determined or adjudicated and as a result it is difficult to predict how future enforcement initiatives may impact our business. Also, in some instances our clients may be health insurers that will be subject to limitations on their administrative expenses and new federal review of “unreasonable” rate increases which could impact the prices they pay for our services. If the legislation causes such unintended consequences or indirect impact, it could have a material adverse effect on our business, financial condition and results of operations.

***Ethical and other concerns surrounding the use of stem cell therapy may negatively impact the public perception of our stem cell services, thereby suppressing demand for our services.***

Although our stem cell business pertains to adult stem cells only, and does not involve the more controversial use of embryonic stem cells, the use of adult human stem cells for therapy could give rise to similar ethical, legal and social issues as those associated with embryonic stem cells, which could adversely affect its acceptance by consumers and medical practitioners. Additionally, it is possible that our business could be negatively impacted by any stigma associated with the use of embryonic stem cells if the public fails to appreciate the distinction between adult and embryonic stem cells. Delays in achieving public acceptance may materially and adversely affect the results of our operations and profitability.

***We are exposed to fluctuations in currency exchange rates.***

A significant portion of our business, particularly our research and development, is conducted outside the United States. Therefore, we are exposed to currency exchange fluctuations in other currencies such as the New Israeli Shekels (“NIS”) and the Euro. Moreover, a portion of our expenses in Israel and Europe are paid in NIS and Euros, respectively, which subjects us to the risks of foreign currency fluctuations. Our primary expenses paid in NIS are employee salaries, fees for consultants and subcontractors and lease payments on our Israeli facilities.

***The dollar cost of our operations in Israel will increase to the extent increases in the rate of inflation in Israel are not offset by a devaluation of the NIS in relation to the dollar, which would harm our results of operations.***

Since a considerable portion of our expenses such as employees' salaries are linked to an extent to the rate of inflation in Israel, the dollar cost of our operations is influenced by the extent to which any increase in the rate of inflation in Israel is or is not offset by the devaluation of the NIS in relation to the dollar. As a result, we are exposed to the risk that the NIS, after adjustment for inflation in Israel, will appreciate in relation to the dollar. In that event, the dollar cost of our operations in Israel will increase and our dollar-measured results of operations will be adversely affected. During the past few years inflation-adjusted NIS appreciated against the dollar, which raised the dollar cost of our Israeli operations. We cannot predict whether the NIS will appreciate against the dollar or vice versa in the future. Any increase in the rate of inflation in Israel, unless the increase is offset on a timely basis by a devaluation of the NIS in relation to the dollar, will increase labor and other costs, which will increase the dollar cost of our operations in Israel and harm our results of operations.

***We may be subject to significant product liability claims and litigation which could adversely affect our future earnings and financial condition.***

Our business exposes us to potential product liability risks inherent in the testing, processing and marketing of stem cell therapy products. Specifically, the conduct of clinical trials in humans involves the potential risk that the use of our stem cell therapy products will result in adverse effects. Such liability claims may be expensive to defend and result in large judgments against us. We currently maintain liability insurance for our clinical trials; however such liability insurance may not be adequate to fully cover any liabilities that arise from clinical trials of our stem cell therapy products. We also maintain errors and omissions, directors and officers, workers' compensation and other insurance appropriate to our business activities. If we were to be subject to a claim in excess of this coverage or to a claim not covered by our insurance and the claim succeeded, we would be required to pay the claim from our own limited resources, which could have a material adverse effect on our financial condition, results of operations and business. Additionally, liability or alleged liability could harm our business by diverting the attention and resources of our management and damaging our reputation and that of our subsidiaries.

***Political, economic and military instability in Israel may impede our ability to execute our plan of operations.***

Our principal operations and the research and development facilities of the scientific team funded by us under the Second Ramot Agreement are located in Israel. Accordingly, political, economic and military conditions in Israel may affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have occurred between Israel and its Arab neighbors. Acts of random terrorism periodically occur which could affect our operations or personnel. Ongoing or revived hostilities or other factors related to Israel could harm our operations and research and development process and could impede our ability to execute our plan of operations.

In addition, Israeli-based companies and companies doing business with Israel have been the subject of an economic boycott by members of the Arab League and certain other predominantly Muslim countries since Israel's establishment. Although Israel has entered into various agreements with certain Arab countries and the Palestinian Authority, and various declarations have been signed in connection with efforts to resolve some of the economic and political problems in the Middle East, we cannot predict whether or in what manner these problems will be resolved. Wars and acts of terrorism have resulted in damage to the Israeli economy, including reducing the level of foreign and local investment.

Furthermore, certain of our officers and employees may be obligated to perform annual reserve duty in the Israel Defense Forces and are subject to being called up for active military duty at any time. Israeli citizens who have served in the army may be subject to an obligation to perform reserve duty until they are between 40 and 49 years old, depending upon the nature of their military service.

***Man-Made Problems Such as Computer Viruses or Terrorism May Disrupt Our Operations and Harm Our Operating Results***

Despite our implementation of network security measures our servers are vulnerable to computer viruses, break-ins, and similar disruptions from unauthorized tampering with our computer systems. Any such event could have a material adverse effect on our business, operating results, and financial condition. Efforts to limit the ability of malicious third parties to disrupt the operations of the internet or undermine our own security efforts may meet with resistance. In addition, the continued threat of terrorism and heightened security and military action in response to this threat, or any future acts of terrorism, may cause further disruptions to the economies of the United States, Israel and other countries and create further uncertainties or otherwise materially harm our business, operating results, and financial condition. Likewise, events such as widespread blackouts could have similar negative impacts. To the extent that such disruptions or uncertainties result in delays or access to data or personal information, our business, operating results, and financial condition could be materially and adversely affected.

**Risks related to our Common Stock**

***The price of our stock is expected to be volatile.***

The market price of our Common Stock has fluctuated significantly, and is likely to continue to be highly volatile. To date, the trading volume in our stock has been relatively low and significant price fluctuations can occur as a result. An active public market for our Common Stock may not continue to develop or be sustained. If the low trading volumes experienced to date continue, such price fluctuations could occur in the future and the sale price of our Common Stock could decline significantly. Investors may therefore have difficulty selling their shares.

***Your percentage ownership will be diluted by future issuances of our securities.***

In order to meet our financing needs, we may issue additional significant amounts of our Common Stock and warrants to purchase shares of our Common Stock. The precise terms of any future financings will be determined by us and potential investors and such future financings may also significantly dilute your percentage ownership in the Company.

***ACCBT holds equity participation rights and other rights that could affect our ability to raise funds.***

Pursuant to the Subscription Agreement with ACCBT Corp. (“ACCBT”), a company under the control of Mr. Chaim Lebovits, our President and Chief Executive Officer, we granted ACCBT the right to acquire additional shares of our Common Stock whenever we issue additional shares of Common Stock or other securities of the Company, or options or rights to purchase shares of the Company or other securities directly or indirectly convertible into or exercisable for shares of the Company (including shares of any newly created class or series). This participation right could limit our ability to enter into equity financings and to raise funds from third parties. ACCBT is entitled to purchase its pro rata share of any additional securities we offer, so that its percentage ownership of the Company remains the same after any such issuance of additional securities. Such additional securities will be offered to ACCBT at the same price and on the same terms as the other investors in the transaction. ACCBT will have 30 days from the date of our notice to ACCBT of any intended transaction, to decide whether it wishes to exercise its participation rights in the transaction. We also are prohibited from taking certain corporate actions without the consent of ACCBT, including issuing shares, acquiring or divesting assets and making payment of cash compensation over \$60,000 per year. Further, ACCBT also has the right to appoint a majority of our Board of Directors. In connection with the Subscription Agreement, we entered into a registration rights agreement with ACCBT pursuant to which we granted piggyback registration rights to ACCBT. In addition, we issued ACCBT warrants to purchase up to 2,016,666 shares of Common Stock, of which 2,016,666 warrants are presently outstanding. The outstanding warrants contain cashless exercise provisions, which permit the cashless exercise of up to 50% of the underlying shares of Common Stock. 672,222 of such warrants have an exercise price of \$3.00 and the remainder have an exercise price of \$4.35. We registered 1,920,461 shares of Common Stock and 2,016,666 shares of Common Stock underlying the ACCBT Warrants on registration statement No. 333-201705 dated January 26, 2015 pursuant to ACCBT’s registration rights. ACCBT has waived its participation rights and anti-dilution rights with respect to issuances that were made on or prior to January 8, 2015. In March 2014, we entered into an agreement with ACCBT according to which ACCBT waived certain anti-dilution rights. On May 25, 2014, the Company entered into a Warrant Amendment Agreement with ACCBT, pursuant to which the expiration date of each Warrant held by ACCBT was extended until November 5, 2017, in consideration of ACCBT having provided a series of waivers of their rights, including the anti-dilution rights waiver.

***You may experience difficulties in attempting to enforce liabilities based upon U.S. federal securities laws against us and our non-U.S. resident directors and officers.***

Our principal operations are located through our subsidiary in Israel and our principal assets are located outside the U.S. Our Chief Financial Officer and some of our directors are foreign citizens and do not reside in the U.S. It may be difficult for courts in the U.S. to obtain jurisdiction over our foreign assets or these persons and as a result, it may be difficult or impossible for you to enforce judgments rendered against us or our directors or executive officers in U.S. courts. Thus, should any situation arise in the future in which you have a cause of action against these persons or entities, you are at greater risk in investing in our Company rather than a domestic company because of greater potential difficulties in bringing lawsuits or, if successful, collecting judgments against these persons or entities as opposed to domestic persons or entities.

***If we fail to implement and maintain an effective system of internal controls, we may be unable to accurately report our results of operations or prevent fraud, and investor confidence and the market price of our Common Stock may be materially and adversely affected.***

As a public company in the United States, we are subject to the reporting obligations under the U.S. securities laws. The SEC, as required under Section 404 of the Sarbanes-Oxley Act of 2002, has adopted rules requiring every public company to include a report of management on the effectiveness of such company's internal control over financial reporting in its annual report. In prior years, management has identified material weaknesses in our internal control over financial reporting. If any of our prior material weaknesses recurs, or if we identify additional weaknesses or fail to timely and successfully implement new or improved controls, our ability to assure timely and accurate financial reporting may be adversely affected, and we could suffer a loss of investor confidence in the reliability of our financial statements, which in turn could negatively impact the trading price of our shares of Common Stock, result in lawsuits being filed against us by our stockholders, or otherwise harm our reputation. If material weaknesses are identified in the future, it could be costly to remediate such material weaknesses, which may adversely affect our results of operations. In addition, our auditor is not required to attest to the effectiveness of our internal controls over financial reporting due to our status of qualifying as a smaller reporting company. As a result, current and potential investors could lose confidence in our financial reporting, which could harm our business and have an adverse effect on our share price.

***Delaware law could discourage a change in control, or an acquisition of us by a third party, even if the acquisition would be favorable to you, and thereby adversely affect existing stockholders.***

The Delaware General Corporation Law contain provisions that may have the effect of making more difficult or delaying attempts by others to obtain control of our Company, even when these attempts may be in the best interests of stockholders. Delaware law imposes conditions on certain business combination transactions with "interested stockholders." These provisions and others that could be adopted in the future could deter unsolicited takeovers or delay or prevent changes in our control or management, including transactions in which stockholders might otherwise receive a premium for their shares over then current market prices. These provisions may also limit the ability of stockholders to approve transactions that they may deem to be in their best interests.

*We do not expect to pay dividends in the foreseeable future, and accordingly you must rely on stock appreciation for any return on your investment.*

We have paid no cash dividends on our Common Stock to date, and we currently intend to retain our future earnings, if any, to fund the continued development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future. Further, any payment of cash dividends will also depend on our financial condition, results of operations, capital requirements and other factors, including contractual restrictions to which we may be subject, and will be at the discretion of our Board of Directors.

#### **Item 1B. UNRESOLVED STAFF COMMENTS**

None.

#### **Item 2. PROPERTIES**

Our executive offices and United States corporate headquarters are located at 3 University Plaza Drive, Suite 320, Hackensack, NJ 07601 ("the Headquarters").

In October 2014, we entered into a lease agreement for the Headquarters, according to which we leased approximately 220 square meters of office space for a term of 63 months commencing October 1, 2014. Rent is paid on a monthly basis in the amount of approximately U.S. \$4,300.

On December 1, 2004, our Israeli Subsidiary entered into a lease agreement (the Lease Agreement) for the lease of premises in 12 Basel Street, Petach Tikva, Israel, which include approximately 600 square meters of office and laboratory space. The original term of the lease was 36 months (the Lease Term), commencing on April 1, 2005, with two options to extend: one for an additional 24 months (the First Option); and one for an additional 36 months (the Second Option).

On November 11, 2012, the Israeli Subsidiary entered into an amendment to the Lease Agreement, pursuant to which the Lease Term (including the First Option and the Second Option) was extended by an additional five years, through March 31, 2018. After three years, we will have the right to cancel the agreement with 6 months' notice. Rent is paid on a monthly basis in the amount of NIS 40,000 (approximately U.S. \$10,000).



We expanded our Petach Tikva facility in 2008 to include an animal research facility.

As part of the clinical trials with Hadassah, we pay \$31,250 per month for rental and operation of clean room facilities at Hadassah facilities in Jerusalem.

We believe that the current office and laboratory space is adequate to meet our needs or will be available in the U.S. to meet the needs of U.S. clinical trials.

### **Item 3. LEGAL PROCEEDINGS**

From time to time, we may become involved in litigation relating to claims arising out of operations in the normal course of business, which we consider routine and incidental to our business. We currently are not a party to any legal proceedings the adverse outcome of which, in management's opinion, would have a material adverse effect on our business, results of operation or financial condition.

### **Item 4. MINE SAFETY DISCLOSURES.**

Not applicable.

## **PART II**

### **Item MARKET FOR COMMON EQUITY AND RELATED STOCKHOLDER MATTERS AND ISSUER 5. PURCHASES OF EQUITY SECURITIES.**

#### *Market Information*

Our Common Stock is currently traded on the Nasdaq Capital Market under the symbol "BCLI". The following table contains information about the range of high and low sales prices for our Common Stock.



Quarter Ended	High	Low
December 31, 2015	\$3.13	\$2.22
September 30, 2015	\$3.68	\$2.17
June 30, 2015	\$5.43	\$3.54
March 31, 2015	\$8.47	\$3.75
December 31, 2014	\$4.94	\$2.81
September 30, 2014	\$5.70	\$3.35
June 30, 2014	\$5.70	\$3.45
March 31, 2014	\$5.55	\$2.55

The source of these high and low prices was the OTCQB Marketplace for all periods prior to September 24, 2014, and thereafter the Nasdaq Capital Market. The high and low prices listed have been rounded up to the next highest two decimal places. All sales prices are adjusted to reflect our September 15, 2014 one-for-fifteen reverse stock split.

#### *Record Holders*

As of January 29, 2016, there were approximately 46 holders of record of our Common Stock.

#### *Dividends*

We have not paid or declared any cash or other dividends on our Common Stock within the last two fiscal years. Any future determination as to the payment of dividends will depend upon our results of operations, and on our capital requirements, financial condition and other factors relevant at the time.

#### *Equity Compensation Plans*

Information regarding our equity compensation plans and the securities authorized under the plans is included in Item 12 below.

#### *Recent Sales of Unregistered Securities*

On January 16, 2013, we issued 4,800 and 9,600 shares of Common Stock to Dani Offen and Eldad Melamed, respectively, for consulting services. The issuance of these securities was effected without registration in reliance on Section 4(2) of the Securities Act as a sale by the Company not involving a public offering. No underwriters were involved with the issuance of such securities.

On February 4, 2013, we issued 8,407 shares of Common Stock to Aaron Lasry in accordance with a settlement agreement with Mr. Lasry. The issuance of these securities was effected without registration in reliance on Section 4(2) of the Securities Act as a sale by the Company not involving a public offering. No underwriters were involved with the issuance of such securities.

On February 7, 2013, we issued 55,555 shares of Common Stock at a purchase price of \$4.50 per share (for a total purchase price of \$250,000) and a 32-month warrant to purchase up to 55,556 shares of our Common Stock with an exercise price equal to \$7.50 per share to E.E.B Investments and Holdings (2009) Ltd. and pursuant to a Securities Purchase Agreement with E.E.B Investments and Holdings (2009) Ltd. dated February 7, 2013. These securities were issued without registration pursuant to the exemption afforded by Regulation S promulgated under the Securities Act. No underwriters were involved with the issuance of these securities and no commissions were paid in connection with this transaction.

In March 2013, we issued 16,666 shares of Common Stock to Emerging Markets Consulting, LLC for consulting, marketing and public relations services pursuant to our March 2013 Agreement with Emerging Markets Consulting, LLC. The issuance of these securities was effected without registration in reliance on Section 4(2) of the Securities Act as a sale by the Company not involving a public offering. No underwriters were involved with the issuance of such securities.

In March 2013, we issued 10,000 shares of Common Stock to LifeSci Advisors, LLC for consulting, marketing and public relations services pursuant to our March 2013 Agreement with LifeSci Advisors, LLC. The issuance of these securities was effected without registration in reliance on Section 4(2) of the Securities Act as a sale by the Company not involving a public offering. No underwriters were involved with the issuance of such securities.

On April 13, 2013, pursuant to the April 2010 agreement with Hadasit, we issued a warrant to purchase up to 2,222 shares of our Common Stock at an exercise price of \$0.00075 per share, exercisable for a period of 10 years, to Hadasit Medical Research Services and Development Ltd. The issuance of these securities was effected without registration in reliance upon Regulation D promulgated under the Securities Act. No underwriters were involved with the issuance of such securities and no commissions were paid in connection with such transaction. On October 22, 2014, Hadasit paid the exercise amount and exercised the warrants.

On March 24, 2014, the Company issued 12,000 and 24,000 shares of Common Stock to Dani Offen and Eldad Melamed, respectively, for consulting services. The issuance of these securities was effected without registration in reliance on Section 4(2) of the Securities Act as a sale by the Company not involving a public offering. No underwriters were involved with the issuance of such securities.

On April 13, 2014, pursuant to the April 2010 agreement with Hadasit, the Company issued a warrant to purchase up to 2,222 shares of its Common Stock at an exercise price of \$0.00075 per share, exercisable for a period of 10 years, to Hadasit Medical Research Services and Development Ltd. The issuance of these securities was effected without registration in reliance upon Regulation D promulgated under the Securities Act. No underwriters were involved with the issuance of such securities and no commissions were paid in connection with such transaction. As a result of the April 25, 2014 termination of the Hadasit Agreement, any outstanding and unvested grants made pursuant to the Agreement ceased to vest, and the grant shall be valid until and may be exercised only on or before October 25, 2014.

On April 25, 2014 (the "Effective Date"), the Company entered into agreements with certain holders of 2013 Warrants to exchange outstanding 2013 Warrants entitling the holder to purchase an aggregate of 777,470 shares of Common Stock for an aggregate of 388,735 unregistered shares of Common Stock. On the Effective Date, each share of Common Stock issuable pursuant to the 2013 Warrants (the "Warrant Shares") was exchanged for shares of unregistered Common Stock equal to one-half (0.5) of the number of Warrant Shares (the "Exchange Shares"), provided that in the event the number of Exchange Shares resulted in a fractional number it was rounded up to the nearest whole share. As of the Effective Date, the 2013 Warrants were cancelled and of no further force and effect. The offer and sale of the Exchange Shares were made in reliance upon the exemption from registration provided for by Rule 506 of Regulation D promulgated under the Securities Act. No form of general solicitation or general advertising was used by the Company, or any representative of the Company, in connection with the offer or sale of the Exchange Shares. No underwriters were involved with the issuance of the Exchange Shares and no commissions were paid in connection with the exchange. Each of the investors represented to the Company that they are an accredited investor.

On June 19, 2014, we issued 2.8 million shares of Common Stock at a price per share of \$3.75 and warrants to purchase up to 2.8 million shares of Common Stock at an exercise price of \$5.22 per share to a group of investors, including several healthcare-focused funds, pursuant to the Securities Purchase Agreement dated June 13, 2014 between the Company and the investors. The Company received gross proceeds of \$10.5 million. The warrants were exercisable immediately upon closing of the private placement and have a term of three (3) years. Maxim Group LLC acted as sole placement agent (the "Placement Agent") for the private placement. In connection with the private placement, the Company paid the Placement Agent a cash fee equal to 6.9% of the gross proceeds of the private placement, as well as fees and expenses of the Placement Agent of \$35,000. In addition, the Company issued to the Placement Agent a 5-year warrant to purchase up to 84,000 shares of Common Stock, with an exercise price equal to \$4.50. The issuance of the shares, the warrants and the Placement Agent warrant was exempt from the registration requirements of the Securities Act pursuant to the exemption for transactions by an issuer not involving any public offering under Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D promulgated under the Securities Act. The Company made this determination based on the representations that each party is an "accredited investor" within the meaning of Rule 501 of Regulation D and has access to information about the Company and its investment.

In June and in July 2014, the Company issued to several investors 150,651 shares of Common Stock pursuant to the exercise of warrants issued in the July 19, 2012 fund raising. The issuance of these securities was effected without registration in reliance upon Regulation D promulgated under the Securities Act. No underwriters were involved with the issuance of such securities and no commissions were paid in connection with such transaction.

On July 9, 2014, the Company issued to Avi Szenberg 6,666 shares of Common Stock pursuant to an agreement with Mr. Szenberg for marketing services provided to the Company. The issuance of these securities was effected without registration in reliance upon Regulation D promulgated under the Securities Act. No underwriters were involved with the issuance of such securities and no commissions were paid in connection with such transaction.

On July 28, 2014, the Company issued to Thomas B. Rosedale 10,752 shares of Common Stock pursuant to an agreement with BRL Law Firm LLC for legal services provided to the Company. The issuance of these securities was effected without registration in reliance upon Regulation D promulgated under the Securities Act. No underwriters were involved with the issuance of such securities and no commissions were paid in connection with such transaction.

On September 3, 2014, the Company issued to Rainbow Biotechnologies Sarl 7,144 shares of Common Stock pursuant to an exercise of warrants issued under the August 2005 Consulting Agreement with Rainbow Biotechnologies Sarl, for an aggregate exercise price of \$16,000. The issuance of these securities was effected without registration in reliance on Section 4(2) of the Securities Act as a sale by the Company not involving a public offering. No underwriters were involved with the issuance of such securities.

On October 22, 2014, the Company issued to Hadasit Medical Research Services and Development Ltd., 8,889 shares of Common Stock pursuant to the exercise of warrants issued under the April 2010 Agreement with Hadasit Medical Research Services and Development Ltd. The issuance of these securities was effected without registration in reliance upon Regulation D promulgated under the Securities Act. No underwriters were involved with the issuance of such securities and no commissions were paid in connection with such transaction.

On January 8, 2015, pursuant to a Warrant Exercise Agreement (the “Exercise Agreement”), holders of warrants to purchase an aggregate of approximately 2.5 million shares of the Company’s Common Stock, at an exercise price of \$5.22 per share (the “2014 Warrants”), issued in a private placement to accredited investors that was consummated on June 13, 2014, agreed to exercise their 2014 Warrants in full and the Company agreed to issue new warrants to the holders to purchase up to an aggregate of approximately 3.8 million unregistered shares of Common Stock at an exercise price of \$6.50 (the “New Warrants”). The Company received an aggregate of approximately \$13 million in proceeds from the exercises of the 2014 Warrants (the “Exercise Proceeds”). Maxim Group LLC (“Maxim”) acted as solicitation agent for the Exercise Agreement. In connection with the Exercise Agreement, the Company agreed to pay Maxim a cash fee equal to 6.0% of the Exercise Proceeds, as well as fees and expenses of Maxim of \$20,000. In addition, the Company issued Maxim a warrant to purchase up to approximately 38,000 shares of Common Stock (equal to 1.5% of the exercised 2014 Warrants) upon substantially the same terms as the New Warrants (the “Maxim Warrant”). The Company filed a registration statement covering the resale of the additional shares of Common Stock underlying the New Warrants and the Maxim Warrant (together the “Warrants”) on January 26, 2015. The Warrants have not been registered under the Securities Act, or state securities laws. The issuance of the Warrants is exempt from the registration requirements of the Securities Act pursuant to the exemption for transactions by an issuer not involving any public offering under Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D promulgated under the Securities Act. The Company made this determination based on the representations that each party is an “accredited investor” within the meaning of Rule 501 of Regulation D.

On November 19, 2015, the Company issued to Hadasit Medical Research Services and Development Ltd., 100,000 shares of Common Stock pursuant to the exercise of warrants issued under the February 17, 2010 Clinical Trial Agreement, as amended May 30, 2011, with Hadasit Medical Research Services and Development Ltd. The issuance of these securities was effected without registration in reliance upon Regulation D promulgated under the Securities Act. No underwriters were involved with the issuance of such securities and no commissions were paid in connection with such transaction.

## **Item 6. SELECTED FINANCIAL DATA**

Not required.

## **Item 7. MANAGEMENT’S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

### **Company Overview**

We are a biotechnology company developing novel adult stem cell therapies for debilitating neurodegenerative disorders such as ALS, MS, and PD among others. These diseases for the most part have no or limited treatment

options and as such represent unmet medical needs. We believe that NurOwn®, our proprietary process for the propagation of MSC and their differentiation into neurotrophic factor-secreting cells, and their transplantation at, or near, the site of damage, offers the hope of more effectively treating neurodegenerative diseases. Our core technology was developed in collaboration with Prof. Daniel Offen of the Felsenstein Medical Research Center of Tel Aviv University and the late Prof. Eldad Melamed, who passed away in October 2015, and was former head of Neurology of the Rabin Medical Center and former member of the Scientific Committee of the Michael J. Fox Foundation for Parkinson's Research. Our wholly-owned Israeli Subsidiary holds rights to commercialize the technology, through a licensing agreement with Ramot. We currently employ 17 employees in Israel and 3 in the United States.

## Results of Operations

For the period from inception (September 22, 2000) until December 31, 2015, the Company did not generate any revenues from operations. The Company does not expect to earn revenues from operations until at least 2020, if ever. In addition, the Company incurred operating costs and expenses of approximately \$8,536,000 during the year ended December 31, 2015.

### *Research and Development, net*

Our business model calls for significant investments in research and development. Our research and development expenditures, net in the year ended December 31, 2015 were \$4,949,000, an increase of \$177,000 compared to \$4,772,000 for the year ended December 31, 2014. Included in these amounts were OCS research and development grants that are recorded as an offset to expenses as well as stock based compensation expenses. OCS grants included as an offset were \$1,386,000 in 2015 and \$1,344,000 in 2014 while stock based compensation expenses included in research and development expenses were \$130,000 in 2015 and \$176,000 in 2014. Excluding OCS grants and stock based compensation expenses, research and development expenses increased by \$266,000 from \$6,047,000 in 2014 to \$6,313,000 in 2015.

This increase is primarily due to an increase of \$492,000 to \$4,343,000 for the year ended December 31, 2015, from \$3,851,000 for the year ended December 31, 2014 for costs of activities related to the U.S. Clinical Trial, primarily due to higher payments to the Mayo Clinic and higher fees to our PRC Clinical (our US CRO) offset by a reduction of \$147,000 in the costs of activities related to the Israeli clinical trials and costs of materials as well as net reduction of \$21,000 of various other expenses.



*General and Administrative*

General and administrative expenses for the years ended December 31, 2015 and 2014 were \$3,587,000 and \$2,649,000, respectively. The increase of \$938,000 in general and administrative expenses is mainly due to: (i) an increase of \$527,000 in payroll expenses primarily due to the hiring of a new CEO in June 2014 and his replacement in September 2015, as well as a hiring of a new CFO in August 2015, (ii) an increase of \$371,000 in the cost of our investor relations and public relations activities and rent, and (iii) an increase of \$263,000 in the cost of our Delaware Franchise tax and (iv) an increase of \$10,000 of various other expenses offset by a decrease of \$233,000 in stock based compensation expenses.

*Financial Expenses*

The financial income of \$48,000 for the year ended December 31, 2015 is mainly due to interest earned on our cash, cash equivalents and short term deposits.

Financial expenses for the year ended December 31, 2014 were \$1,825,000. The financial expenses for the year ended December 31, 2014 included a charge \$1,743,000 due to revaluation of warrants issued to investors in the August 2013 public offering ("2013 Warrants") which included certain anti-dilution provisions. Under generally accepted accounting principles, the anti-dilution provisions require those 2013 Warrants to be valued and classified as a warrant liability on the balance sheet, resulting in a reduction of stockholders' equity. On January 6, 2015, the remaining 2013 Warrants, that did not participate in the redemption and that did not provide a waiver of their anti-dilution rights, exercised their warrants. Therefore, the liability related to the 2013 Warrants has been cancelled.

*Net Loss*

Net loss for the year ended December 31, 2015 was \$8,488,000, as compared to a net loss of \$9,246,000 for the year ended December 31, 2014. Net loss per share for the year ended December 31, 2015 was \$0.46, compared to net loss per share of \$0.68 for the year ended December 31, 2014.

The decrease in the net loss for the year ended December 31, 2015 compared to the year ended December 31, 2014 is due to an increase in our research and development expenses and general and administrative expenses offset by a decrease in our financial expenses as explained above.

The weighted average number of shares of Common Stock used in computing basic and diluted net loss per share for the year ended December 31, 2015 was 18,405,610, compared to 13,662,758 for the year ended December 31, 2014.

The increase in the weighted average number of shares of Common Stock used in computing basic loss per share for the year ended December 31, 2015 was due to: (i) the issuance of shares of Common Stock in a private placement in June 2014 and pursuant to a Warrant Exercise Agreement in January 2015, as described in more detail below, (ii) the exercise of options and warrants, and (iii) the issuance of shares to service providers.

### **Going Concern**

To date the Company has not generated any revenues from its activities and has incurred substantial operating losses. Management expects the Company to continue to generate substantial operating losses and to continue to fund its operations primarily through utilization of its current financial resources and through additional raises of capital. 2015 net cash inflows from issuances of Common Stock through the exercise of equity warrants as well as from issuances of new equity warrants amounted to approximately \$14.8 million, net. Management believes that the Company's current resources are sufficient to fund its operations for the next 12 months, however there can be no assurance that additional funds necessary for the Company's long term operations will be available on terms acceptable to the Company, or that the Company will not incur additional unforeseen costs or expenses. Such conditions raise substantial doubts about the Company's long term ability to continue as a going concern. The Company's financial statements do not include any adjustments relating to the recoverability and classification of assets, carrying amounts or the amount and classification of liabilities that may be required should the Company be unable to continue as a going concern.

### **Liquidity and Capital Resources**

The Company has financed its operations since inception primarily through public and private sales of its Common Stock and warrants and the issuance of convertible promissory notes. At December 31, 2015, the Company had net working capital of \$13,836,000 including cash, cash equivalents and short term bank deposits amounting to \$15,955,000.

Net cash used in operating activities for the year ended December 31, 2015 was \$7,408,000. Cash used for operating activities was primarily attributed to cost of clinical trials, rent of clean rooms and materials for clinical trials, payroll costs, rent, outside legal fee expenses and public relations expenses.

Net cash used in investing activities for the year ended December 31, 2015 was \$11,283,000 representing primarily a net increase in short-term deposits.

Net cash provided by financing activities for the year ended December 31, 2015 was \$14,868,000, including net proceeds of \$12,409,000 from the January 8, 2015 agreement described below as well as \$2,459,000 from the exercises of other warrants and options during the year.

On June 13, 2014, we entered into a securities purchase agreement with a group of investors, including several healthcare-focused funds (the “Investors”) to effect a private placement (the “2014 Private Placement”) of the Company’s Common Stock and warrants to purchase Common Stock. On June 19, 2014, upon the closing of the 2014 Private Placement, we received gross proceeds of \$10.5 million, resulting from the issuance and sale of 2.8 million shares of Common Stock at a price per share of \$3.75, a 15% discount to the 30 day volume-weighted average price of \$4.41. The Investors also received warrants to purchase up to 2.8 million shares of Common Stock at an exercise price of \$5.22 per share (the “2014 Warrants”). The 2014 Warrants were exercisable immediately upon closing of the 2014 Private Placement and have a term of three (3) years.

On January 8, 2015, the Company signed an agreement according to which the Company issued 2.5 million shares of Common Stock, pursuant to the exercise of the 2014 Warrants for consideration of \$13.3 million dollars. In addition, the Company granted new warrants to the warrant holders to purchase up to an aggregate of approximately 3.8 million unregistered shares of Common Stock at an exercise price of \$6.50.

Maxim Group LLC (“Maxim”) acted as solicitation agent for the exercise of the 2014 Warrants on January 8, 2015, for a cash fee equal to 6.0% of the exercise proceeds, as well as fees and expenses of Maxim of \$20,000. In addition, the Company issued Maxim a warrant to purchase up to approximately 38,000 shares of Common Stock (equal to 1.5% of the exercised 2014 Warrants) upon substantially the same terms as the new warrants.

On June 4, 2015, we filed a shelf registration statement, effective June 10, 2015, relating to Common Stock, warrants and units that we may sell from time to time in one or more offerings, up to a total dollar amount of \$100,000,000. We have not filed any supplemental prospectus defining particular terms of securities to be offered under the shelf registration statement.

Our material cash needs for the next 12 months will include (i) costs of the clinical trial in the U.S. (ii) employee salaries, (iii) costs expected for the upcoming multi-dose clinical trial in Israel, (iv) payments to Hadassah for rent and operation of the GMP facilities, and (v) fees to our consultants and legal advisors, patents, and fees for facilities to be used in our research and development.

Future operations are expected to be highly capital intensive and will require substantial capital raisings. We expect our current cash position will allow us to meet our obligations in the upcoming 12 months.

Over the longer term if we are not able to raise substantial additional capital, we may not be able to continue to function as a going concern and may have to cease operations or the Company will reduce its costs, including curtailing its current plan to pursue larger clinical trials in ALS and move new indications into clinical testing. We will be required to raise a substantial amount of capital in the future in order to reach profitability and to complete the commercialization of our products. Our ability to fund these future capital requirements will depend on many factors, including the following:

- our ability to obtain funding from third parties, including any future collaborative partners;
- the scope, rate of progress and cost of our clinical trials and other research and development programs;
- the time and costs required to gain regulatory approvals;
- the terms and timing of any collaborative, licensing and other arrangements that we may establish;
- the costs of filing, prosecuting, defending and enforcing patents, patent applications, patent claims, trademarks and other intellectual property rights;
- the effect of competition and market developments; and
- future pre-clinical and clinical trial results.

### **Critical Accounting Policies**

Our significant accounting policies are more fully described in Note 2 to our consolidated financial statements appearing in this Annual Report. We believe that the accounting policies below are critical for one to fully understand and evaluate our financial condition and results of operations.

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which we prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate such estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions.

### **Financial statements in U.S. dollars:**

The functional currency of the Company is the U.S dollar ("dollar") since the dollar is the currency of the primary economic environment in which the Company has operated and expects to continue to operate in the foreseeable future. Part of the transactions of the Company are recorded in new Israeli shekels ("NIS"); however, a substantial portion of the Company's costs are incurred in dollars or linked to the dollar. Accordingly, management has designated the dollar as the currency of the Company's primary economic environment and thus it is their functional and reporting currency.

Transactions and balances denominated in dollars are presented at their original amounts. Non-dollar transactions and balances have been re-measured to dollars in accordance with the provisions of ASC 830-10 (formerly Statement of Financial Accounting Standard 52), "Foreign Currency Translation". All transaction gains and losses from re-measurement of monetary balance sheet items denominated in non-dollar currencies are reflected in the statement of operations as financial income or expenses, as appropriate.

**Fair value of financial instruments:**

The carrying values of cash and cash equivalents, accounts receivable and prepaid expenses, trade payables and other accounts payable approximate their fair value due to the short-term maturity of these instruments.

The Company utilizes the Black Scholes Merton formula to measure the fair value of the warrants issued. The assumptions included in the Black-Scholes model were: (i) the market price of the Company's shares; (ii) the exercise price of the warrant; (iii) risk-free interest; (iv) term available to exercise or redeem the security and (v) the volatility of the shares during the relevant term. The Company determines the volatility of its shares using daily historical quotes of the shares. The risk free interest rate is determined as the interest rate on governmental bonds with maturity commensurate with the term of the warrant.

**Accounting for stock-based compensation:**

In accordance with ASC 718-10 (formerly Statement of Financial Accounting Standards 123 (Revised 2004)) the Company estimates the fair value of equity-based payment awards on the date of grant using an option-pricing model. The value of the portion of the award that is ultimately expected to vest is recognized as expense over the requisite service periods in the Company's consolidated statement of operations.

The Company recognizes compensation expense for the value of non-employee awards, which have graded vesting, based on the straight-line method over the requisite service period of each award.

The Company recognizes compensation expense for the value of employee awards that have graded vesting, based on the straight-line method over the requisite service period of each of the awards, net of estimated forfeitures.

The Company estimates the fair value of restricted shares based on the market price of the shares at the grant date and estimates the fair value of stock options granted using a Black-Scholes options pricing model. The option-pricing model requires a number of assumptions, of which the most significant are, expected stock price volatility and the expected option term (the time from the grant date until the options are exercised or expire). Expected volatility was calculated based upon actual historical stock price movements over the period, equal to the expected option term. The Company has historically not paid dividends and has no foreseeable plans to issue dividends. The risk-free interest rate is based on the yield from U.S. Treasury zero-coupon bonds with an equivalent term.

**Research and development expenses, net:**

Research and development expenses, are charged to the statement of operations as incurred.

Royalty-bearing grants from the Government of Israel for funding approved research and development projects are recognized at the time the Company is entitled to such grants, on the basis of the costs incurred and applied as a deduction from research and development expenses. Such grants are included as a deduction of research and development costs since at the time received it is not probable the Company will generate sales from these projects and pay the royalties resulting from such sales.

**Off Balance Sheet Arrangements**

We have no off balance sheet arrangements that have or are reasonably likely to have a current or future material effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources.

**Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK**

Not required.

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**Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

BRAINSTORM CELL THERAPEUTICS INC. AND SUBSIDIARIES

**CONSOLIDATED FINANCIAL STATEMENTS**

**AS OF DECEMBER 31, 2015**

**U.S. DOLLARS IN THOUSANDS**

(Except share data and exercise prices)

BRAINSTORM CELL THERAPEUTICS INC. AND SUBSIDIARIES

**CONSOLIDATED FINANCIAL STATEMENTS**

**AS OF DECEMBER 31, 2015**

U.S. DOLLARS IN THOUSANDS

(Except share data and exercise prices)

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

**To the Board of Directors and Stockholders of**

**BRAINSTORM CELL THERAPEUTICS Inc.**

We have audited the accompanying consolidated balance sheet of BRAINSTORM CELL THERAPEUTICS Inc. and its subsidiaries (the "Company") as of December 31, 2015 and 2014, and the related consolidated statement of income, stockholders' deficiency, and cash flows for each of the two years in the period ended December 31, 2015. These financial statements are the responsibility of the Company's Board of Directors and management. Our responsibility is to express an opinion on the financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, based on our audits, such consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2015 and 2014, and the results of its operations and cash flows for each of the two years in the period ended December 31, 2015 in conformity with accounting principles generally accepted in the United States of America.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. The Company is engaged in the development of stem cell therapeutic products, and to-date has not generated revenues from such activities. The resulting operating losses raise substantial doubts about its ability to continue as a going concern. Management's plans concerning these matters are described in Note 1 to the financial statements. The financial statements do not include any adjustments that might result from the outcome of these uncertainties.

/s/ Brightman Almagor Zohar & Co.

Brightman Almagor Zohar & Co.

Certified Public Accountants

A Member of Deloitte Touche Tohmatsu Limited

Tel Aviv, Israel

March 9, 2016

BRAINSTORM CELL THERAPEUTICS INC. AND SUBSIDIARIES

CONSOLIDATED BALANCE SHEETS

U.S. dollars in thousands

(Except share data)

**December 31,**  
2 0 1 5   2 0 1 4  
U.S. \$ in  
thousands

ASSETS

Current Assets:

Cash and cash equivalents	\$428	\$4,251
Short-term deposit	15,527	4,290
Account receivable (Note 4)	759	1,005
Prepaid expenses and other current assets	74	32