Neuralstem, Inc.
Form 10-K
March 14, 2016

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2015.

or

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

For the transition period from_____ to_____.

Commission File Number 001-33672

NEURALSTEM, INC.

(Exact name of registrant as specified in its charter)

Delaware	**52-2007292**
State or other jurisdiction of	(I.R.S. Employer
incorporation or organization	Identification No.)
20271 Goldenrod Lane	**20876**

Germantown, Maryland
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code **(301)-366-4841**

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

Title of each class	**Name of each exchange on which registered**
Common stock, $0.01 par value	NASDAQ Stock Market

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

None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. ¨ Yes x 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. x 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). x Yes ¨ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

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.

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the Company’s common equity was last sold as of the last business day of the registrant’s most recently completed second fiscal quarter based upon the closing price of the common stock as reported by NASDAQ on such date, was $168,902,179.

The number of shares outstanding of Registrant’s common stock, $0.01 par value at March 1, 2016 was **92,044,042**.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant’s definitive proxy statement relating to its 2016 annual meeting of shareholders (the “2016 Proxy Statement”) are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The 2016 Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

NEURALSTEM, INC

ANNUAL REPORT ON FORM 10-K

FOR THE YEAR ENDED DECEMBER 31, 2015

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PART I

We urge you to read this entire Annual Report on Form 10-K, including the "Risk Factors" section, the financial statements and related notes included herein. As used in this Annual Report, unless context otherwise requires, the words "we," "us," "our," "the Company," "Neuralstem" and "Registrant" refer to Neuralstem, Inc. and its subsidiary Also, any reference to "common share" or "common stock," refers to our $.01 par value common stock.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements in this annual report that are not strictly historical are forward-looking statements and include statements made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 such as statements about products in development, results and analyses of pre-clinical studies, clinical trials and studies, research and development expenses, cash expenditures, regulatory applications and approvals, and third party relationships, among other matters. You can identify these forward-looking statements because they involve our expectations, intentions, beliefs, plans, projections, anticipations, or other characterizations of future events or circumstances and may often be identified by words such as "expect," "anticipate," "intend," "plan," "believe," "seek" or "will.". These forward-looking statements are not guarantees of future performance and are subject to substantial risks and uncertainties that may cause actual results to differ materially from those in the forward-looking statements These Forward-looking statements by their nature address matters that are, to different degrees, uncertain. Specific risks and uncertainties that could cause our actual results to differ materially from those expressed in our forward-looking statements include risks inherent in our ability to conduct and obtain successful results from our clinical trials, our ability to commercialize our technology, our ability to obtain regulatory approval for our product candidates, our ability to contract with third parties to adequately test and manufacture our proposed products, our ability to protect our intellectual property rights and our ability to obtain additional financing to continue development efforts. These forward-looking statements are based on current expectations and assumptions that are subject to risks and uncertainties, which could cause our actual results to differ materially from those reflected in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this Annual Report, and in particular, the risks discussed under the caption "Risk Factors" in Item 1A and those discussed in other documents we file with the Securities and Exchange Commission (SEC). We undertake no obligation to revise or publicly release the results of any revision to these forward-looking statements, except as required by law. Given these risks and uncertainties, readers are cautioned not to place undue reliance on such forward-looking statements.

The information contained herein is current as of the date of this Annual Report (December 31, 2015), unless another date is specified.

ITEM 1. BUSINESS

Overview

We are focused on the research, development and commercialization of central nervous system therapies based on our proprietary human neuronal stem cells and our stem-cell derived small molecule compounds. We are headquartered in Germantown, Maryland and have a wholly-owned subsidiary in China, Suzhou Neuralstem Biopharmaceutical Co. Ltd., or Neuralstem China.

Our technology base has produced three primary assets: Our NSI-189 small molecule program, our NSI-566 stem cell therapy program and our novel and proprietary new chemical entity screening platform.

Our patented technology enables the commercial-scale production of multiple types of central nervous system stem cells, which are under development for the potential treatment of central nervous system diseases and conditions. In addition, this ability to generate human neural stem cell lines provides a platform for chemical screening and discovery of novel compounds that Neuralstem believes may stimulate the brain's capacity to generate neurons, potentially reversing pathologies associated with certain central nervous system (CNS) conditions. This proprietary screening platform led to the discovery of NSI-189.

We have developed and maintain a portfolio of patents and patent applications that form the proprietary base for our research and development efforts. We own or exclusively license one hundred fourteen (114) U.S. and foreign issued patents and forty-seven (47) U.S. and foreign patent applications in the field of regenerative medicine, related to our stem cell technologies as well as our small molecule compounds. At times we have licensed the use of our intellectual property to third parties.

We believe our technology base, in combination with our expertise, and collaborative projects with major research institutions, could facilitate the development and commercialization of products for use in the treatment of a wide array of central nervous system disorders including neurodegenerative conditions and regenerative repair of acute disease.

There can be no assurances that we will ultimately produce any viable products or processes. Even if we are able to produce a commercially viable product, there are strong competitors in this field and our products may not be able to successfully compete against them.

All of our research efforts to date are at the pre-clinical or clinical stage of development. We are focused on leveraging our key assets, including our intellectual property, proprietary technology, scientific team and facilities, to advance our technologies and clinical programs. In addition, we are pursuing strategic collaborations with members of academia and industry.

Clinical Programs

We have devoted substantially all our efforts to the pre-clinical and clinical development of our small molecule compounds and our stem cell therapeutics. Below is a description of our most advanced clinical programs, their intended indication, current stage of development and our expected future development plans:

In January, 2016, we announced a strategic refocusing to concentrate the Company's resources on the NSI-189 small molecule program. As part of this refocusing, the Company announced that it will seek external funding to defray all, or substantially all, of the costs associated with the NSI-566 stem cell therapy program. The Company is in active conversations with a number of sources of funding to achieve this goal and minimize any delay in progressing our stem cell therapy programs.

NSI - 189 (Small Molecule Pharmaceutical Compound).

Major Depressive Disorder (MDD)

Major depressive disorder, or MDD (also known as recurrent depressive disorder, clinical depression, major depression, unipolar depression, or unipolar disorder), is a mental disorder characterized by episodes of all-encompassing low mood accompanied by low self-esteem and loss of interest or pleasure in normally enjoyable activities. NSI-189 is being developed for the treatment of major depressive disorder and other psychiatric and/or cognitive impairment indications associated with hippocampal atrophy. NSI-189 is the lead compound in our neurogenic small molecule drug platform. We believe that NSI-189 may provide an effective treatment for patients suffering from MDD by promoting synaptogenesis or neurogenesis in the hippocampus.

In February of 2011, we commenced a Phase I clinical trial (Phase Ia portion), NSI-189, at California Clinical Trials, LLC, in Glendale, California. The purpose of the Phase Ia portion of the trial was to evaluate the safety of the drug in healthy volunteers. The Phase Ia portion tested a single oral administration of NSI-189 in 24 healthy volunteers and was completed in October of 2011.

In December of 2011, we received authorization from the FDA to commence the Phase Ib randomized, dose-escalating, placebo controlled clinical trial for the treatment of MDD. The purpose of the Phase Ib portion of the clinical trial was to determine the drug safety and tolerability in three dosages in diagnosed MDD patients. The Phase Ib portion consisted of patients with MDD receiving daily doses for 28 consecutive days with an eight week observation period. The trial was completed in November 2013 and met its primary endpoints of safety and tolerability and showed a promising reduction in depressive and cognitive symptoms across the secondary, explorative endpoints.

In September, 2015 we filed the regulatory and clinical protocol with the Food and Drug Administration (FDA) for a Phase II, multi-site clinical trial in approximately 220 patients. In late February, Neuralstem received the Food and Drug Administration (FDA) approval for the Phase II clinical trial which is expected to enroll the first subject in Q2 of 2016.

In February 2016, the Company received approval from the FDA to commence its Phase 2 Major Depressive Disorder (MDD) trial.

Second Study:

We are exploring the expansion of the NSI-189 program to include a second short-term study. The Company will provide an update in 2016.

NSI - 566 (Stem Cells).

Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis, or ALS, is a disease of the nerve cells in the brain and spinal cord that control voluntary muscle movement. In ALS, nerve cells (neurons) waste away or die, and can no longer send messages to muscles. This eventually leads to muscle weakening, twitching, and an inability to move the arms, legs, and body. The condition slowly gets worse. When the muscles in the chest area stop working, it becomes hard or impossible to breathe. NSI-566 is under development as a potential treatment for ALS by providing cells designed to nurture and protect the patients' remaining motor neurons; and possibly repair some motor neurons which have not yet died but which are diseased. Neuralstem received orphan designation by the FDA for NSI-566 in ALS.

In January 2010, we commenced the Phase I trial of NSI-566 in ALS at Emory University in Atlanta Georgia. The purpose of the Phase I trial was to evaluate the safety and transplantation technique of our proposed treatment and procedure. The dosing of patients in the Phase I trial, as designed, was completed in August of 2012. We commenced our Phase II clinical trial for ALS in September of 2013. The Phase II dose escalation trial enrolled 15 ambulatory patients in five different dosing cohorts, under an accelerated dosing and treatment schedule. Each patient in the final cohort had two transplants, for a total of 18 surgeries. We have now completed all of the transplantations. The observation period of six months after the last surgery concluded in January 2015. The Phase II ALS clinical trial met the primary safety endpoints and established what we believe to be the maximum safe tolerated dose of 16 million cells delivered in 40 injections. In September 2015, nine-month Phase II and combined Phase I and Phase II data on the NSI-566 trial in amyotrophic lateral sclerosis (ALS) was presented at the American Neurological Association Meeting by principal investigator Eva Feldman, MD, PhD, Director of the A. Alfred Taubman Medical Research Institute and Director of Research of the ALS Clinic at the University of Michigan Health. The Company is in discussion with the FDA for planning of a larger registration directed, controlled trial.

In January, 2016, the Company announced that it is in discussions with various governmental, state and non-profit organizations regarding funding grants for a registration directed, controlled trial and that initiation of such a trial would, in part, be dependent upon significant funding from such sources. To date, substantially all of the clinical costs of ALS studies undertaken by the Company have been funded by such grants.

Chronic Spinal Cord Injury

A spinal cord injury, or SCI, generally refers to any injury to the spinal cord that is caused by trauma instead of disease although in some cases, it can be the result of diseases. Chronic spinal cord injury refers to the time after the initial hospitalization. Spinal cord injuries are most often traumatic, caused by lateral bending, dislocation, rotation, axial loading, and hyperflexion or hyperextension of the cord or cauda equina. Motor vehicle accidents are the most common cause of SCIs, while other causes include falls, work-related accidents, sports injuries, and penetrations such as stab or gunshot wounds. In certain instances, SCIs can also be of a non-traumatic origin, as in the case of cancer, infection, intervertebral disc disease, vertebral injury and spinal cord vascular disease. We believe that NSI-566 may provide an effective treatment for chronic spinal cord injury by "bridging the gap" in the spinal cord circuitry created in traumatic spinal cord injury and providing new cells to help transmit the signal from the brain to points at or below the point of injury.

During the first quarter of 2013, we received authorization from the United States Food and Drug Administration, or FDA, to commence our proposed Phase I clinical trial to treat chronic spinal cord injury. The entire trial will take place at The University of California, San Diego. The trial commenced during the third quarter of 2014 and the first subject was treated in October 2014. The study enrolled four AIS A thoracic-spinal cord injury subjects (motor and sensory complete), one-to-two years post-injury at the time of stem cell treatment. In January, 2016 we reported six month follow-up data on all four subjects. The stem cell treatment demonstrated feasibility and safety; there were no serious adverse events. A self-reported ability to contract some muscles below the level of injury was confirmed via clinical and electrophysiological follow-up examinations in one of the four subjects treated. There was no change in the clinical status of the three other subjects.

To date, substantially all of the clinical costs of this study have been funded by grants arranged through the University of California, San Diego (UCSD).

Motor Deficits Due to Ischemic Stroke

Ischemic strokes, the most common type of stroke, occur as a result of an obstruction within a blood vessel supplying blood to the brain. Post-stroke motor deficits include paralysis in arms and legs and can be permanent. We believe that NSI-566 may provide an effective treatment for restoring motor deficits resulting from ischemic stroke by both creating new circuitry in the area of injury and through repairing and or nurturing diseased cells to improve function in patients.

In the fourth quarter of 2013 the Company commenced a human clinical trial for treatment of motor deficits due to ischemic stroke. The trial is being conducted by Neuralstem China, at BaYi Brain Hospital in Beijing, China utilizing our spinal cord stem cells. The trial authorization encompasses a combined phase I/II/III design and will test direct injections of NSI-566 into the brain. The Phase I portion of the trial is designed to confirm the maximum safe tolerated dose. To date, we have completed dosing the second of three planned cohorts.

To date, the Ischemic Stroke program has been funded substantially by Neuralstem.

Markets

The table below summarizes the potential United States patient populations by indication, for our proposed stem cell and small molecule products:

Medical Condition	**Estimated Number of Patients in United States**	
Small molecule compounds		
Major Depressive Disorder	14.8 million	(1)
Stem cells		
ALS	20,000	(2)
Alzheimer's Disease	5.3 million	(3)
Spinal Cord Injury	240,000 – 337,000	(4)
Stroke	6.5 million	(5)

(1) Anxiety and Depression Association of America (ADAA), website: http://www.adaa.org/about-adaa/press-room/facts-statistics retrieved March 2016

(2) The ALS Association (ALSA), website: http://www.alsa.org/about-als/facts-you-should-know.html retrieved March 2016

(3) Alzheimer's Association (AA), The 2015 Alzheimer's Disease Facts and Figures, website: https://www.alz.org/facts/downloads/facts_figures_2015.pdf retrieved March 2016

(4) National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance. Birmingham, AL: University of Alabama at Birmingham, website: https://www.nscisc.uab.edu/Public/Facts%202015.pdf retrieved March 2016

(5) National Stroke Association (NSA), website: retrieved March 2016 from www.stroke.org **Technology**

Stem Cells.

Our technology enables the isolation and large-scale expansion of regionally specific, human neural stem cells from all areas of the developing human brain and spinal cord, thus enabling the generation of physiologically relevant human neurons of all types. We believe that our stem cell technology will assist the body in producing new cells to replace malfunctioning or dead cells as a way to treat disease and injury. Many significant and currently untreatable human diseases arise from the loss or malfunction of specific cell types in the body. Our focus is the development of effective methods to generate replacement cells from neural stem cells. We believe that replacing damaged, malfunctioning or dead neural cells with fully functional ones may be a useful therapeutic strategy in treating many diseases and conditions of the central nervous system. We own or exclusively license fifty-two (52) and foreign issued patents and thirty-three (33) U.S. and foreign patent applications related to our stem cell technologies.

Small Molecule Pharmaceutical Compounds.

Utilizing our proprietary stem cell derived, screening capability, we have developed and patented a series of small molecule compounds. We believe the low molecular weight organic compounds can efficiently cross the blood/brain barrier. In mice, research indicated that the small molecule compounds both stimulate neurogenesis of the hippocampus and increase its volume. Our collaborators at Massachusetts General Hospital have presented the human data from the MDD trial which showed clinically meaningful and statistically significant improvement in depressive and cognitive scales. We believe the small molecule compounds may assist promoting synaptogenesis or neurogenesis in the human hippocampus documented in indications such as MDD.

Our small molecule compounds are covered by sixty-two (62) exclusively owned U.S. and foreign issued patents and fourteen (14) exclusively owned U.S. and foreign patent applications related to our small molecule compounds.

Research

Substantial resources are devoted to our research programs in order to isolate and develop a series of neural stem cell banks that we believe can serve as a basis for our therapeutic product candidates. Our efforts are directed at developing therapies utilizing our stem cells and small molecule regenerative drug candidates. This research is conducted internally, through the use of third party laboratories and consulting companies under our direct supervision, and through collaboration with academic institutes.

Manufacturing

We currently manufacture our cells both in-house and on an outsourced basis. We outsource the manufacturing of our pharmaceutical compounds to third party manufacturers. We manufacture, in-house, cells that are not required to meet stringent FDA requirements. We use these cells in our research and collaborative programs. During 2015, we are began the process of bringing the manufacturing of our spinal cord stem cells, in-house. We believe this will better assure the availability of our stem cells and to also lead to a reduction in per patient manufacturing costs.

Intellectual Property

Our research and development is supported by our intellectual property. We own or exclusively license one hundred fourteen (114) U.S. and foreign issued patents and forty-seven (47) U.S. and foreign patent applications in the field of regenerative medicine, related to our stem cell technologies as well as our small molecule compounds. Our issued patents have expiration dates ranging from 2016 through 2034. In our opinion the patents expiring in 2016 are not critical to our business.

Our success will likely depend upon our ability to preserve our technologies and operate without infringing the proprietary rights of other parties. However, we may rely on certain proprietary technologies and know-how that are not patentable. We protect our proprietary information, in part, by the use of confidentiality agreements with our employees, consultants and certain of our contractors.

When appropriate, we seek patent protection for inventions in our core technologies and in ancillary technologies that support our core technologies or which we otherwise believe will provide us with a competitive advantage. We accomplish this by filing patent applications for discoveries we make, either alone or in collaboration with scientific collaborators and strategic partners. Typically, although not always, we file patent applications both in the United States and in select international markets. In addition, we plan to obtain licenses or options to acquire licenses to patent filings from other individuals and organizations that we anticipate could be useful in advancing our research, development and commercialization initiatives and our strategic business interests.

In addition to patenting our technologies, we also rely upon trade-secret protection for our confidential and proprietary information and take active measures to control access to that information.

Our policy is to require our employees, consultants and significant scientific collaborators and sponsored researchers to execute confidentiality and assignment of invention agreements upon the commencement of an employment or consulting relationship with us. These agreements generally provide that all confidential information developed or made known to the individual by us during the course of the individual's or entity’s relationship with us, is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees and

consultants, the agreements generally provide that all inventions conceived by the individual or entity in the course of rendering services to us shall be our exclusive property.

The patent positions of pharmaceutical and biotechnology companies, including ours, are uncertain and involve complex and evolving legal and factual questions. The coverage sought in a patent application can be denied or significantly reduced before or after the patent is issued. Consequently, we do not know whether any of our pending applications will result in the issuance of patents, or if any existing or future patents will provide significant protection or commercial advantage or will be circumvented by others. Since patent applications are secret until the applications are published (usually eighteen months after the earliest effective filing date), and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make the inventions covered by each of our pending patent applications or that we were the first to file patent applications for such inventions. There can be no assurance that patents will issue from our pending or future patent applications or, if issued, that such patents will be of commercial benefit to us, afford us adequate protection from competing products, or not be challenged or declared invalid.

In the event that a third party has also filed a patent application relating to inventions claimed in our patent applications, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office or USPTO, to determine priority of invention, which could result in substantial uncertainties and costs, even if the eventual outcome is favorable to us. There can be no assurance that our patents, if issued, would be held valid by a court of competent jurisdiction.

A number of pharmaceutical, biotechnology and other companies, universities and research institutions have filed patent applications or have been issued patents relating to cell therapy, stem cells and other technologies potentially relevant to or required by our proposed products. We cannot predict which, if any, of such applications will issue as patents or the claims that might be allowed.

If third party patents or patent applications contain claims infringed by our technology and such claims are ultimately determined to be valid, there can be no assurance that we would be able to obtain licenses to these patents at a reasonable cost, if at all, or be able to develop or obtain alternative non-infringing technology. If we are unable to obtain such licenses or develop or obtain alternative non-infringing technology at a reasonable cost, we may not be able to develop certain products commercially. There can be no assurance that we will not be obliged to defend ourselves in court against allegations of infringement of third party patents. Patent litigation is very expensive and could consume substantial resources and create significant uncertainties. An adverse outcome in such a suit could subject us to significant liabilities to third parties, require us to seek licenses from third parties, or require us to cease using such technology.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly evolving technology and intense competition. Our competitors include major multinational pharmaceutical companies, specialty biotechnology

companies and chemical and medical products companies. Many of these companies are well-established and possess greater resources for technical, research, development, financial, sales and marketing initiatives than we do. Other, less well-established companies have formed or may form strategic collaborations, partnerships and other types of joint ventures with larger, well established industry competitors that may provide research and development and commercialization advantages to these competitors. Academic institutions, governmental agencies and other public and private research organizations are also conducting and financing research activities which may produce products directly competitive to those we are developing. Moreover, many of these competitors may be able obtain patent protection, or FDA and other regulatory approvals that may impede our freedom to develop and commercialize our programs.

The diseases and medical conditions we are targeting have a demographic in which there are large numbers of patients who do not respond to current therapies or have limited therapies available. Nevertheless, we expect that our technologies and product candidates, if or when approved, will compete with a variety of therapeutic products and procedures offered by other pharmaceutical and biotechnology companies. Many pharmaceutical and biotechnology companies are investigating new drugs and therapeutic approaches for the same or similar indications. These companies' efforts may achieve new efficacy profiles, extend the therapeutic window for such products, alter the prognosis of these diseases, or prevent their onset. We believe that our products, if or when approved, will attempt to compete with these products principally on the basis of improved and extended efficacy and safety and their overall economic benefit to the health care system. Competition for our products may be in the form of existing and new drugs, other forms of cell transplantation, surgical procedures, gene therapy or other proprietary technology and expertise. We expect that all of these products will compete with our product candidates, if or when approved, based on efficacy, safety, cost and intellectual property positions. We cannot be certain that that other entities have not filed patents that block our freedom to commercialize our programs and we may be required to seek licenses from these entities in order to commercialize certain of our proposed products, and such licenses may not be granted or be extremely expensive to obtain.

If we develop products that receive regulatory approval, they would then have to compete for market acceptance and market share. For our potential products, an important success factor will be the timing of market introduction of competitive products. This timing will be a function of the relative speed with which we and our competitors can develop products, complete the clinical testing and approval processes, and supply commercial quantities of a product to the market. These competitive products may also impact the timing of clinical testing and approval processes by limiting the number of clinical investigators and subjects available to test our potential products.

Government Regulation

Regulation by governmental authorities in the United States and other countries is a significant factor in our research and development and will be a significant factor in the manufacture and marketing of our proposed products. The nature and extent to which such regulation applies to us will vary depending on the nature of any products we may develop. Governmental authorities, including the FDA and comparable regulatory authorities in other countries, regulate the design, development, testing, manufacturing, safety, efficacy, labeling, storage, record-keeping, advertising, promotion and marketing of pharmaceutical products, including drugs and biologics, under the Federal Food, Drug, and Cosmetic Act, or FFDCA, and its implementing regulations, and, for biologics, under the Public Health Service Act, or PHSA, and its implementing regulations. Non-compliance with applicable requirements can result in fines and other judicially imposed sanctions, including product seizures, import restrictions, injunctive actions and criminal prosecutions of both companies and individuals. In addition, administrative remedies can involve requests to recall violative products; the refusal of the government to enter into supply contracts; or the refusal to approve pending product approval applications until manufacturing or other alleged deficiencies are brought into compliance. The FDA also has the authority to cause the withdrawal of approval of a marketed product or to impose labeling restrictions. The process of obtaining approvals and the subsequent compliance with appropriate statutes and regulations require the expenditure of substantial time and money, and there can be no guarantee that approvals will be granted.

United States Product Development Process

We believe that, in the United States, our human neuronal stem cell candidates are regulated as biologic pharmaceuticals, or biologics, and our small-molecule compounds are regulated as drugs.

The process required by the FDA before a drug or biological product may be marketed in the United States generally involves the following:

- Completion of preclinical testing of new pharmaceutical or biological products, generally conducted in the laboratory and in animal studies in accordance with GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations to evaluate the potential efficacy and safety of the product candidate;
- Submission of the results of these studies to the FDA as part of an IND application, which must become effective before clinical testing in humans can begin;
- Performance of adequate and well-controlled human clinical trials according to cGMPs and any additional requirements for the protection of human research patients and their health information, to establish the safety and efficacy of the product candidate for its intended use;
- Submission to the FDA of a biological license application, or BLA, for any biologic or a new drug application, or NDA, for any new chemical entity drug we seek to market that includes substantive evidence of safety, purity, and

potency, or safety and effectiveness from results of nonclinical testing and clinical trials;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the product is produced, packaged and distributed, to assess compliance with cGMPs, to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity, and, if applicable, the FDA's current good tissue practices, or GTPs, for the use of human cellular and tissue products;
- Potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA or NDA; and
- FDA review and approval of the NDA, or licensure, of the BLA.

Typically, human clinical evaluation involves a time-consuming and costly three-phase process.

- Phase 1. The product is initially introduced into healthy human volunteers and tested for safety. 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 is often conducted in patients.
- Phase 2. The product is evaluated 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, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk to benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval clinical trials, sometimes referred to as Phase IV clinical trials, may be required and conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk, including risks inferred from other unrelated similar trials. Similarly, an institutional review board, or 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 product has been associated with unexpected serious harm to patients.

Human cell-based therapies in the field of regenerative medicine are relatively novel. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of such products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval.

United States Review and Approval Process

After the completion of clinical trials of a product candidate, FDA approval of a BLA or NDA must be obtained before commercial marketing of the product. The BLA or NDA must include results of product development, laboratory and animal studies, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information as well as a significant user fee. The FDA may grant deferrals for submission of data, or full or partial waivers. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA or NDA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

The FDA may refuse to file any BLA or NDA that it deems incomplete or not properly reviewable at the time of submission, and may request additional information. Once the submission is accepted for filing, the FDA reviews the BLA or NDA to determine, among other things, whether the proposed product is safe, potent, and/or effective for its intended use, and has an acceptable purity profile, and whether the product is safe and effective for its intended use, and in each case, whether the product is being manufactured in accordance with cGMP or GTP, if applicable. During the product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the BLA or NDA must submit a proposed REMS. The FDA will not approve a BLA or NDA without a REMS, if required.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA or NDA does not satisfy its regulatory criteria for approval and deny approval via a letter detailing such deficiencies. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the FDA denies an application, the applicant may either resubmit the BLA or NDA, addressing all of the deficiencies identified by the FDA, or withdraw the application.

United States Post-Approval Requirements

Any products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved uses, known as off-label use, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long-term stability of the product. We rely, and expect to continue to rely, on third parties for the production of some, or all, clinical and commercial quantities of our products in accordance with cGMP and GTP regulations, as applicable. Manufacturers and other entities involved in the manufacture and distribution of approved products 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 and other laws.

The FDA also may require post-marketing testing, known as Phase 4 testing, and surveillance to monitor the effects of an approved product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our product candidates under development.

European, China and Other Regulatory Review and Approval

Whether or not FDA approval has been obtained, approval of a product by comparable regulatory authorities in Europe, China and other countries will be necessary prior to commencement of marketing the product in such countries. The regulatory authorities in each country may impose their own requirements and may refuse to grant an approval, or may require additional data before granting it, even though the relevant product has been approved by the FDA or another authority. As with the FDA, the regulatory authorities in the European Union, China and other developed countries have lengthy approval processes for biological and pharmaceutical products. The process for gaining approval in particular countries varies, but generally follows a similar sequence to that described for FDA approval.

Other Health Care Laws

In the event any of proposed products are ever approved for marketing, we may also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments where we may market our product candidates, if approved. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, physician sunshine and privacy and security laws and regulations.

Other Regulations

We are also subject to various U.S. federal, state, local and international laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our business. We cannot accurately predict the extent of government regulation which might result from future legislation or administrative action.

For additional information about governmental regulations as well as risk related to our business that could affect our planned and intended business operations, see the *"Risk Factors"* Section of this Annual Report.

Executive Officers

The following sets forth our current executive officers and information concerning their age and background:

Name	Position	Age	Position Since
Richard J. Daly	Chief Executive Officer, President,	54	2016
Karl Johe, Ph.D.	Chief Scientific Officer	55	1996
Jonathan Lloyd Jones	Chief Financial Officer	55	2015

Mr. Richard J. Daly, age 54, has been Chief Executive Officer, President and a director since February of 2016. Mr. Daly has over 25 years of commercial pharmaceutical experience working in positions of progressive responsibility in sales, marketing and operations. From November 2015 until February 2016, Mr. Daly was a managing partner at

Ravine Rock Partners, LLC, a bio-pharmaceutical consulting company. Prior to that, from August 2013 until November 2014, Mr. Daly was the President of U.S. Diabetes, a subsidiary of AstraZeneca Pharmaceutical LP. From October 2011 until November 2012, Mr. Daly was a founding partner, board member and investor in SagePath Partners LLC, a commercial outsourcing provider to the pharmaceutical industry. Between July 2008 and October 2011, Mr. Daly was executive vice president of North and South America for Takeda NA, the north American subsidiary of Takeda Pharmaceuticals (TSE: TYO). Since June 2015, Mr. Daly has served on the board of directors and on the Compensation and Commercial Committees for Synergy Pharmaceuticals (NASDAQ: SGYP). Since February 2015, Mr. Daly has also served on the board of directors and on the Compensation Committee of Catalyst Pharmaceuticals (NASDAQ: CPRX). Mr. Daly holds a BS in Microbiology from The University of Notre Dame and an MBA from Northwestern University's Kellogg Graduate School of Management. In evaluating Mr. Daly's specific experience, qualifications, attributes and skills in connection with his appointment to our board, we took into account his prior work with both public and private organizations, including his experience in building biopharmaceutical organizations, his strong business development background and his past experience and relationships in the biopharma and biotech fields.

Dr. Karl Johe, Ph.D., age 55***,*** has been a director, Chairman of the Board and our Chief Scientific Officer since 1996. Dr. Johe has over 15 years of research and laboratory experience. Dr. Johe is the sole inventor of Neuralstem's granted stem cell patents and is responsible for the strategic planning and development of our therapeutic products. Dr. Johe received his Bachelor of Arts Degree in Chemistry and a Master's Degree from the University of Kansas. Dr. Johe received his doctorate from the Albert Einstein College of Medicine of Yeshiva University. From 1993 to January 1997, Dr. Johe served as a Staff Scientist at the Laboratory of Molecular Biology of the National Institute of Neurological Disease and Stroke in Bethesda, Maryland. While holding this position, Dr. Johe conducted research on the isolation of neural stem cells, the elucidation of mechanisms directing cell type specification of central nervous system stem cells and the establishment of an in vitro model of mammalian neurogenesis. In evaluating Dr. Johe's specific experience, qualifications, attributes and skills in connection with his appointment to our board, we took into account his extensive experience in international science and business communities. Dr. Johe is also multilingual.

Mr. Jonathan Lloyd Jones, ACA, MBA, age 55***,*** has been our Chief Financial Officer since May of 2015. Mr. Lloyd Jones has over 30 years of experience in finance and corporate development. Mr. Lloyd Jones was previously the Chief Financial Officer of Juniper Pharmaceuticals, Inc. (formerly Columbia Pharmaceuticals) (NASDAQ: JNP) from 2013 to 2014 and served as the Chief Financial Officer and Vice President of Corporate Development at TetraLogic Pharmaceuticals, Inc. (NASDAQ: TLOG) from 2011 to 2012. Prior to that, Mr. Lloyd Jones served as an independent consultant for bio-tech companies from 2010 to 2011. Mr. Lloyd Jones served as Vice President, Finance for TransMolecular, Inc., a privately held bio-tech company from 2006 to 2010. From 1996 to 2006, Mr. Lloyd Jones held positions of increasing seniority at Genzyme, Inc. (now Sanofi-Aventis) (NYSE: ADR) most recently, as Senior Director of Corporate Development. Mr. Lloyd Jones is a member of the Institute of Chartered Accountants in England & Wales. He received his bachelor of science in business studies from the University of Bradford in England (1981), and a master of business administration with a dual major in strategic management and finance from The Wharton School of the University of Pennsylvania.

Employees

As of January 31, 2016, we had thirty three (33) full-time employees. Of these full-time employees, twenty five (25) work on research and development and clinical operations eight (8) in administration. We also use the services of numerous outside consultants in business and scientific matters.

Our Corporate Information

We were incorporated in Delaware in 2001. Our principal executive offices are located at 20271 Goldenrod Lane, Germantown, Maryland 20876, and our telephone number is (301) 366-4841. Our website is located at www.neuralstem.com.

In addition to announcing material financial information through our investor relations website, press releases, SEC filings and public conference calls and webcasts, we also intend to use the following social media channels as a means of disclosing information about the company, its services and other matters and for complying with our disclosure obligations under Regulation FD:

· Neuralstem’s Twitter Account (https://twitter.com/Neuralstem_Inc)

· Neuralstem’s Facebook Page (https://www.facebook.com/Neuralstem)

· Neuralstem's Company Blog (http://neuralstem.com/neuralstem-ceo-blog)

· Neuralstem's Google+ Page (https://plus.google.com/u/0/b/104875574397171789280/104875574397171789280/posts)

· Neuralstem's LinkedIn Company Page (http://www.linkedin.com/company/neuralstem-inc-)

· Neuralstem Asia's Tencent Weibo Account (http://t.qq.com/neuralstem)

The information we post through these social media channels may be deemed material. Accordingly, investors should monitor these accounts and the blog, in addition to following the company's press releases, SEC filings and public conference calls and webcasts. This list may be updated from time to time.

We have not incorporated by reference into this report the information in, or that can be accessed through, our website or social media channels, and you should not consider it to be a part of this report.

Where to Find More Information

We make our public filings with the SEC, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all exhibits and amendments to these reports. Also our executive officers, directors and holders of more than 10% of our common stock, file reports with the SEC on Forms 3, 4 and 5 regarding their ownership of our securities. These materials are available on the SEC's web site, http://www.sec.gov. You may also read or copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, DC 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Alternatively, you may obtain copies of these filings, including exhibits, by writing or telephoning us at:

NEURALSTEM, INC

20271 Goldenrod Lane

Germantown, Maryland 20876

Attn: Chief Financial Officer

Tel: (301) 366-4841

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. We have described below a number of uncertainties and risks which, in addition to uncertainties and risks presented elsewhere in this Annual Report, may adversely affect our business, operating results and financial condition. The uncertainties and risks enumerated below as well as those presented elsewhere in this Annual Report should be considered carefully in evaluating our company and our business and the value of our securities.

Risks Relating to Our Stage of Development and Capital Structure

We may not be able to continue as a going concern if we do not obtain additional financing by June 2016.

The Company has incurred losses since its inception and has not demonstrated an ability to generate revenues from sales or services. These factors create substantial doubt about the Company's ability to continue as a going concern. The consolidated financial statements do not include any adjustment that might be necessary if the Company is unable to continue as a going concern.

The ability of the Company to continue as a going concern is dependent on generating cash from the sale of its common stock and/or obtaining debt financing.

Our cash and cash equivalents balance at December 31, 2015 was approximately $12,234,000. Based on our current expected level of operating expenditures, we expect to be able to fund our operations for the next five to six months from that date. Our ability to continue as a going concern is wholly dependent upon obtaining sufficient financing to fund our operations. Management has discussed various financing options with financial institutions and believes that it will receive cash adequate to fund operations through December 31, 2016 however, there can be no assurance the Company will be successful in these efforts.

Accordingly, despite our ability to secure capital in the past, there is no assurance that additional equity or debt financing will be available to us when needed. In the event that we are not able to secure financing, we may be forced to curtail operations, delay or stop ongoing clinical trials, cease operations altogether or file for bankruptcy.

Our auditors have expressed substantial doubt about our ability to continue as a going concern.

Our auditors' report on our December 31, 2015 financial statements expressed an opinion that our capital resources as of the date of their Audit Report were not sufficient to sustain operations or complete our planned activities for the upcoming year unless we raised additional funds. Accordingly, our current cash level raises substantial doubt about our ability to continue as a going concern past June 2016. If we do not obtain additional funds by such time, we may no longer be able to continue as a going concern and will cease operation which means that our shareholders may lose their entire investment.

Risks Relating to Our Stage of Development and Capital Structure

We have a history of losses.

Since inception in 1996 and through December 31, 2015, we have accumulated losses totaling approximately $171,959,000. On December 31, 2015, we had a working capital surplus of approximately $7,006,000 and stockholders' equity of approximately $4,967,000. Our net losses for the three most recent fiscal years have been approximately $20,904,000, $22,629,000, and $19,832,000 for 2015, 2014, and 2013, respectively. Although from 2013 through 2015 we recognized revenue as a result of us providing subcontractor services and the licensing of our intellectual property, we have generated no significant revenue from the sales of our proposed products.

Our ability to generate revenues and achieve profitability will depend upon our ability to complete the development of our proposed products, obtain the required regulatory approvals, manufacture and market and sell our proposed products. To date, we have not generated any revenue from the commercial sale of our proposed products. No assurances can be given as to exactly when, if at all, we will be able to fully develop, commercialize, market, sell and/or derive any, let alone material, revenues from our proposed products.

We will need to raise additional capital to continue operations.

Since our inception, we have funded our operations through the sale of our securities, credit facilities, the exercise of options and warrants, and to a lesser degree, from grants and research contracts and other revenue generating activities such as licensing. As of December 31, 2015, we had cash, cash equivalents and short-term investments on hand of approximately $12,234,000. We cannot assure you that we will be able to secure additional capital through financing transactions, including issuance of debt, licensing agreements or grants. Our inability to license our intellectual property, obtain grants or secure additional financing will materially impact our ability to fund our current and planned operations.

We have spent and expect to continue spending substantial cash in the research, development, clinical and pre-clinical testing of our proposed products with the goal of ultimately obtaining FDA approval to market such products. We will require additional capital to conduct research and development, establish and conduct clinical and pre-clinical trials, enter into commercial-scale manufacturing arrangements and to provide for marketing and distribution of our products. We cannot assure you that financing will be available if needed. If additional financing is not available, we may not be able to fund our operations, develop or enhance our technologies, take advantage of business opportunities or respond to competitive market pressures. If we exhaust our cash reserves and are unable to secure adequate additional financing, we may be unable to meet operating obligations which could result in us initiating bankruptcy proceedings or delaying, or eliminating some or all of our research and product development programs.

We will need to raise additional capital to pay our indebtedness as it comes due.

We have a substantial level of debt. As of December 31, 2015, we had approximately $8,335,000 in aggregate principal amount long-term indebtedness outstanding. Under our amended loan and security agreement, we were required to make monthly interest only payments through September 2015; and are required to make monthly interest and principal payments of approximately $435,000 per month from October 2015 through March 2017 and make a balloon payment for the remaining principal in April 2017. As security for such indebtedness, we have pledged substantially all of our assets, including our intellectual property. If we are unable to make the required payments, or if we fail to comply with the various requirements and covenants of our indebtedness, we would be in default, which would permit the holders of our indebtedness to accelerate the maturity and require immediate repayment and lead to potential foreclosure on the assets securing the debt. Any default under our indebtedness would have a material adverse effect on our business, operating results and financial condition. Additionally, our amended loan and security agreement governing our $10 million loan also contains a number of affirmative and restrictive covenants, including reporting requirements and other collateral limitations, certain limitations on liens and indebtedness, dispositions, mergers and acquisitions, restricted pa