

Nile Therapeutics, Inc.
Form 10-K
June 21, 2013

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

**Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 for the fiscal year
X ended December 31, 2012**

or

Transition Report Under Section 13 or 15(d) of the Securities Exchange Act of 1934

For the transition period from to

Commission File Number: 001-34058

NILE THERAPEUTICS, INC.

(Exact Name Of Registrant As Specified In Its Charter)

Delaware **88-0363465**
(State or other jurisdiction of incorporation or organization) (I.R.S. Employer Identification No.)

63 Bovet Rd., Suite 421, San Mateo, California

(Address of principal executive offices)

94402

(Zip Code)

(650) 918-7489
(Registrant's telephone number, including area code)

Not Applicable
(Former name, former address and former fiscal year, if changed since last report)

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

None

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

Common Stock, par value \$0.001 per share

Warrants (expiring April 21, 2015)

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 Section 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

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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 in response to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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 Accelerated filer

Non-accelerated filer 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

State 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 common equity was last sold, or the average bid and asked price of such common equity, as of the last business day of the registrant's most recently completed second fiscal quarter.

As of June 30, 2012: \$3,763,041

Indicate the number of shares outstanding of each of the registrant's classes of common stock, as of the last practicable date.

As of June 19, 2013, there were 43,062,231 shares of the issuer's common stock, par value \$0.001 per share, issued and outstanding.

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References to “the Company”, “Nile”, “we”, “us” or “our” in this Annual Report on Form 10-K refer to Nile Therapeutics, Inc., a Delaware corporation, unless the context indicates otherwise.

FORWARD-LOOKING STATEMENTS

This Form 10-K contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. The forward-looking statements are only predictions and provide our current expectations or forecasts of future events and financial performance and may be identified by the use of forward-looking terminology, including the terms “believes,” “estimates,” “anticipates,” “expects,” “plans,” “potential,” “projects,” “intends,” “may,” “will” or “should” or, in each case, their negative, or other variations or comparable terminology, though the absence of these words does not necessarily mean that a statement is not forward-looking. Forward-looking statements include all matters that are not historical facts and include, without limitation, statements concerning our business strategy, outlook, objectives, future milestones, plans, intentions, goals, future financial conditions, obtaining financing of our operations, our research and development programs and planning for and timing of any clinical trials, the possibility, timing and outcome of submitting regulatory filings for our products under development, potential investigational new drug applications, or INDs, and new drug applications, or NDAs, research and development of particular drug products, the development of financial, clinical, manufacturing and marketing plans related to the potential approval and commercialization of our drug products, and the period of time for which our existing resources will enable us to fund our operations. These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from those expressed or implied by such forward-looking statements. For a detailed discussion of these risks and uncertainties, see the “Risk Factors” section in Item 1A of this Form 10-K. We caution the reader not to place undue reliance on these forward-looking statements, which reflect management's analysis only as of the date of this Form 10-K.

We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are subject to many risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Pharmaceutical and biotechnology companies have suffered significant setbacks in advanced clinical trials, even after obtaining promising earlier trial results. Data obtained from such clinical trials are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Additional factors that could cause actual results to differ materially from projected results include, but are not limited to, those discussed in “Risk Factors” elsewhere in this Annual Report. Readers are expressly advised to review and consider those Risk Factors, which include risks associated with (1) our ability to successfully conduct clinical and pre-clinical trials for our product candidates, (2) our ability to obtain required regulatory approvals to develop and market our product candidates, (3) our ability to raise additional capital or to license our products on favorable terms, (4) our ability to execute our development plan on time and on budget, (5) our ability to identify and obtain additional product candidates, and (6) our ability to raise enough capital to fund our operations. Although we believe that the assumptions underlying the forward-looking statements contained in this Report are reasonable, any of the assumptions could be inaccurate, and therefore there can be no assurance that such statements will be accurate. In light of the significant uncertainties inherent in the forward-looking statements included herein, the inclusion of such information should not be regarded as a representation by us or any other person that the results or conditions

described in such statements or our objectives and plans will be achieved. Furthermore, past performance in operations and share price is not necessarily indicative of future performance. Except to the extent required by applicable laws or rules, we do not undertake to update any forward-looking statements or to announce publicly revisions to any of our forward-looking statements, whether resulting from new information, future events or otherwise.

PART I

ITEM 1. BUSINESS

Company Overview

We are a development stage, biopharmaceutical company developing innovative products for the treatment of cardiovascular and renal diseases, with an initial focus on heart failure. We currently have exclusive rights to develop two drug candidates:

Cenderitide (formerly *CD-NP*), our lead product candidate, is a chimeric natriuretic peptide that we are developing for the treatment of heart failure. To date, we have developed cenderitide for the treatment of patients for up to 90 days following admission for acutely decompensated heart failure, or ADHF. We refer to this setting as the “post-acute” period. In 2011, we completed a 58-patient Phase 1 clinical trial of cenderitide in the post-acute setting. We conducted this clinical trial in collaboration with Medtronic, Inc., delivering cenderitide through continuous intravenous infusion using Medtronic’s pump technology. Following that Phase 1 clinical trial, we had planned to initiate a Phase 2 clinical trial of cenderitide, pending availability of capital resources. However, to date we have been unable to raise the capital necessary to conduct the next phase of development of cenderitide. Any further development of cenderitide is subject to our ability to either raise additional capital or enter into a strategic transaction in which an acquirer or strategic partner provides the capital necessary to continue development activities. In addition to treating heart failure, we believe cenderitide may be useful in several other cardiovascular and renal indications.

CU-NP, is a pre-clinical rationally-designed natriuretic peptide that consists of amino acid chains identical to those produced by the human body, specifically the ring structure of C-type natriuretic peptide, or CNP, and the N- and C-termini of Urodilatin, or URO. All development of CU-NP is on hold pending the results of our efforts to pursue additional financing or strategic alternatives

We were originally incorporated under Delaware law in August 2005 under the name Nile Pharmaceuticals, Inc. and we changed our name to Nile Therapeutics, Inc. in January 2007. On September 17, 2007, we were acquired by SMI Products, Inc., or SMI, which was then a public shell company, in a reverse merger transaction whereby a wholly-owned subsidiary of SMI merged with, and into, Nile Therapeutics, with Nile Therapeutics remaining as the surviving corporation and a wholly-owned subsidiary of SMI. In accordance with the terms of this transaction, the stockholders of Nile Therapeutics exchanged all of their shares of Nile Therapeutics common stock for shares of SMI common stock, which immediately following the transaction represented approximately 95 percent of the issued and outstanding common stock of SMI. Upon completion of the merger, the sole officer and director of SMI resigned and was replaced by the officers and directors of Nile Therapeutics. Additionally, following the merger, Nile Therapeutics, or Old Nile, was merged into SMI, and SMI changed its name to Nile Therapeutics, Inc., or Nile, and adopted the business plan of Old Nile. We collectively refer to these two merger transactions in this Annual Report as the “Merger.”

Because the Merger was accounted for as a reverse acquisition under generally accepted accounting principles, the financial statements for periods prior to September 17, 2007 reflect only the operations of Old Nile.

We do not currently own or lease any real property. Our mailing address is 63 Bovet Rd., Suite 421, San Mateo, California 94402. Our telephone number is 650-918-7489 and our Internet address is www.nilethera.com. The information on, or accessible through, our website is not part of this Form 10-K.

Our Product Candidates

The following table summarizes our product development programs:

Product	Indications	Commercial Rights	Ongoing Studies / Status
Cenderitide	Heart failure	Nile	Completed single-blind, placebo-controlled Phase 1 study of cenderitide in chronic heart failure patients in October 2011. The primary objective of the study was to assess the pharmacokinetics of cenderitide delivered through a subcutaneous micro-needle pump to patients in the post-acute heart failure setting. All future studies are on hold pending the results of our efforts to pursue additional financing or strategic alternatives.
CU-NP	Cardiovascular / Renal	Nile	Preclinical. All development is on hold pending the results of our efforts to pursue additional financing or strategic alternatives.

Background on Heart Failure

Heart failure, or HF, is a condition that exists when the heart cannot pump blood to the body as quickly as needed. Blood returning to the heart faster than the heart can eject it, congests the system behind it. Decreased blood flow to organs, such as the kidneys, causes the body to retain more fluid, which further complicates the problem. As a result, HF can often cause damage to the kidneys and other organs, which in turn can worsen the condition of the heart.

HF is the fastest-growing clinical cardiac disease in the United States according to the American Heart Association, affecting over 5 million Americans. Over 1.2 million patients in the U.S. each year are hospitalized with ADHF, an acute exacerbation of their condition. This hospitalization rate is almost double the rate seen 15 years ago. HF is the most frequent cause of hospital admission in the U.S. for patients older than 65 years, generating annual inpatient costs of more than \$35 billion, according to the American Heart Association. We believe that approval of a novel agent with safety and efficacy improvements over existing therapies could significantly expand the HF market.

Patients with heart failure are treated with a combination of drugs in an attempt to improve cardiac output and reverse fluid overload. Diuretics, such as furosemide, are used as a first-line treatment to relieve the symptoms of ADHF patients by helping to remove excess fluid from the body, which then helps to increase cardiac output. However, some studies have correlated high doses of intravenous (i.v.) furosemide, a diuretic, with a decreased kidney function and some patients can become resistant to the effects of furosemide. Second-line treatments are often palliative, and can come at the cost of an increased mortality rate. Despite aggressive therapy, 1 in 3 patients die of the disease within a year of diagnosis, reflecting a substantial need for novel treatments.

Only one new treatment for ADHF patients has been approved by the FDA in over 20 years: nesiritide, which is also known as Natrecor®, or B-type natriuretic peptide, or BNP. Nesiritide, a drug marketed by Johnson & Johnson, is a natriuretic peptide that targets the A-type natriuretic peptide receptor and was approved in 2001 by the FDA.

Within 90 days following hospital admission for ADHF, which we refer to as the “post-acute” period, approximately 40% of patients with ADHF return to the hospital or pass away. To prevent a return to the hospital, post-acute patients need sustained cardiac and renal function support to prevent a recurrence of their acute symptoms. While this post-acute indication is a novel indication in the HF space, we believe that post-acute patients represent one of the greatest areas of unmet need in the HF market.

Cenderitide Program

Cenderitide is a novel chimeric natriuretic peptide in clinical development for the treatment of HF patients. Cenderitide was rationally designed by scientists at the Mayo Clinic's cardio-renal research labs. Current therapies for ADHF, including nesiritide, have been associated with favorable pharmacologic effects, but have also been associated with hypotension, which limit their utility outside the hospital setting. Cenderitide was designed to preserve the favorable effects of existing natriuretic peptide therapies while reducing or attenuating the hypotensive response and enhancing or preserving renal function. We believe that cenderitide has potential utility in multiple cardio-renal indications, including preservation of cardiac function following acute myocardial infarction and prevention of renal damage following cardiac surgery.

Prior Clinical Studies

In 2007, we completed a Phase 1 dose-escalation study in healthy volunteers to examine the safety and pharmacodynamic effects of various doses of cenderitide. The study placed particular emphasis on the effects of cenderitide on blood pressure and renal function. Data from the completed Phase 1 study in healthy volunteers was consistent with several pre-clinical findings, including that cenderitide was associated with increased levels of plasma cGMP, a secondary messenger of the target receptor, preserved renal function, increased urinary excretion of sodium, or natriuresis, and increased urination, or diuresis. The study also showed that cenderitide had a minimal effect on mean arterial pressure, a measurement of pumped blood flow in the arteries.

In 2008, we initiated two additional dose-escalation studies to assess the safety and pharmacodynamic profile of cenderitide in heart failure patients. The first study was a Phase 1 study in chronic heart failure patients with signs of fluid overload designed to understand the maximum tolerated dose of the product candidate. Patients with chronic heart failure with signs of fluid overload were enrolled into the study. The effects of 24 hours of cenderitide delivered through intravenous (i.v.) infusion was compared to the patient's baseline established in the 24 hours prior to cenderitide infusion. The patient's oral diuretic and vasoactive medications were withheld during the cenderitide infusion. While the study was not powered for statistical analysis, data from the Phase 1 study indicate the following:

Cenderitide was tolerated at doses of up to 20 ng/kg/min;

Cenderitide blood pressure effects were dose-dependent and well characterized;

Cenderitide infusion resulted in increases in diuresis at doses of 3, 10 and 20 ng/kg/min as compared to each patient's base-line, which included oral diuretic medication;

With a 24-hour infusion, cenderitide produced decreases in serum creatinine and cystatin-c in stable heart failure patients, consistent with enhanced renal function; and

As expected, the limiting toxicity of cenderitide was shown to be symptomatic hypotension, which was experienced by one of six patients at the maximum tolerated dose of 20 ng/kg/min, and by two of two patients at a dose of 30 ng/kg/min.

The second study initiated in 2008 was a Phase 2 study in acute heart failure patients designed to better understand the hemodynamic properties of cenderitide, or how cenderitide affected blood circulation. The subjects were enrolled 24-48 hours after admission to the hospital for acute heart failure. In the first 24-48 hours after admission, subjects were treated with the standard of care. The subjects were enrolled into the study only after an investigator had determined that the patient needed a Swan-Ganz catheter to better monitor pulmonary capillary wedge pressure, or PCWP, and after the patient's acute condition had stabilized. All patients received a continuous i.v. infusion of furosemide throughout the administration of cenderitide. Data from this Phase 2 study indicate the following:

Cenderitide was tolerated at all study doses, including 1, 3, 10 and 20 ng/kg/min;

Cenderitide had minimal blood pressure effects at all doses;

In the first cohort, where patients were dosed at 3 and then 10 ng/kg/min, the cenderitide infusions produced clinically relevant reductions in PCWP;

In the second cohort, where patients were dosed at 1 and 20 ng/kg/min, the cenderitide infusions did not result in clinically relevant reductions in PCWP;

Cenderitide produced a clinically relevant increase in diuresis at doses of 3, 10 and 20 ng/kg/min when administered concurrently with i.v. furosemide; and

There was no clinically relevant change in serum creatinine and there were no cases of symptomatic hypotension in any subject.

In March 2009, the FDA placed a clinical hold on the cenderitide program. The FDA requested additional data on our Phase 2 clinical trial, which was finalized in March 2009, and modifications to cenderitide's current investigator brochure. We submitted a full response to the FDA in April 2009 and the cenderitide program was released from clinical hold in May 2009.

In June 2010, we completed dosing of a 77 patient, open-label, placebo controlled Phase 2 study of cenderitide in patients with ADHF and mild to moderate renal dysfunction. Cenderitide infusion at 1.25, 2.5 and 3.75 ng/kg/min appeared to be well tolerated. A dose-related effect on blood pressure was observed, with minimal or mild blood pressure reduction at 1.25 and 2.5 ng/kg/min, and moderate blood pressure reduction at 3.75 ng/kg/min. Dose escalation was limited by significant blood pressure reduction at 5 ng/kg/min. Secondary and exploratory analyses demonstrated favorable effects of cenderitide on renal function, particularly at the 1.25 and 2.5 ng/kg/min doses. At these doses, cenderitide appeared to preserve or enhance renal function compared to placebo, as evidenced by favorable trends in several biomarkers correlated with kidney function, including creatinine and cystatin-c.

In March 2011, the FDA granted Fast Track designation to our post-acute heart failure development program for cenderitide.

In October 2011, we completed dosing of a 58 patient, open-label, placebo controlled Phase I clinical trial that was designed to understand the doses required to achieve pre-determined plasma levels of cenderitide when delivered through a subcutaneous infusion pump. The target cenderitide plasma levels were based on our previous Phase 2 clinical trials, in which cenderitide was delivered through continuous i.v. infusion. The Phase 2 study enrolled patients in three parts. In Part A of the trial, 12 patients received two subcutaneous bolus injections of cenderitide. In Part B of the trial, 34 patients received a 24-hour continuous subcutaneous infusion of either of two fixed doses of cenderitide or placebo. In Part C, 12 patients received a 24-hour continuous subcutaneous infusion of either a weight-based dose of cenderitide, or placebo. All infusions were delivered through subcutaneous pump technology of Medtronic, Inc. pursuant to the parties' February 2011 collaboration agreement. In accordance with the terms of that agreement, Medtronic agreed to reimburse us for certain expenses of this Phase 1 study and provided the subcutaneous pumps used in the study.

The top line results from the Phase 1 trial are as follows:

The primary end-point was met – cenderitide achieved target pharmacokinetic, or PK, levels when delivered through Medtronic's subcutaneous pump technology;
24 hour subcutaneous delivery of cenderitide through Medtronic's pump technology was well-tolerated, with no injection site irritation;

- Subcutaneously delivered cenderitide has an acceptable bioavailability profile;
- Cenderitide's PK profile achieved steady-state when delivered through subcutaneous infusion;
- Weight-based dosing reduced PK variability, as compared to a fixed dosing regimen.

In addition to our own studies, in July 2008, the Mayo Clinic initiated a Phase 1 study, under an investigator-sponsored investigational new drug application, or IND, to better understand cenderitide's renal properties.

Future Clinical Studies

We believe the next step in the clinical development of cenderitide is a Phase 2 single-blind, placebo-controlled, dose ranging study in post-acute patients, with the primary objective of ensuring that patients can tolerate subcutaneous infusion for up to 90 days in an outpatient setting. We estimate the costs to conduct this Phase 2 study, up to 296 patients, will be approximately \$15 million to \$20 million and will take approximately 30 months to complete. However, we have lacked the necessary capital to conduct any additional development activities of cenderitide, and until we obtain such capital, we will not proceed with any further development. During the last 12 months, we have been actively pursuing additional financing or other strategic transaction alternatives that would provide the capital necessary to continue development of cenderitide. Such alternatives could include collaborating with another biotechnology or pharmaceutical company to further develop cenderitide, or engaging in a merger or other corporate transaction in which the control of cenderitide's development would be assumed by a purchaser of our company. There can be no assurance that we will be able to successfully resolve our lack of capital resources or otherwise find a strategic alternative. See "Risk Factors – Risks Relating to Our Business – We need substantial additional funding before we can complete the development of our product candidates. If we are unable to obtain such additional capital, we will be forced to delay, reduce or eliminate our product development programs and may not have the capital required to otherwise operate our business."

CU-NP Program

CU-NP is our novel natriuretic peptide rationally designed by scientists at the Mayo Clinic's cardio-renal research labs. CU-NP was designed to combine the favorable hemodynamic venodilating effects of CNP generated via NPR-B receptor agonism, with the beneficial renal effects of Urodilatin generated via NPR-A receptor agonism. In animal models, CU-NP was shown to increase natriuresis, diuresis, and glomerular filtration rate in a dose dependent manner, decrease cardiac filling pressure, and inhibit the renin-angiotensin system without inducing significant hypotension. As with cenderitide, all development of CU-NP is on hold pending the results of our efforts to pursue strategic alternatives.

Intellectual Property, License and Collaboration Agreement

Our goal is to obtain, maintain and enforce patent protection for our products, formulations, processes, methods and other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and abroad. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates and any future product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the United States and abroad. Even patent protection, however, may not always afford us with complete protection against competitors who seek to circumvent our patents. If we fail to adequately protect or enforce our intellectual property rights or secure rights to patents of others, the value of our intellectual property rights would

diminish.

We have depended upon the skills, knowledge and experience of scientific and technical personnel, as well as that of advisors, consultants and other contractors, none of which is patentable. To help protect such proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we have relied and will in the future rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

License Agreements

Cenderitide

On January 20, 2006, we entered into an exclusive, worldwide, royalty-bearing license agreement, or the Cenderitide License Agreement, with Mayo Foundation for Medical Education and Research, or the Mayo Foundation, for the rights to issued patents, patent applications and know-how relating to the use of cenderitide in all therapeutic uses. We were also entitled to rights to improvements to cenderitide that arose out of the laboratory of Dr. John Burnett, the co-inventor of cenderitide, until January 19, 2009.

Under the terms of the Cenderitide License Agreement, we paid the Mayo Foundation an up-front cash payment and reimbursed it for past patent expenses. We issued to the Mayo Foundation 1,379,419 shares of common stock. Additionally, we agreed to make contingent cash payments up to an aggregate of \$31.9 million upon successful completion of specified clinical and regulatory milestones relating to cenderitide. This aggregate amount is subject to increase upon the receipt of regulatory approval for each additional indication of cenderitide as well as for additional compounds or analogues contained in the intellectual property. In July 2008, we made a milestone payment of \$400,000 to the Mayo Foundation upon the dosing of the first patient in a Phase II trial. There were no such milestone payments due for the year ended December 31, 2012. Based on the current stage of research we do not expect to make any milestone payments for the year ending December 31, 2013. Pursuant to the Cenderitide License Agreement, we is required to pay the Mayo Foundation an annual maintenance fee and a percentage of net sales of licensed products, as well as \$50,000 per year for the consulting services of Dr. Burnett while serving as chairman of the Company's Scientific Advisory Board.

In addition to the potential milestone payments discussed above, the Cenderitide License Agreement requires us to issue shares of common stock to the Mayo Foundation for an equivalent dollar amount of grants received in excess of \$300,000, but not to exceed \$575,000. For the period from August 1, 2005 (inception) through December 31, 2011, the Company received \$482,235 in grant income for which it has issued to the Mayo Foundation 63,478 shares (representing \$182,236) of common stock. No such shares have been issued since the year ended December 31, 2008.

The Cenderitide License Agreement, unless earlier terminated, will continue in full force and effect until January 20, 2026. However, to the extent any patent covered by the license is issued with an expiration date beyond January 20, 2026, the term of the agreement will continue until such expiration date. Mayo may terminate the agreement earlier (i) for our material breach of the agreement that remains uncured after 90 days' written notice to us, (ii) our insolvency or bankruptcy, or (iii) if we challenge the validity or enforceability of any of the patents in any manner. We may terminate the agreement without cause upon 90 days' written notice.

Pursuant to the Cenderitide License Agreement, we have exclusive rights to 3 issued U.S. patents and 3 pending U.S. patent applications, 16 issued foreign patents and 3 pending foreign applications, covering composition of matter and methods of use. These patents and patent applications cover cenderitide, and other similar natriuretic peptides, as well as methods of use of the peptides in the treatment of multiple cardiovascular and renal indications. The issued composition of matter patent expires in 2019 and, if allowed, the last of the pending U.S. patents would expire in 2028.

As of the end of 2012, we were not in compliance with several terms of the Cenderitide License Agreement, including, but not limited to, provisions requiring us to pay the Mayo Foundation an annual maintenance fee and actively pursue the development of cenderitide. We are in discussions with the Mayo Foundation to amend the agreement, but we cannot guarantee that we will be able to reach an agreement with Mayo that allows us to maintain our rights to cenderitide. See "Risk Factors – Risks Relating to Our Business – We are not in compliance with various provisions of our license agreements with the Mayo Foundation. If we are unable to renegotiate these agreements, then we will lose our rights to cenderitide and CU-NP."

CU-NP

On June 13, 2008, we entered into an exclusive, worldwide, royalty-bearing license agreement, or the CU-NP License Agreement, with the Mayo Foundation for the rights to intellectual property and to develop commercially CU-NP for all therapeutic indications. We were also entitled to rights to improvements to CU-NP that arose out of the Mayo Clinic laboratory of Dr. John Burnett and Dr. Candace Lee, the inventors of CU-NP, until June 12, 2011.

Under the terms of the CU-NP License Agreement, we made an up-front cash payment to the Mayo Foundation and agreed to make future contingent cash payments up to an aggregate of \$24.3 million upon achievement of specific clinical and regulatory milestones relating to CU-NP, including a milestone payment due in connection with the initiation of the first Phase 2 clinical trial of the licensed product. This aggregate amount of \$24.3 million is subject to increase upon the receipt of regulatory approval for each additional indication of CU-NP, as well as for additional compounds or analogues contained in the intellectual property. There were no such milestone payments due for the year ended December 31, 2012. Based on the current stage of research, we do not expect to make any milestone payments for the year ending December 31, 2013. Pursuant to the agreement, we must also pay the Mayo Foundation an annual maintenance fee and a percentage of net sales of licensed products.

In addition to these cash payments payable with respect to the CU-NP License Agreement, we also agreed to issue shares of our common stock and warrants to the Mayo Foundation. In June 2008, we issued 49,689 shares of common stock to the Mayo Foundation having a fair market value as of June 13, 2008 equal to \$250,000.

The CU-NP License Agreement, unless earlier terminated, will continue in full force and effect until June 13, 2028. However, to the extent any patent covered by the license is issued with an expiration date beyond June 13, 2028, the term of the agreement will continue until such expiration date. The Mayo Foundation may terminate the agreement earlier (i) for our material breach of the agreement that remains uncured after 90 days' written notice to us, (ii) our insolvency or bankruptcy, (iii) if we challenge the validity or enforceability of any of the patents in any manner, or (iv) or upon receipt of notice from us that we have terminated all development efforts under the agreement. We may terminate the agreement without cause upon 90 days' written notice.

Pursuant to our CU-NP license agreement with Mayo Foundation, we have exclusive rights to 1 U.S. patent and 3 pending foreign applications, covering composition of matter and methods of use. These patents and patent applications cover CU-NP, and other similar natriuretic peptides, as well as methods of use of the peptides in the treatment of multiple cardiovascular and renal indications. If allowed, the pending U.S. patent would expire in 2028.

As of the end of 2012, we were not in compliance with several terms of the CU-NP license agreement, including, but not limited to, provisions requiring us to pay the Mayo Foundation an annual maintenance fee and actively pursue the development of CU-NP. We are in discussions with the Mayo Foundation to amend the agreement, but we cannot guarantee that we will be able to reach an agreement with Mayo that allows us to maintain our rights to CU-NP. See "Risk Factors – Risks Relating to Our Business – We are not in compliance with various provisions of our license agreements with the Mayo Foundation. If we are unable to renegotiate these agreements, then we will lose our rights to cenderitide and CU-NP."

Collaboration Agreement

In February 2011, we entered into a Clinical Trial Funding Agreement with Medtronic, Inc. Pursuant to the agreement, Medtronic provided the funding and equipment necessary for us to conduct our Phase 1 clinical trial to assess the pharmacokinetics and pharmacodynamics of cenderitide when delivered to heart failure patients through continuous subcutaneous infusion using Medtronic's diabetes pump technology.

Under the agreement, we agreed not to enter into an agreement with a third party to develop or commercialize cenderitide or any drug/device combination developed under the agreement until the earlier of: (i) three months following delivery to Medtronic of a final database with respect to the Phase 1 trial; and (ii) 15 months after the date of the agreement. The final database was delivered to Medtronic on November 19, 2011.

The agreement provides that intellectual property conceived in or otherwise resulting from the performance of the Phase I clinical trial shall be jointly owned by us and Medtronic (the "Joint Intellectual Property"), and that we shall pay royalties to Medtronic based on the net sales of any Nile product, the manufacture, use or sale of which is covered or claimed in one or more issued patents constituting Joint Intellectual Property. The agreement further provides that, if the parties fail to enter into a definitive commercial license agreement with respect to cenderitide, then each party shall have a right of first negotiation to license exclusive rights to any Joint Intellectual Property.

Pursuant to its terms, the agreement expired in February 2012, following the completion of the Phase 1 clinical trial and the delivery of data and reports related to such study.

Government Regulation

The research, development, testing, manufacture, labeling, promotion, advertising, distribution, and marketing, among other things, of our product candidates are extensively regulated by governmental authorities in the United States and other countries. In the United States, the Food and Drug Administration, or FDA, regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. Failure to comply with the applicable United States requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve a pending NDA, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecution.

Drug Approval Process

A drug or drug candidate may not be marketed or sold in the United States until it has received FDA approval. The process to receiving such approval is long, expensive and risky, and includes the following steps:

- pre-clinical laboratory tests, animal studies, and formulation studies;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practices, or cGMPs; and
- FDA review and approval of the NDA.

Pre-clinical tests include laboratory evaluation of product chemistry, toxicity, and formulation, as well as animal studies. The conduct of the pre-clinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. There can be no assurance that submission of an IND will result in the FDA allowing clinical trials to begin.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND.

Clinical trials are typically conducted in three sequential “Phases”, although the Phases may overlap. The study protocol and informed consent information for study subjects in clinical trials must also be approved by an Institutional Review Board for each institution where the trials will be conducted. Study subjects must sign an informed consent form before participating in a clinical trial. Phase I usually involves the initial introduction of the investigational drug into human patients to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness. Phase II usually involves trials in a limited patient population to (i) evaluate dosage tolerance and appropriate dosage; (ii) identify possible adverse effects and safety risks; and (iii) evaluate preliminarily the efficacy of the drug for specific indications. Phase III trials usually further evaluate clinical efficacy and test further for safety by using the drug in its final form in an expanded patient population. There can never be any assurance that Phase I, Phase II, or Phase III testing will be completed successfully within any specified period of time, if at all. Furthermore, clinical trials may be suspended at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The FDCA permits the FDA and the IND sponsor to agree in writing on the design and size of clinical studies intended to form the primary basis of an effectiveness claim in an NDA. This process is known as Special Protocol Assessment. These agreements may not be changed after the clinical studies begin, except in limited circumstances.

Assuming successful completion of the required clinical testing, the results of the pre-clinical studies and of the clinical studies, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. The testing and approval process requires substantial time, effort, and financial resources. The FDA reviews the application and may deem it to be inadequate to support the registration, and companies cannot be sure that any approval will be granted on a timely basis, if at all. The FDA may also refer the application to the appropriate advisory committee, typically a panel of clinicians, for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee.

The FDA has various programs, including fast track, priority review, and accelerated approval, that are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that may be eligible for one or more of these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that provide meaningful benefit over existing treatments. There can be no assurance that a drug will qualify for any of these programs, or that, if a drug does qualify, the review time will be reduced.

Section 505(b)(2) of the FDCA allows the FDA to approve a follow-on drug on the basis of data in the scientific literature or a prior FDA approval of an NDA for a related drug. This procedure potentially makes it easier for generic drug manufacturers to obtain rapid approval of new forms of drugs based on proprietary data of the original drug manufacturer.

Before approving an NDA, the FDA usually will inspect the facility or the facilities at which the drug is manufactured and will not approve the product unless cGMP compliance is satisfactory. If the FDA evaluates the NDA and the manufacturing facilities as acceptable, the FDA may issue an approval letter, or in some cases, an approvable letter followed by an approval letter. Both letters usually contain a number of conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter. The approval letter authorizes commercial marketing of the drug for specific indications. As a condition of NDA approval, the FDA may require post-marketing testing and surveillance to monitor the drug's safety or efficacy, or impose other conditions.

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes, or making certain additional labeling claims, are subject to further FDA review and approval. Before we can market our product candidates for additional indications, we must obtain additional approvals from the FDA. Obtaining approval for a new indication generally requires that additional clinical studies be conducted. We cannot be sure that any additional approvals for new indications for any product candidate will be approved on a timely basis, or at all.

Post-Approval Requirements

Often times, even after a drug has been approved by the FDA for marketing and sales of the approved product, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. If such post-approval requirements are not satisfied, the FDA may withdraw its approval of the drug. In addition, holders of an approved NDA are required to report certain adverse reactions to the FDA, comply with certain requirements concerning advertising and promotional labeling for their products, and continue to have quality control and manufacturing procedures conform to cGMP after approval. The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing facilities; this latter effort includes assessment of compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. If we obtain the capital necessary for us to continue the development of our product candidates, whether through a strategic transaction or otherwise, we intend to use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market.

Manufacturing

We do not currently have our own manufacturing facilities. If we obtain the capital necessary for us to continue the development of our product candidates, whether through a strategic transaction or otherwise, we intend to continue to use our financial resources to accelerate development of our product candidates rather than diverting resources to establish our own manufacturing facilities. To date, we have met our pre-clinical and clinical trial manufacturing requirements by establishing relationships with third-party manufacturers and other service providers to perform these services for us. We have historically relied on individual proposals and purchase orders to meet our needs and have typically relied on terms and conditions proposed by the third party or us to govern our rights and obligations under each order (including provisions with respect to intellectual property, if any). We do not have any long-term agreements or commitments for these services. Likewise, we do not have any long-term agreements or commitments with vendors to supply the underlying component materials of our product candidates, some of which are available from only a single supplier.

Competition

Even if we obtain the capital necessary for us to continue the development of our product candidates, whether through a strategic transaction or otherwise, we will face significant competition from companies with substantial financial, technical, and marketing resources, which could limit our future revenues from sales of cenderitide and CU-NP. Our success will depend, in part, upon our ability to achieve market share at the expense of existing and future products in the relevant target markets. Existing and future products, therapies, technologies, technological innovations,