Zacks Small-Cap Research

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Neurocrine Biosciences, Inc.

(NBIX-NASDAQ)

NBIX: Neurocrine Continues To Execute On Plan…

UPDATE

Neurocrine Biosciences is expecting data from eight clinical trials in 2015. The first came earlier in the year when elagolix partner AbbVie reported positive top-line data from the Violet Petal study. That leaves another seven trials to read out in the next ten months. Key data read outs include Phase 3 results from the Solstice study and Phase 2 results from the uterine fibroids study with elagolix, Phase 3 data from Kinect 3 and Phase 1b data from T-Force with NBI-98854, and Phase 1 data from NBI-77860.

We continue to believe that Neurocrine represents an attractive long-term investment in the biotech sector. Our sum-of-parts valuation pegs fair value at $38 per share.

Current Recommendation	**Buy**
Prior Recommendation	Neutral
Date of Last Change	06/16/2010
Current Price (02/10/15)	$33.54
Target Price	**$38.00**

SUMMARY DATA

52-Week High	**$34.35**
52-Week Low	**$12.78**
One-Year Return (%)	**98.79**
Beta	**-0.43**
Average Daily Volume (sh)	**1,577,740**
Shares Outstanding (mil)	**76**
Market Capitalization ($mil)	**$2,504**
Short Interest Ratio (days)	**4.76**
Institutional Ownership (%)	**91**
Insider Ownership (%)	**5**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/M**
P/E using 2015 Estimate	**N/A**
P/E using 2016 Estimate	**N/A**

Risk Level	**Below Avg.**
Type of Stock	**Small-Growth**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	0 A	0 A	0 A	0 A	0 A
2015	0 E	0 E	0 E	0 E	0 E
2016					50.0 E
2017					50.0 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	-$0.17 A	-$0.18 A	-$0.21 A	-$0.26 A	-$0.81 A
2015	-$0.29 E	-$0.30 E	-$0.30 E	-$0.35 E	-$1.24 E
2016					-$0.50 E
2017					-$0.56 E

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WHAT'S NEW

Fourth Quarter Financial Review

On February 9, 2015, Neurocrine Biosciences, Inc. (NBIX) reported financial results for the fourth quarter and full year ending December 31, 2014. The company did not have any revenues for the quarter, as expected. Neurocrine reported a net loss of $19.4 million, or $0.26 per share in the quarter, roughly in-line with our modeling that was looking for a loss of $0.25 per share. For the full year 2014, net loss totaled $60.5 million, or $0.81 per share. This compared to a net loss of $46.1 million, or $0.69 per share in the full year ending 2013.

The net loss in 2014 was composed of $46.4 million in research and development expenses and $18.0 million in general and administrative expenses. Stock-based compensation totaled $10.4 million in 2014. Neurocrine burned approximately $47.1 million in cash from operating activities in 2014. The company exited December 31, 2014 with $243.0 million in total assets, of which $193.8 million in cash and short-term investments. The company held another $37.5 million in long-term investments.

Neurocrine has provided some initial financial guidance for 2015. Management expects total cash burn in 2015 to be between $80 and $85 million, with total operating expenses in the range of $106 to $111 million. The sizable increase in expected operating expenses in 2015 is due to advancement of the company's clinical pipeline, which includes completing the Phase 3 Kinect 3 and Phase 1b T-Force study with NBI-98854 (valbenazine), as well as advancing NBI-77860, the company's Phase 1 CRF candidate, into Phase 2 studies. Management plans to file an IND on a new candidate during the second quarter of 2015. Based on current guidance, the company should still exit 2015 with still around $150 million in total cash and investments, although we would not be surprised to see management raise additional cash in the near-term to sure-up the balance sheet ahead of multiple clinical catalysts throughout the coming next several quarters.

Kinect 3 Top Line Expected Mid Year

On October 20, 2014, Neurocrine announced the initiation of a Phase 3 clinical trial called Kinect 3 (NCT02274558) of NBI-98854 for the treatment of tardive dyskinesia (TD). The study is a randomized, parallel-group, double-blind, placebo-controlled trial of approximately 240 patients with moderate to severe tardive dyskinesia and an underlying diagnosis of mood disorder, schizophrenia, or schizoaffective disorder. The trial will consist of a six week treatment period of 80 mg and 40 mg NBI-98854 dosed once daily against placebo. This will then be followed by a 46-week long-term safety assessment where all study subjects will be randomized in a blinded fashion to either 80 mg or 40 mg NBI-98854.

The primary endpoint for the Kinect 3 trial is change from baseline in the Abnormal Involuntary Movement Score (AIMS) as measured by blinded central raters, just as was done in Neurocrine's previous and successful Kinect 2 study (see our analysis of Kinect 2 here). The Kinect 3 study, along with the previous efficacy studies of NBI-98854, is designed to complete the clinical efficacy evaluation of the drug in tardive dyskinesia. In parallel to the Kinect 3 study, the company will be running an open-label safety trial with 100-150 subjects taking either 40 or 80 mg of NBI-98854, with that trial expected to commence in March 2015. Management is referring to this study as Kinect 4. Alongside the Kinect 3 pivotal trial and open-label Kinect 4 assessment, Neurocrine is planning to perform additional Phase 1 work that includes a QTc study, a study involving patients with renal impairment, and another drug interaction study. Top-line efficacy results from Kinect 3 are expected in the second half of 2015 (likely the third quarter of the year).

…FDA Awards Breakthrough Therapy Designation…

On October 30, 2014, Neurocrine announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for NBI-98854 in tardive dyskinesia. The breakthrough therapy designation is granted for a drug that is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on clinically significant endpoints over available therapies. The FDA had previously granted Fast Track status to NBI-98854 for tardive dyskinesia. Breakthrough therapy designation is quite similar to the Fast Track designation in that both programs are designed to expedite the development and review of drugs, which includes the following:

- ✓ Increased number of meetings with the FDA throughout the development of the drug,
- ✓ Maintaining an interactive dialogue with the FDA regarding drug development to ensure the sponsor is obtaining the proper nonclinical and clinical data necessary for approval expeditiously,
- ✓ Working with the FDA to ensure the clinical trials are being run as efficiently as possible,
- ✓ Rolling review and priority review.

NBI-98854 was granted breakthrough therapy designation based in part on the results of the Phase 2b studies of the drug in patients with tardive dyskinesia. Interestingly, breakthrough therapy has typically been designated for compounds in hematology and oncology with few compounds attaining the designation thus far in the neurology and psychiatry areas. Thus, by granting breakthrough designation to NBI-98854, the FDA has indicated it views tardive dyskinesia as a serious condition and one worthy of the agency's increased time and attention. Neurocrine is targeting an New Drug Application (NDA) for NBI-98854 in 2016.

…Phase 1 Tourette Syndrome…

On October 2, 2014, Neurocrine announced the initiation of a Phase 1b clinical trial called T-FORCE (NCT02256475) of NBI-98854 in both children and adolescents with Tourette syndrome. The T-FORCE study is an open-label, multiple ascending dose, two-week study of 36 subjects with Tourette syndrome. The study participants will receive once-daily dosing of NBI-98854 during a two-week treatment period to assess both the safety and tolerability of NBI-98854 in Tourette patients followed by seven days off-drug. The study is taking place at approximately 10 centers in the U.S.

The study will be divided into two dosing groups: children (ages 6-11) and adolescents (ages 12-18). Each group will then be divided into three dosing cohorts of six patients each. Following the initial two weeks of dosing with the first adolescent cohort, an independent review of both safety and pharmacokinetic results will occur prior to escalating the dose level for the second cohort of adolescents. Concurrently, when the second group of adolescents is dosed the first group of children will be administered NBI-98854. Continued dose escalations for both children and adolescents will be contingent upon the pharmacokinetic and safety data from the previous cohort in each age group. Lastly, each patient's Tourette symptoms will be evaluated weekly using the Yale Global Tic Severity Scale, the Premonitory Urge for Tics Scale, and the Clinical Global Impression in Tourette syndrome Scale. However, management indicated during the third quarter conference call that this study is not powered to show efficacy in treating Tourette syndrome, but is rather a pharmacokinetic and pharmacodynamics focused study. Data from the T-FORCE study should be available in the second half of 2015 (guidance is this fall).

AbbVie Reports Positive Top-Line From Violet Petal In January 2015

On January 8, 2015, AbbVie Inc. reported positive top-line data from a Phase 3 trial evaluating the safety and efficacy of elagolix in the treatment of endometriosis in premenopausal women. According to the press release, results from the Phase 3 trial, dubbed Violet Petal (NCT01620528), show that after three and six months of treatment, both doses of elagolix (150 mg once daily and 200 mg twice daily) met the study's co-primary endpoints ($p<0.001$) of reducing scores of non-menstrual pelvic pain (NMPP) and menstrual pain (or dysmenorrhea), associated with endometriosis as measured by the Daily Assessment of Endometriosis Pain scale. If you're scoring at home, that's eight total endpoints that all hit statistical significance. Unfortunately, no actual figures on efficacy were reported in the press release, protecting the data we suspect from competitors' eyes and so that AbbVie can present full results at a medical meeting later this year.

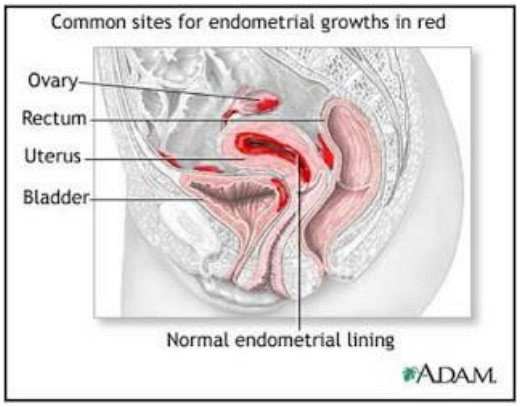
A brief summary of the safety data and adverse event profile was presented in the release. According to AbbVie, the observed safety profile of elagolix in this Phase 3 trial was consistent with observations from prior studies (which we discuss below). The most common adverse events (AEs) were hot flush, headache, nausea and fatigue. Adverse events, particularly hot flush, were dose-dependent. No DXA scan data was presented in the press release, only the mention that bone mineral density (BMD) loss was dose-dependent and the 150 mg results were similar to the results for the 150 mg cohort seen in the previous Phase 2b studies (< 0.5% change). A six month follow-up / open-label analysis from Violet Petal is still going, with data expected in May / June 2015.

Discontinuation rates specifically due to AEs for the trial are presented below:

Discontinuation Rates Phase 3 Violet Petal	
Placebo	*5.9%*
150 mg QD	*6.4%*
200 mg BID	*9.7%*

...Background On Endometriosis...

Endometriosis is a gynecological medical disorder that occurs when cells from the lining of the uterus (endometrium) grow in other areas of the body, most commonly on the peritoneum which lines the abdominal cavity, the ovaries, bowel, rectum, and bladder. These endometrial tissue implants are influenced by hormonal changes and respond similar to the cells found inside the uterus. Only they are not shed during menstruation. Instead, they may grow and shrink with hormonal changes, bleed irregularly, and lead to severe cramping or pelvic pain. Endometriosis is a common finding in women with infertility.



The cause of endometriosis is unknown. One theory is that the shed endometrial cells during menstruation travel backwards through the fallopian tubes into the pelvis, where they implant and grow. This is called retrograde menstruation. This backward menstrual flow occurs in many women, but researchers think the immune system may be different in women with endometriosis. As such, genetic predisposition plays a role in the development of endometriosis, with about a 10-fold increased incidence in women with an affected first-degree relative.

Endometriosis can affect any female, from premenarche to post-menopause; however, it is primarily a disease of the reproductive years. Accordingly, endometriosis is typically diagnosed between the ages of 25 and 35, although researchers believe the condition probably begins about the time that regular menstruation begins. Its prevalence varies, but sources suggest up to 10% of the general reproductive age female population is affected. Nearly 25% of women with endometriosis are asymptomatic.

As noted above, infertility is common with endometriosis. About 25 to 50% of infertile women have endometriosis, and 30 to 50% of women with endometriosis are infertile. Endometriosis is an estrogen-dependent process, and can persist beyond menopause and in up to 40% of patients following hysterectomy. Approximately 400,000 hysterectomies per year are attributed to endometriosis. For additional information on endometriosis, we recommend this detailed medical report.

...Background On Elagolix...

Elagolix is a novel, oral gonadotropin-releasing hormone (GnRH) antagonist developed by Neurocrine Biosciences. Neurocrine licensed the worldwide rights to elagolix to Abbott Labs in June 2010. Neurocrine received $75 million upfront from Abbott. Neurocrine has the potential to earn up to an additional $480 million in regulatory and development payments and $50 million in commercial payments, along with royalties on sales. Since June 2010, Neurocrine has earned $30 million of the $480 million in milestones plus an additional $37 million in sponsored development revenue. We suspect the next earnable milestone for Neurocrine in the initiation of the uterine fibroid Phase 3 trial perhaps in 2016. Filing the NDA in endometriosis will likely also earn Neurocrine a handsome milestone payment in 2016.

GnRH is a peptide that stimulates the secretion of the pituitary hormones that are responsible for sex steroid production and normal reproductive function. Researchers have found that chronic administration of GnRH agonists, after initial stimulation, reversibly shuts down this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as endometriosis. Several companies have developed peptide GnRH agonists on this principle, such as Lupron (Abbott Labs) and Zoladex (AstraZeneca).

However, since these drugs are peptides, they must be injected via a depot formulation rather than the preferred oral route of administration. In addition, GnRH agonists can take up to several weeks to exert their desired effect once the initial stimulation has occurred, a factor not seen with the use of Neurocrine's GnRH antagonists. More importantly, until the desired effects are maximized, GnRH agonists have shown a tendency to exacerbate the condition via a hormonal flare. And, ultimately profound suppression of GnRH is similar to that seen after menopause and can be associated with hot flashes and the loss of bone mineral density.

Elagolix, an orally active, non-peptide GnRH antagonist potentially offers several advantages over injectable GnRH peptide drugs, including rapid onset of hormone suppression without a hormonal flare. Also, injection site reactions commonly observed in peptide depots are avoided and dosing can be rapidly discontinued if necessary – a clinical management option not available with long-acting depot injections. And importantly, with elagolix, it may be possible to alter the level of pituitary GnRH suppression thereby titrating circulating estrogen levels. Using this approach, an oral GnRH antagonist may provide patients relief from the painful symptoms of endometriosis while avoiding the need for the active management of bone loss.

In summary, we see the following advantages to elagolix over existing medications such as Lupron, Zoladex, or depot formulation contraceptives such as medroxy-progesterone (Depo Provera):

- ✓ **Orally active:** Elagolix is given as a once-daily oral tablet, avoiding injection-site reaction seen with depo formulations. Elagolix can be dose-titrated and quickly discontinued if necessary.

- ✓ **Reversible:** Because elagolix can be quickly discontinued, ovulation returns typically after the first month of cessation of therapy. Women receiving long-acting formulations of Lupron and Pepo Provera can take months to see normal return to ovulation.

- ✓ **Rapid effect:** Elagolix does not cause the initial GnRH flare effect seem with agonists (drugs that simulate GnRH which the body then shuts down via feedback loop), which can worsen symptoms near-term and take weeks or even months before they reduce symptoms.

- ✓ **Less side-effects:** The mechanism of action of a GnRH antagonist (GnRH suppression seems to have a benign effect on changes in bone mineral density and hot flash as elagolix does not suppress estradiol levels to the effect of Lupron).

...Background On Violet Petal & Solstice...

Violet Petal (NCT01620528) was a 24-week, multinational, randomized, double-blind, placebo-controlled study designed to evaluate the safety and efficacy of elagolix in 872 women, age 18 to 49, with moderate-to-severe endometriosis-associated pain. The trial was conducted at approximately 160 sites in the United States, Puerto Rico and Canada.

The primary endpoint was a dual-endpoint in reduction in dysmenorrhea (painful menstruation) and non-menstrual pelvic pain (NMPP) for women on two doses of elagolix (150 mg QD & 200 mg BID) vs. placebo in a 1-1-2 randomization over six months. Efficacy will be assessed by a responder analysis for statistical evaluation. The inclusion of a higher dose allows for a potential full label with dose titration and prescribing options post approval.

A second Phase 3 trial, Solstice (NCT01931670), is ongoing. This study is similar in design to the Violet Petal Study and will assess 788 women, age 18 to 49, with moderate to severe endometriosis-associated pain at more than 200 sites globally. Data from Solstice is expected late 2015.

...Review Of Previous Clinical Data...

In total, Neurocrine has presented data from 12 Phase 1 programs and 6 Phase 2 programs (2 Phase 2a and 4 Phase 2b) on roughly 1,000 patients. Results from the Phase 2b (n=137) Daisy Petal program first released in May 2010 provided the best proof-of-concept data for the Phase 3 program. Results for Daisy Petal were statistically significant in all primary and secondary endpoints.

Data at Week 8	Baseline	Elagolix	Placebo
Change in Baseline (ITT population) of...			
Dysmenorrhea (mean, 0-3)	2.1 / 2.1	-1.13	-0.37
Non-Menstrual Pelvic Pain (mean, 0-3)	1.4 / 1.3	-0.47	-0.19
Dyspareunia (pain, 0-3)	1.6 / 1.3	-0.61	-0.23
All p<0.01			

Data at Week 8	Elagolix	Placebo
Responder Analysis (>30%)...		
Dysmenorrhea	63% [1]	33%
Non-Menstrual Pelvic Pain	63% [1]	33%
Dyspareunia	58% [2]	34%
1 = p<0.01 2 = p<0.05		

Data at Week 8	Elagolix	Placebo
Secondary Efficacy Endpoints (ITT population) on...		
Patient Global Impression of Change (PGIC) "much" or "very much improved"	60%	30%
Endometriosis Health Profile 5 (EHP-5) Related-Pain Assessment, 0-100	-28 pts	-13 pts
Composite Pelvic Signs & Symptoms Scale (CPSSS) Reduction from Baseline (9.5), 0-15)	-4.45 pts	-2.19 pts
All p<0.001		

Source: Neurocrine Bio & Zacks (Jason Napodano, CFA)

Market Opportunity

We believe that AbbVie is an excellent partner for Neurocrine Bio. AbbVie is a pioneer and market leader in GnRH agonists with Lupron for the treatment of hormone-responsive cancers such as prostate cancer or breast cancer. AbbVie has a strong appreciation for the GnRH mechanism and the company is clearly committed to see elagolix a success with Lupron expected to lose patent protection in 2015. We believe that AbbVie will look to replace Lupron in the Ob/Gyn market with elagolix thanks to superior efficacy and tolerability, as well as patent protection.

Above we noted sources that site the prevalence of endometriosis at around 10% of the general female population between the ages of 18 and 49. This is roughly 10 million women in the U.S. However, we also note that nearly 25% of these women are asymptomatic. Our findings are consistent with research done by Datamonitor in 2009 citing 7.5 million women in the U.S. alone are believed to suffer from clinically significant endometriosis.

Neurocrine notes that 75% of endometriosis sufferers have symptoms defined as moderate or severe. Data from IMS Health suggests that 10-20% of all oral contraceptive prescriptions are written off-label for endometriosis, and that Ob/Gyn's prescribe NSAIDs and opioids off-label to approximately 25% of their endometriosis patients.

The question is, what percent of moderate to severe endometriosis patients are adequately treated by NSAIDs, oral contraceptives, and opioids? Above we noted that approximately 400,000 hysterectomies per year are attributed to endometriosis. We suspect that another 300-400,000 women are to the point that they are failing these other medications and nearing a hysterectomy (essentially pulling forward one year all the women that are heading towards a hysterectomy next year). As such, we believe there are approximately 750,000 women in the U.S. that are ideal potential candidates for elagolix. We think it is realistic for AbbVie to penetrate 30% of this market.

We believe that elagolix will launch competitively priced with branded neurological or fibromyalgia pain medications such as Cymbalta or Lyrica, or around $12 per day. We believe a typical course of treatment will include eight months on therapy. Elagolix' intellectual property is protected by a composition of matter patent through 2024, but we suspect that AbbVie will file additional applications and extensions (through Hatch-Waxman) that could protect the drug to 2029. We suspect that elagolix pricing can peak at $15 per day by 2025.

> ***Multiplying all this through, we arrive at a peak U.S. opportunity for elagolix in endometriosis of $825 million (750k patients x 30% penetration x $15 per day x 245 days).***

We remind investors that AbbVie is also evaluating elagolix in women with uterine fibroids (UF). AbbVie is conducting a Phase 2b clinical trial (NCT01817530) evaluating the change in menstrual blood loss of 520 women, age 18-51, with heavy menstrual bleeding associated with uterine fibroids. Management described this as an "add back" study because women in the study will also be receiving low dose oral contraceptives. The goal of the study is to fine the right balance of dosing between elagolix and oral contraceptives, while mitigating risk on bone mineral density. Data on this study is expected in the third quarter of 2015. The doses for the trial have not been disclosed, but Neurocrine describes them as a broad range with previous work done in Phase 1 and Phase 2a programs.

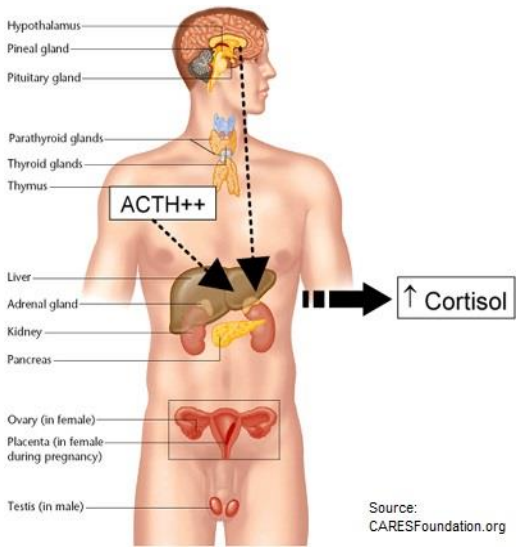
Also, we think this is an important step forward for AbbVie and Neurocrine because development of elagolix outside the U.S. will probably focus on uterine fibroids. The opportunity in uterine fibroids may be as large as in endometriosis. As such, globally, we think elagolix is a blockbuster drug, with peak sales that could eclipse $2.5 billion if the drug is approved for both endometriosis and uterine fibroids.

Neurocrine Gets Orphan Designation For NBI-77860 In CAH

On January 16, 2015, Neurocrine Bio announced that NBI-77860, the company's proprietary corticotropin releasing factor 1 (CRF-1) receptor antagonist, has been granted orphan drug status by the U.S. FDA for the treatment of congenital adrenal hyperplasia (CAH). CRF is a peptide released directly from the hypothalamus in the central nervous system into a discrete network of blood vessels where it functions via specific G-Protein Coupled Receptors on cells in the anterior pituitary gland to regulate the release of pituitary hormones. One such hormone is adrenocorticotropic hormone (ACTH), the primary role of which is the stimulation of synthesis and release of adrenal steroids including cortisol.

…Background On CAH…

The glucocorticoid cortisol is tightly coupled in a negative manner to the release of both hypothalamic CRF and pituitary ACTH thus providing a very tightly regulated feedback loop. This is commonly known as the Hypothalamic-Pituitary-Adrenal Axis (HPA). In diseases or disorders of dysregulated cortisol, levels of ACTH and CRF increase and if left uncontrolled, lead to an overproduction of a number of adrenal steroids including androgens.



Classic CAH is a collection of recessive genetic disorders that results in an enzyme deficiency altering the production of adrenal steroids, namely cortisol, but also may affect other hormones included mineralcorticoids such as aldosterone and androgens such as testosterone. Deficiency of 21-hydroxylase, resulting from mutations or deletions of CYP21A, is the most common form of CAH, accounting for more than 90% of cases. The disorder is considered life-threatening, and if left untreated, classic CAH can result in salt wasting, dehydration and eventually death. CAH can cause problems with normal growth and development in children, including normal development of the genitals. It affects both males and females.

Blockade of the specific CRF receptors on the pituitary gland has been shown to decrease the release of ACTH and subsequently attenuate the production and release of adrenal steroids. This effect may potentially alleviate the symptoms associated with an overproduction or excess of adrenal steroids in a number of endocrine disorders.

However, even with cortisol replacement, persistent elevation of ACTH from the pituitary gland results in excessive androgen levels leading to virilization of females including precocious puberty, menstrual irregularity, short stature, hirsutism, acne, and fertility problems. Metabolic syndrome, bone loss, growth impairment, and Cushing's syndrome are also common and serious side effects of long-term corticosteroid use.

The incidence of CAH varies geographically. In the U.S., CAH is particularly common in Native Americans and Yupic Eskimos, with an incidence rate of 1 out of 280. Among American Caucasians, the incidence is approximately 1 out of 15,000 births for the classic form (Merke D, et al 2001). The non-classic or mild form occurs in approximately 1 out of 1,000 births worldwide. Neurocrine Bio estimates the total CAH population in the U.S. is between 20,000 and 30,000 people.

…Status…

In late 2014, Neurocrine announced it had successfully completed the 1501 study in adult females with classic CAH. This was a small, single-dose pilot study designed to show that a single dose of NBI-77860 results in a pharmacokinetic/pharmacodynamic effect on key biomarkers of interest. The study was not designed as an efficacy trial, and management obviously received no information about chronic repeated dose exposure or what happens in children with CAH, which ultimately are the target population, but they were very pleased with what they saw with respect to the biomarker levels. Management has also confirmed with the U.S. FDA that these biomarkers are indeed the appropriate endpoints for this stage of clinical development.

Specifically, eight study participants visited the investigative site for three separate overnight visits consisting of bedtime dosing with placebo or one of two active doses of NBI-77860. Each of the visits was separated by a three-week washout period. Key biomarker measurements included ACTH, 17-hydroxyprogesterone (17-OHP), androgen, and cortisol levels collected in the morning after dosing. Data from this initial single dose exploratory study demonstrated a robust decrease in ACTH and 17-OHP. Neurocrine is planning to present the data via an oral presentation at the 97th Annual Meeting of the Endocrine Society (ENDO 2015) on Thursday, March 5, 2015 in San Diego. The session is entitled "HPA Axis and Adrenal: Receptors to Clinical Impact." ENDO is the world's largest endocrinology meeting drawing over 10,000 experts from around the world.

Neurocrine is preparing to initiate a second repeat dose study with NBI-77860 in the near future dubbed 1401. The 1401 study is a Phase 1/2 open-label, sequential cohort, single ascending dose pharmacokinetic/pharmacodynamic study assessing three doses of NBI-77860. The fifteen adolescent females with classic CAH will be split into three cohorts and each will receive one dose of NBI-77860 at bedtime. Biomarker measurements include ACTH, 17-OHP, androgen, and cortisol levels collected the morning after dosing.

NBI-77860 is a drug that the company has studied extensively under its previous collaboration with Glaxo looking at the potential role for CRF-1 antagonists in the treatment of depression and anxiety. Although no meaningful efficacy was seen with the drug in anti-depression studies, Neurocrine amassed significant exposure data with the drug showing excellent safety and tolerability. As a result of the significant exposure data generated in previous studies, management believes they will be in position to hold a Type-B (end of Phase 2) meeting with the U.S. FDA later this year. The goal is to start Phase 3 trials with NBI-77860 in 2016. We suspect that management will engage with and even looking to collaborate with the CARES Foundation for development of NBI-77860.

As noted above, Neurocrine has been granted Orphan Drug status for NBI-77860 for the treatment of CAH. The company believes the U.S. CAH population is between 20,000 and 30,000 individuals. However, this number would encompass all CAH patients including both male and female from young to old. In the Phase 1 pilot study noted above the company enrolled only adult female CAH patients. In the Phase 1/2 1401 study the company is targeting fifteen adolescent females with classic CAH. Ultimately the target population for the company may be around 10,000 patients in the U.S. We are anticipating learning more about NBI-77860, the target population, and development pathway prior to the initiation of the Phase 2 studies later this year. However, given the potential for strong pricing and limited competition, we believe NBI-77860 could have peak sales in the billion-dollar range (5,000 patients x$200,000 per year).

New IND on New Molecule Coming

On Neurocrine's fourth quarter update call management informed investors that they plan to file an investigational new drug (IND) application on a new molecule for a new indication in the second quarter 2015. This was the only information noted on the call.

Conclusion: Valuation and Recommendation

Neurocrine is off to a solid start to 2015. The shares are already up 55% following the positive elagolix Phase 3 data from Violet Petal reported by AbbVie in January 2015. Up next from AbbVie with elagolix is another Phase 3 trial in endometriosis called Solstice and the Phase 2b uterine fibroid trial. We expect data from both these studies in the second half of the year. We expect that AbbVie will be in position to file the New Drug Application (NDA) on elagolix late 2016. Our model assumes commercial launch for endometriosis in the U.S. in early 2018.

Back in Neurocrine's internal pipeline, results from the Phase 3 Kinect 3 study are expected this fall. Management is also planning to initiate an open-label study in March called Kinect 4, as well as some Phase 1 safety and drug-drug interaction studies. We believe the company will be in position to file the NDA on NBI-98854 for tardive dyskinesia during the second half of 2016. We see tardive dyskinesia as a meaningful market opportunity for Neurocrine. There are an estimated 500,000 TD patients in the U.S. with no real treatment options besides tetrabenazine. For valuation purposes, we assume U.S. approval of NBI-98854 in tardive dyskinesia will target roughly 150,000 of the total TD patients in the U.S. that are moderate-to-severe in disease state. We assume Neurocrine will charge pricing comparable to atypical antipsychotics, or around $12,000 per year. If Neurocrine can capture 33% market share, which we believe is reasonable given the superior characteristics of NBI-98854 (valbenazine) vs. generic tetrabenazine, then peak sales estimates are approximately $1.0 billion in this indication in the U.S. alone. We remind investors that NBI-98854 has received breakthrough designation from the U.S. FDA for the treatment of TD. Neurocrine is also pursuing development of NBI-98854 in Tourette syndrome. Phase 1b data are expected this fall. We believe the opportunity for NBI-98854 in TS is another billion-dollar opportunity.

We have also begun to factor NBI-77860 into our valuation model. Data from a pilot study reported late last year gave encouraging pk/pd results. We will have a better sense of the true efficacy and market opportunity for the drug after results from the Phase 1/2 1401 study reports out later in 2015. However, just given the potential for orphan disease pricing in the $200,000 range and a target population of approximately 10,000 in the U.S., Neurocrine looks to have another potential blockbuster in its hands, albeit still in very early-stage development.

We continue to be positive on the Neurocrine story. The company is one-for-one so far in 2015 with clinical trial read-outs. Management plans to offer-up data from another seven studies in 2015. Our sum-of-parts analysis pegs fair-value at $38 per share.

Neurocrine Biosciences Inc.
Income Statement

Neurocrine Bio	2014 A	Q1 E	Q2 E	Q3 E	Q4 E	2015 E	2016 E	2017 E
R&D / Milestones & Fees	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$50.0**	**$50.0**
YOY Growth	-	-	-	-	-	-	-	-
elagolix Royalties	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
NBI-77860 (CRF1)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-					-	-	-
NBI-98854 (VMAT2)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$50.0**	**$50.0**
YOY Growth	-	-	-	-	-	-	-	*0.0%*
CoGS / Royalties	$0	$0	$0	$0	$0	$0	$0	$0
Gross Margin	-	-	-	-	-	-	-	-
SG&A	$18.0	$6.5	$6.6	$6.8	$7.0	$26.9	$22.5	$30.0
R&D	$46.4	$16.5	$17.5	$20.0	$23.5	$77.5	$75.0	$75.0
Operating Income	($64.4)	($23.0)	($24.1)	($26.8)	($30.5)	($104.4)	($47.5)	($55.0)
Operating Margin	-	-	-	-	-	-	-	-
Interest / Other Income	$3.9	$0.9	$0.9	$0.9	$0.9	$3.6	$4.0	$5.0
Pre-Tax Income	($60.5)	($22.1)	($23.2)	($25.9)	($29.6)	($100.8)	($43.5)	($50.0)
Taxes	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*15%*	*0%*	*0%*	*0%*	*0%*	*30%*	*30.0%*	*30.0%*
Net Income	($60.5)	($22.1)	($23.2)	($25.9)	($29.6)	($100.8)	($43.5)	($50.0)
YOY Growth	-	-	-	-	-	-	-	-
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.81)**	**($0.29)**	**($0.30)**	**($0.30)**	**($0.35)**	**($1.24)**	**($0.50)**	**($0.56)**
YOY Growth	-	-	-	-	-	-	-	-
Shares Outstanding	74.6	77.0	78.0	85.0	85.5	81.4	87.5	90.0

Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

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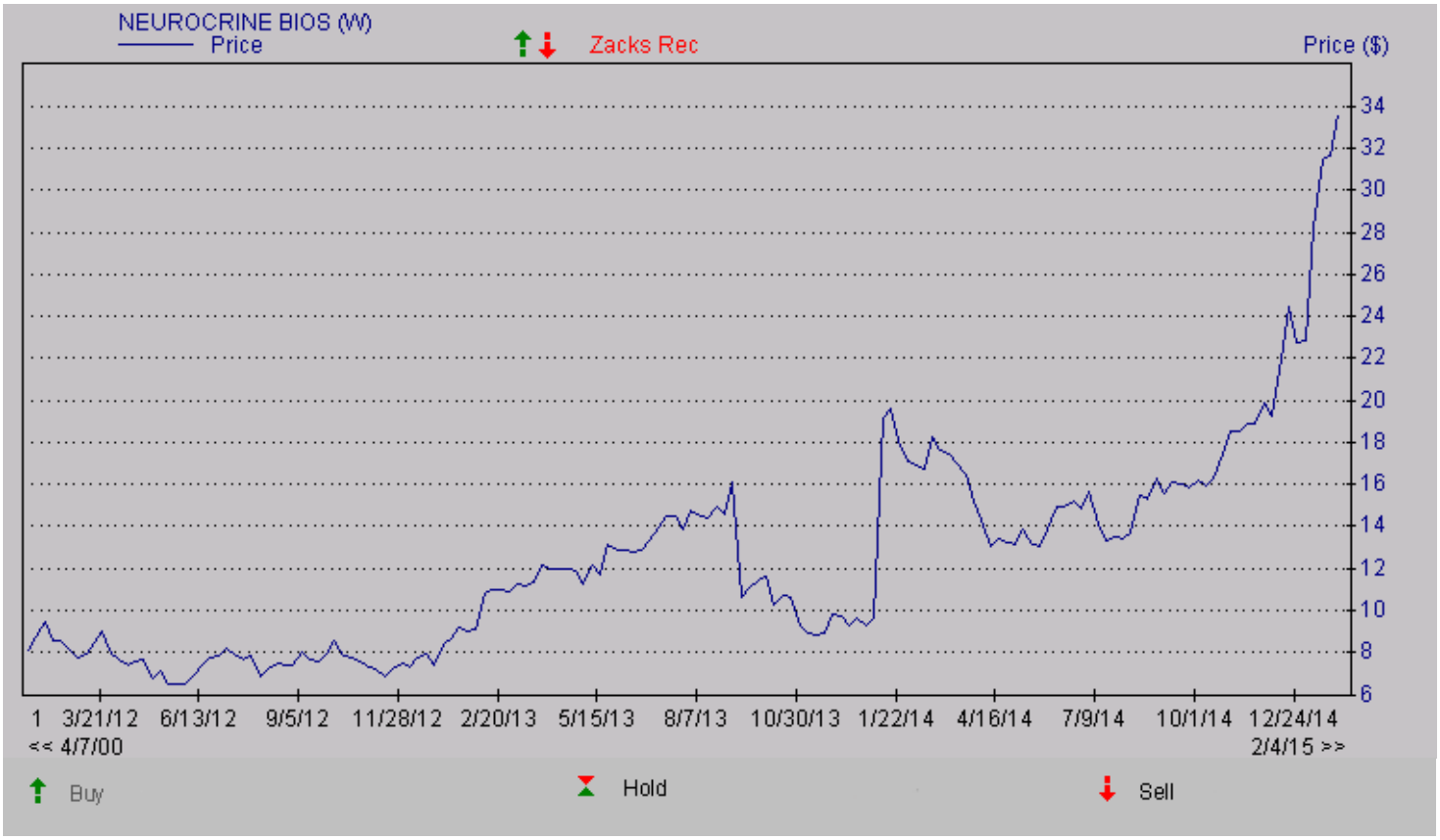

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