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Company Report

December 18, 2018

Strongbridge Biopharma (SBBP - $4.27)

Healthcare / Biotechnology

Initiating Coverage – Growing Late Stage Rare Disease Play

Ticker:	SBBP
Rating:	**Buy**
Price Target:	**$11.00**

We are initiating coverage of Strongbridge Biopharma (SBBP) with a Buy rating and a $11price target. SBBP is focused on development and commercialization of franchises in rare diseases. Their first value driver is Recorlev (next-gen cortisol inhibitor) for the treatment of endogenous Cushing's Syndrome (CS). On 08/08/18, SBBP announced positive topline results from their Phase 3 SONICS trial as it hit its primary endpoint with 30% of patients achieving normalization of mean urinary free cortisol (UFC) after six months without dose increase ($p<0.025$). We were particularly impressed with key secondary endpoints measurements (heart and liver) since Recorlev is an enantiomer of ketoconazole, which has already shown some efficacy in off-label usage for CS treatment. We anticipate topline LOGICS data for supplemental efficacy evidence in 4Q19. Their second value driver consists of Macrilen (oral ghrelin receptor agonist) for diagnosing adult growth hormone deficiency (AGHD). Launched by SBBP in July 2018 as the first FDA approved AGHD diagnostic test due to complexity and safety issues of other current tests like Insulin Tolerance Test (ITT) and Glucagon Stimulation Test (GST); Macrilen was recently acquired by Novo Nordisk (NVO) for $145M upfront and tiered royalty streams. Their third value driver consists of Keveyis (oral carbonic anhydrase inhibitor) for primary periodic paralysis (PPP). As the first and only FDA-approved treatment, SBBP is working on growing awareness and expanding genetic testing to increase PPP diagnosis. Having only launched in the US in April 2017, SBBP is guiding to $16M-$17M in sales for FY18. With a fairly late stage portfolio poised to fulfill unmet medical needs, we view SBBP as undervalued at these levels and are initiating coverage with a Buy rating and a $11price target.

- **Strong PHASE 3 Recorlev data, especially in key secondary endpoints.** While we anticipated solid efficacy due to Recorlev's make-up, we were particularly encouraged by its strong cardiovascular and liver-related values.
- **First FDA approved AGHD diagnostic, Macrilen has impressive commercial potential.** With ITT and GST posing their fair share of obstacles, we believe Macrilen could grow the AGHD diagnostic market.
- **Keveyis making significant strides to fulfill unmet medical need.** While PPP only affects ~4-5K patients in the US, SBBP expects FY18 sales of $16-$17M (launched April 2017).
- **Initiate with a Buy rating, $11PT.** Our price target is based on US Keveyis at $2/share, US Macrilen royalties at $1/share, US Recorlev at $6.5/share and cash & tech at $1.50/share.

Trading Data:

Last Price (12/17/2018)	$4.27
52–Week High (04/02/2018)	$9.25
52–Week Low (09/18/2018)	$3.85
Market Cap. (MM)	$201.5
Shares Out. (MM)	47.2

Earnings Estimates: (per share)

(Dec)	1Q	2Q	3Q	4Q	FY	P/E
FY19E	(0.34)	(0.29)	(0.27)	(0.29)	(1.20)	NA
FY18E	(0.33)A	(0.36)A	(0.47)A	(0.40)	(1.58)	NA
FY17A	(x.xx)	(x.xx)	(x.xx)	(x.xx)	(1.31)	NA
FY16A	(x.xx)	(x.xx)	(x.xx)	(x.xx)	(x.xx)	NA

Source: Laidlaw & Company estimates

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5 Key Reasons to own Strongbridge Biopharma

1. **Strong PHASE 3 Recorlev data, especially in key secondary endpoints.** As ketoconazole monotherapy has been shown to control cortisol in ~50% of patients, we anticipated solid efficacy of Recorlev (ketoconazole enantiomer). However, we were particularly encouraged by the strong key secondary endpoints achieved in the SONICS trial. At six months, Recorlev showed statistically significant ($p<0.0001$) improvements in important cardiovascular measurements (fasting blood glucose, hemoglobin A1c, total cholesterol, body weight and BMI). Liver-related values were also very encouraging as there were no total bilirubin values > 1.5x ULN.

2. **First FDA approved AGHD diagnostic, Macrilen has impressive commercial potential.** Although ITT and GST are currently used to diagnose AGHD, complexity, tolerability and safety issues have restrained their market potential. As the first FDA approved test, Macrilen benefits from a better route of administration (oral), less time for patient and office, fewer blood draws, better safety/tolerability, lack of contraindications and greater evaluability. These advantages should increase AGHD testing by ~33% and potentially much more in traumatic brain injury (TBI). SBBP's recent agreement (10/31/18) to have its US and Canadian Rights acquired by NVO for $145M upfront, tiered royalties and ~$37M of through share purchase represents a testament to Macrilen's potential and reinforces SBBP's balance sheet.

3. **Recorlev to benefit from Macrilen's rare endocrine commercial infrastructure now controlled by NVO.** With Macrilen having recently launched in July 2018, Recorlev (if approved) should leverage SBBP's and NVO's rare endocrine expertise and awareness in the medical community as ~75% who treat AGHD also treat CS.

4. **Keveyis making significant strides to fulfill unmet medical need**. While there are only ~4,000-5,000 patients in the US with PPP, SBBP expects FY18 sales of $16M-$17M (launched April 2017). As the only FDA approved therapy for PPP, we are encouraged by SBBP's progress and see their genetic mutation panel expansion for additional diagnosis and awareness as real positives for this unmet medical need.

5. **With 2 commercial launches progressing, more catalysts around the corner.** As Keveyis and Macrilen progress through their respective launches, SBBP expects SONICS topline one-year data in 1Q19 as well as LOGICS topline data for Recorlev in 4Q19. They also have a third product in their rare endocrine franchise called Veldoreotide for Acromegaly in preclinical stage. Additionally, SBBP intends to expand their Rare neuromuscular franchise and develop a new third rare disease franchise through business development.

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Figure 1: Upcoming Potential Catalysts

Event	Expected Timing
Recorlev SONICS topline 1-year data	1Q19
Recorlev LOGICS topline data	4Q19

Source: Company Reports; Laidlaw and Company estimates

Valuation

We value SBBP at $10/share based on a sum-of-the-parts valuation. Keveyis US sales for PPP is valued at $2/share based on a 3.5x multiple of 2022 sales of $36M, discounted back 3 years at a 7.5% discount rate. Macrilen US Royalties for AGHD diagnosis is valued at $1.25/share based on a 9.5x multiple of 2023 royalties of $10M discounted back 4 years at a 7.5% discount rate. Recorlev US sales for CS is valued at $5.5/share based on a 3.5x multiple of 2024 sales of $222M, discounted back 5 years at a 20% discount rate. We value net cash (end 2019) and technology at $1/share.

Figure 2: Sum-of-the-Parts Analysis

Sum-of-the-parts valuation		
Segment	Valuation (000's)	Per share value
Keveyis US	$100,236	$2.00
Macrilen US royalties	$70,580	$1.50
Recorlev US	$312,150	$5.50
Cash (end '19) & tech value	$65,981	$1.00
	$548,947	**$10.00**
2019 fully diluted shares out (000)		56,678

Source: Company Reports; Laidlaw and Company estimates

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Company Description

SBBP is a global commercial-stage biopharmaceutical company focused on the development and commercialization of therapies for rare diseases with significant unmet needs. Their first commercial product is Keveyis (dichlorphenamide), the first and only treatment approved by the FDA for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis (PPP), a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis. Their second commercial product, Macrilen (macimorelin) is an oral growth hormone secretagogue receptor agonist, and is the first and only oral drug approved by the FDA for the diagnosis of patients with adult growth hormone deficiency (AGHD). They recently (10/31/18) entered into an agreement for NVO to acquire US and Canadian rights to Macrilen. Additionally, they have two clinical-stage product candidates for rare endocrine diseases, Recorlev and Veldoreotide. Recorlev (levoketoconazole) is a cortisol synthesis inhibitor currently being studied for the treatment of endogenous Cushing's syndrome. Veldoreotide is a next-generation somatostatin analog being investigated for the treatment of acromegaly and potential additional applications in other conditions amenable to somatostatin receptor activation. Both Recorlev and veldoreotide have received orphan designation from the FDA and the EMA.

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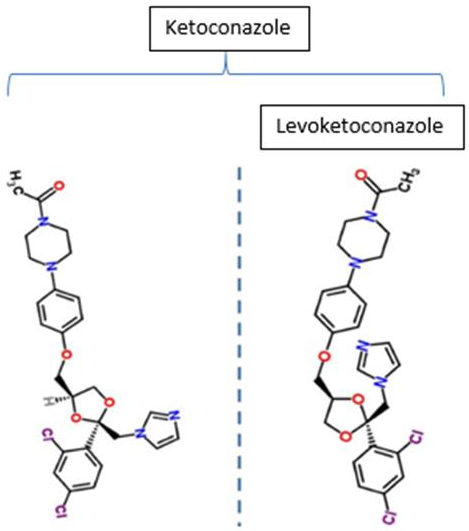
Recorlev for endogenous Cushing's syndrome

Recorlev (levoketoconazole), a cortisol synthesis inhibitor, is in Phase 3 clinical development for the treatment of endogenous Cushing's syndrome, which is a rare endocrine disorder characterized by sustained elevated cortisol levels that usually results from a benign tumor of the pituitary gland. The company believes that Recorlev, which is the isolated, lefthanded mirror image (enantiomer) of ketoconazole, has the potential to become the new standard of care for the drug therapy of endogenous Cushing's syndrome.

Figure 3: Recorlev – An enantiomer of ketoconazole



Source: Erasmus MC

In July 2017, they completed enrollment (n=94) of SONICS, a pivotal, multinational Phase 3 clinical trial for Recorlev and announced topline data for the primary efficacy and safety data on 8/8/18. The study met its primary endpoint as Recorlev was able to demonstrate a statistically significant normalization rate of Urinary Free Cortisol (UFC) at 6 months. Key secondary cardiovascular and liver-related endpoints showed statistically significant and clinically meaningful improvements from baseline. Fasting blood glucose, hemoglobin A1c, total cholesterol, LDL-cholesterol, Body Weight and BMI all showed statistically significant reductions from baseline ($p<0.0001$). We were particularly impressed with 0% of patients showing total bilirubin values > 1.5x ULN, which represents an important number of liver issues. 10.6% of patients showed ALT > 3X ULN and 3.2% demonstrated ALT >5X ULN. We believe

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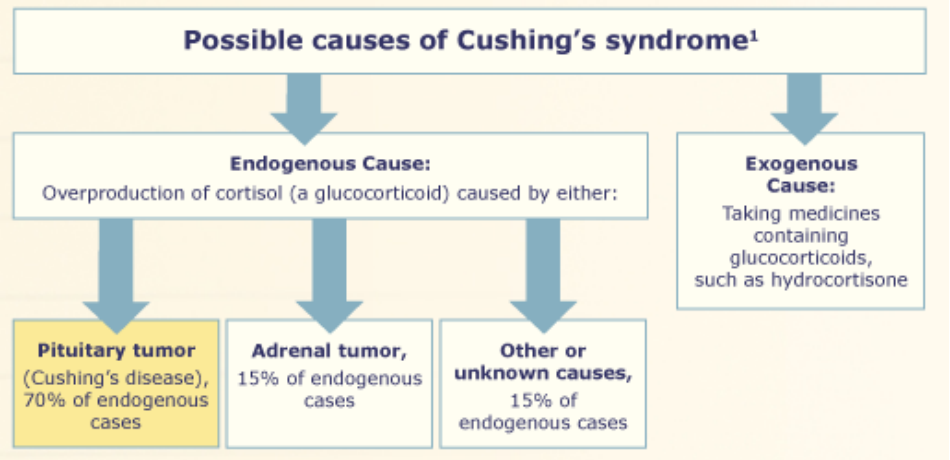
these findings are encouraging as NVS's Signifor was recently approved for Cushing's Disease with 14% ALT > 3X ULN and 5% ALT > 5X ULN and without a black box warning.

Additionally, they have initiated LOGICS, a second pivotal Phase 3 clinical trial of Recorlev. The LOGICS study will supplement the long-term efficacy and safety data from the ongoing SONICS trial via a randomized, double-blind, placebo-controlled design. Top-line data are expected in the 4Q19 from previously guided 1Q19 due to expansion of the randomized-patient target from n=35 to n=54. We believe this should grow the body of evidence and ultimately de-risk topline readout. SBBP intends to conduct a Type C meeting with the FDA in 1Q19 to discuss next steps towards NDA filing. Upon completion of the clinical development program, they intend to file for marketing authorizations in the US and elsewhere through the 505(b)(2) pathway.

Endogenous Cushing's Syndrome

There are two variants of Cushing's syndrome: exogenous, which is caused by factors outside the body such as corticosteroid or cortisol-like medications; and endogenous. While the signs and symptoms may be the same in both forms, the more common form is exogenous Cushing's syndrome, which is often found in people taking cortisol-like medications for long periods of time or for shorter periods of time using very potent forms. Cortisol-like medications are often used to treat inflammatory disorders such as asthma and rheumatoid arthritis.

Figure 4: Cushing's Syndrome Classification



Source: Lancet, 2006

Unlike endogenous Cushing's syndrome, exogenous Cushing's syndrome may be alleviated by withdrawing the inciting medication. Endogenous Cushing's syndrome is a rare endocrine disorder characterized by sustained elevated blood cortisol, which is a hormone produced in the adrenal gland and is naturally secreted as an end-product of the activity of the hypothalamic-pituitary-adrenal axis. Corticotropin-releasing hormone (CRH) is secreted from the hypothalamus

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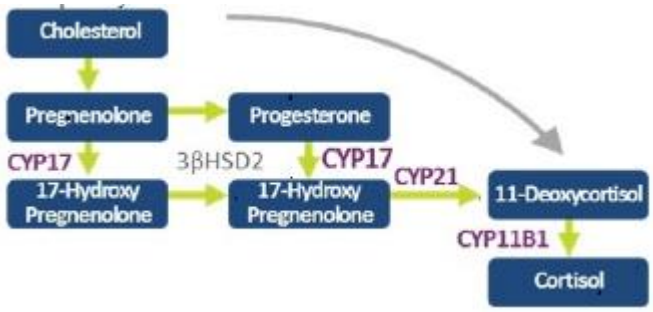
and stimulates the secretion and release of adrenocorticotropin (ACTH) from the pituitary gland, which in turn stimulates cortisol secretion from the adrenal gland. Cortisol itself exerts negative feedback control on both CRH in the hypothalamus and ACTH in the pituitary gland, thereby reducing CRH and ACTH secretion, keeping cortisol levels in a normal range.

Figure 5: Cortisol Synthesis Pathway



Source: Company Reports

The most common form of endogenous Cushing's syndrome is called Cushing's disease, which is typically caused by a benign pituitary tumor that secretes ACTH autonomously. Cushing's disease represents ~70%-80% of patients with endogenous Cushing's syndrome (Lancet, 2006). The most common signs and symptoms of the syndrome include: weight gain, especially in the upper body with a rounded face (moon face) and extra fat on the upper back and above the collarbones; high blood sugar or diabetes mellitus; high blood pressure or hypertension; thin bones or osteoporosis; muscle loss or sarcopenia; thin, fragile skin that bruises easily; purple red stretch marks called striae, usually over the abdomen and under the arms; depression and difficulty thinking clearly; too much facial hair usually noticed only in women; irregular or absent menstrual periods and infertility; reduced sex drive or libido; and in children, poor height growth.

Approximately 25,000 patients in the US and 40,000 patients in EU are diagnosed with endogenous Cushing's syndrome. When first diagnosed, patients are most commonly adults aged 20-50 and occurs in women ~70% of the time (AANS, 2018). However, endogenous Cushing's syndrome is believed to be underdiagnosed due to lack of disease recognition, which often leads to a delay in diagnosis. Endogenous Cushing's syndrome patients are believed to have a mortality risk 2-3X that of the age and gender-matched general population, with cardiovascular disease, venous thrombosis and infections being the primary causes of death.

Recorlev is a cortisol synthesis inhibitor that exerts its therapeutic effect by blocking the synthesis of cortisol in the adrenal glands. Recorlev has been granted ODD by the FDA and the EMA and is being developed using a dose regimen of 2X/day oral administration. Ketoconazole, used off label in the US, is the most frequently prescribed drug therapy for endogenous Cushing's syndrome. It is used to reduce blood cortisol and ameliorate comorbidities associated with Cushing's syndrome.

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Recorlev inhibits the cortisol synthesis pathway at several points. In light of the shared MOA with ketoconazole and the data from Phase 2 clinical trials, which were conducted in diabetes patients without Cushing's syndrome, SBBP believes Recorlev may have a similar beneficial impact on the reduction of significant comorbidities of endogenous Cushing's syndrome. Comorbidities include those associated with CVD risk, such as diabetes, weight gain, hypertension and elevation in LDL- cholesterol. In addition, based on preclinical data and human PK, they believe that Recorlev may offer an improved safety profile relative to existing approved drug therapies for endogenous Cushing's syndrome.

Treatment of endogenous Cushing's syndrome varies depending on the cause of the disease. For patients with Cushing's disease, initial treatment is almost always the attempted surgical removal of the pituitary tumor. In anticipation of surgery and when surgery is not effective, drug or radiation therapy, is used to suppress excessive cortisol production and the accompanying clinical symptoms. Although approved in the EU for this indication, ketoconazole is not approved for this indication by the FDA.

The percentage of endogenous Cushing's syndrome patients treated with ketoconazole monotherapy who achieve normalized levels of cortisol, assessed by measuring urinary free cortisol (UFC) has been reported from retrospective, uncontrolled studies, with varying definitions of normalization, to be between 33% and 100%. Data from a recent retrospective study of 200 patients in 14 French centers solely treated with ketoconazole for endogenous Cushing's syndrome between 1995 and 2012 suggested that ketoconazole controlled cortisol in ~50% of patients and likewise improved clinical symptoms.

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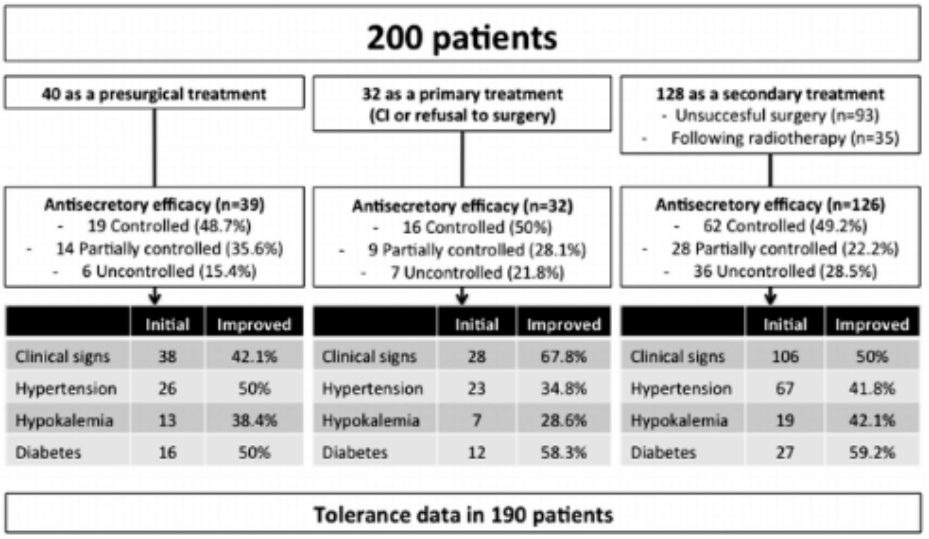
Figure 6: Ketoconazole data in 200 patients



Source: Journal of Clinical Endocrinology, 2014

Also, beneficial effects of oral ketoconazole on clinical symptoms and signs that drive the morbidity and mortality of endogenous Cushing's syndrome have been reported including reduction in high blood pressure, improvement of diabetes, and normalization of hypokalemia, or low potassium blood levels. However, some patients treated with ketoconazole experience tolerability issues and, in some cases, liver injury (also known as hepatotoxicity). As a result of the hepatotoxicity risk the FDA has issued a boxed warning to prescribers concerning the use of ketoconazole to treat fungal infections, the only approved indication for ketoconazole in the US.

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Figure 7: Ketoconazole box warning

WARNING:
NIZORAL® Tablets should be used only when other effective antifungal therapy is not available or tolerated and the potential benefits are considered to outweigh the potential risks.

Hepatotoxicity
Serious hepatotoxicity, including cases with a fatal outcome or requiring liver transplantation has occurred with the use of oral ketoconazole. Some patients had no obvious risk factors for liver disease. Patients receiving this drug should be informed by the physician of the risk and should be closely monitored. See WARNINGS section.

QT Prolongation and Drug Interactions Leading to QT Prolongation
Co-administration of the following drugs with ketoconazole is contraindicated: dofetilide, quinidine, pimozide, cisapride. Ketoconazole can cause elevated plasma concentrations of these drugs and may prolong QT intervals, sometimes resulting in life-threatening ventricular dysrhythmias such as torsades de pointes. See CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS: Drug Interactions sections.

Source: Ketoconazole Label

Although elevations in liver enzymes associated with ketoconazole are generally mild to moderate and reversible upon cessation of drug; in rare cases, severe hepatotoxicity may occur (~1/10,000 to 15,000 patients). In extremely rare cases, ketoconazole related liver injury may be irreversible and result in death or require liver transplantation. In July 2013, the Committee for Medical Products for Human Use (CHMP) recommended that ketoconazole be withdrawn for use as an antifungal agent in the EU.

In a survey they commissioned in 2014 of 89 US physicians treating patients with Cushing's syndrome, when asked, "Of your patients on medication to manage cortisol levels, what percentage are well controlled?", the physicians estimated that only ~37% of such patients were well controlled.

Trials in Type 2 Diabetes

As previously mentioned, levoketoconazole (then called DIO- 902) was studied as a treatment for type 2 diabetes. However, in 2008, in light of negative safety reports for other diabetes treatments such as Avandia, DiObex made the decision to voluntarily terminate the development of levoketoconazole for the treatment of diabetes. Also affecting the decision was the perceived high regulatory and commercial hurdles for its approval and use in type 2 diabetes, and considering the emerging efficacy and safety profile of levoketoconazole in type 2 diabetes. Thereafter, the IND was closed and DiObex terminated the two ongoing Phase 2 clinical trials.

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Figure 8: Key Findings from Phase 2 Trials in Diabetics

Important Findings in Phase 2 trials in Diabetics
AUC and Cmax values: ~50% higher with Levoketoconazole vs ketoconazole at same dose of 400mg.
Post administration, plasma levels of levoketoconazole were ~3X those of the other enantiomer
Levoketoconazole produced decrease in some lipid measures
Significant dose related effect of levoketoconazole for reduction of CRP
Trends for reductions in serum cortisol found after 14 days of treatment

Source: Company reports

SBBP initiated their first Phase 3 pivotal trial SONICS in July 2017 and recently reported positive safety and efficacy data as discussed in the following figure.

Figure 9: Clinical Trial Design

Phase 3: SONICS	
Aim	Evaluate safety and efficacy of Recorlev in subjects with endogenous Cushing's syndrome
Design	Multinational (US, Canada, EU and Middle East), open label, single arm design because placebo in parallel-arm monotherapy considered unethical.
Dosing	After screening phase, 3 distinct treatment phases. During dose titration: 150mg 2X/day and titrate in 150mg increments up to 600mg 2X/day. Then, patients enter maintenance and dose is fix. After 6 months, UFC levels measured and UFC responder rate. Patients who have completed maintenance may enter extended
Endpoints	1) Proportion of subjects with UFC response, defined as reduction in mean 24hour UFC levels to levels equal to or less than upper level of normal range following 6 months of treatment in maintenance phase without dose increase. 2) number of patients with at least 50% decrease in UFC levels, as well as changes in blood sugar, blood pressure, cholesterol and weight compared to baseline and effects on clinical signs and symptoms of endogenous Cushing's syndrome, quality of life measures obtained from endogenous Cushing's syndrome quality of life questionnaire and severity of depression from Beck's Depression Inventory II. Also looking at PK.
Patients	n=94
Safety	generally well-tolerated. 12.8% discontinued treatment due to Aes. 2 most commonly reported Aes that led to 0 discontinuations were nausea. 1 discontinued due to headache. 14.9% had one or more SAEs of whom 4 had Saes deemed drug related. 1 patent death (colon cancer) not considered drug related. Liver-related findings: Liver-related AEs defined in protocol as AE of special interest 7.4%; >3X ULN (includes those >5X ULN) 10.6%; >5X ULN 3.2%. No severe drug-induced liver injury
Results	Achieved stat sig of 1)EP with 30% of patients achieving normalization of mean UFC after 6 months of maitenance treatment without a dose increase ($p<0.025$). Sensitivity analysis as well as 2)EP and exploratory EP of UFC response were supportive of 1)EP. 2): cardiovascular risk (fasting blood glucose, hemoglobin A1C, total cholesterol, LDL, body weight and BMI, Recorlev showed stat sig and clinically meaningful improvements from baseline ($p<0.0001$ for each).

Source: Company reports

SONICS demonstrated consistent and significant clinical benefit by meeting the primary endpoint of the trial, specifically the responder rate measured as normalization of UFC levels at the six-month time point without need for dose increase during the six-month maintenance phase. It also showed consistent improvement of objectively quantifiable biomarkers of endogenous Cushing's syndrome comorbidities. Accordingly, SBBP believes this would be regarded by regulators as adequate proof of efficacy in this rare disease with a high unmet medical need. Additionally, for patients that entered ended the maintenance phase with normalized UFC regardless of dose increase, there was a 38% responder rate. The patients that finished the maintenance phase, 48% had ≥50% UFC decrease or normalization and 76% of completers saw ≥50% UFC reduction, which ultimately demonstrates Recorlev's durable efficacy.

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Figure 10: UFC Responder Analysis at End of Maintenance Phase

Primary endpoint of UFC normalization	30%, CI: 21%, 40% p<.025*
Sensitivity analysis of the primary endpoint (UFC normalization regardless of dose increase)	38%, CI: 28%, 49%
≥50% UFC decrease or normalization, regardless of dose increase	48%, CI: 37%, 58%
Maintenance completers with UFC data had ≥50% UFC reduction from baseline	76% (42/55) **

Source: Company Presentation

We were particularly impressed with cardiovascular key secondary endpoints as they showed strong statistical significance ($p < 0.0001$) across the board. These results are crucial as these secondary endpoints often lead to the demise of Cushing's disease patients.

Figure 11: Key Secondary Endpoints

Outcome Measure @ End of Maintenance Phase	Adjusted p-value of reductions from Baseline
Fasting Blood Glucose	<0.0001
Hemoglobin A1c	<0.0001
Total Cholesterol	<0.0001
LDL-Cholesterol	<0.0001
Body Weight	<0.0001
Body Mass Index	<0.0001

Source: Company Reports and Laidlaw estimates

Therefore, SBBP considers their other Phase 3 pivotal trial LOGICS as a way to provide independent evidence of efficacy of Recorlev, rather than serving as sole or primary evidence of efficacy for Recorlev in endogenous Cushing's syndrome. In total >100 unique subjects with this condition will have been treated with Recorlev during SONICS and LOGICS, and some subjects will be treated with a therapeutic dose of Recorlev for ≥ 1.5 years at the time of first NDA submission.

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Figure 12: Clinical Trial Design

Phase 3: LOGICS	
Aim	Supplement long-term efficacy and safety data from the ongoing SONICS
Design	randomized, double-blind withdrawal, matching placebo-controlled
Dosing	following screening phase, 3 distinct treatment phases for patients who didn't participate in SONICS and 2 distinct phases for most of those who did participate in SONICS. First phase: for patients new to levoketoconazole or for those who require re-establishment of a therapeutic dose, is dose titration and maintenance. start at 150mg 2X/day and titrate in 150mg increments up to max 600mg 2X/day. duration of this is about 14 weeks. Second: randomized-withdrawal, during which patients are randomly assigned to continue active treatment with levoketoconazole or be switched to a matching placebo. lasts no more than 9.5 weeks. Third: Restoration phase during which all patients receive active therapy with 2X # tablets (one active and one placebo).
Endpoints	1) Proportion of patients with loss of established UFC response in the placebo group vs proportion in the levoketoconazole group.
Patients	n=35 to now n=54
Safety	
Results	enrollment anticipated to begin in 1Q18 and topline data expected in 4Q19.

Source: Company reports

In addition to LOGICS, they intend to initiate a long-term open-label extension study with Recorlev to capture even longer-term safety, tolerability and efficacy data from subjects who complete either SONICS or LOGICS and who choose to continue therapy with Recorlev. The open-label extension, named OPTICS, recently began enrollment and will continue to accrue data indefinitely, at least until the drug is first marketed.

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Macrilen for diagnosing AGHD

Macrilen (macimorelin), consists of an oral growth hormone secretagogue receptor agonist and is indicated for the diagnosis of AGHD. Macrilen has been granted ODD by the FDA for use in evaluating growth hormone deficiency (GHD), which affects ~60,000 adults in the US and Canada (Symphony, 2017). On 12/20/17, the FDA granted marketing approval for Macrilen. The company acquired the US and Canadian marketing rights to Macrilen from Aeterna Zentaris (AEZS) in January 2018 and launched it in the US in July 2018. On 10/31/18, SBBP entered into an agreement (expected to close in December) for Novo Nordisk (NVO) to acquire US and Canadian rights to Macrilen for an upfront payment of $145M and tiered royalty stream from NVO. Additionally, NVO will purchase ~5.2M shares of SBBP, resulting in gross proceeds of ~$36.7M and SBBP's current Macrilen sales team will continue to promote the product in the US under a three-year agreement with NVO. We believe this adds significant stability to SBBP's balance sheet and view as positive their intent to pay down their $88M outstanding debt.

AGHD is a condition that is associated with premature mortality, as well as cardiovascular, neuromuscular, metabolic, nervous system, and skeletal abnormalities and its clinical features are nonspecific. Growth hormone stimulation testing is required for its diagnosis.

Growth hormone is produced by the pituitary gland and secreted in pulses, so random measurements of growth hormone levels in the blood are not useful for establishing a diagnosis of AGHD.

Growth hormone stimulation testing provokes the pituitary gland to release levels of growth hormone above resting levels to determine the growth hormone release potential in a patient suspected of having AGHD.

Endocrinologists often use drug to diagnose hormonal issues. Prior to Macrilen, there were only two ways that endocrinologists could diagnose growth hormone deficiencies. These methods were the Insulin Tolerance Test (ITT) and the Glucagon Stimulation Test (GST). Many patients remain underdiagnosed due to the tests' complexity, tolerability, and safety issues.

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Figure 13: 2 Main AGHD Diagnostic Tests Prior to Macrilen

Current tests	Insulin Tolerance Test (ITT)	Glucagon Stimulation Test (GST)
Procedure	IV[1,2]	IM[1,2]
Number of blood draws	6[1]	9[1,2]
Total time	2-3 hours[2]	Minimum 3-4 Hours[1,2]
Requires medical supervision	Yes[1,2]	Yes[3]
Adverse events	• Neuroglycopenia[1,2] • Seizures[1,2] • Loss of consciousness[1,2] • Severe hypoglycemia[2]	• Nausea[1,2] • Vomiting[1,2] • Headache[1,2] • Late hypoglycemia[1,2]

Source: Company Presentation

In comparison to these two tests, Macrilen presents many advantages. It is oral, takes 1.5 hours, requires 4 blood draws, has a better safety/tolerability profile and is FDA approved.

The following figure depicts the design and results of the pivotal trial that led to Macrilen's approval. The goal of the trial was to compare the level of agreement between Macrilen test results and ITT. Results showed a high level of negative agreement. The Macrilen test will not wrongly diagnose and individual without GHD (per the ITT) as having GHD. Additionally, results showed a high level of positive agreement. Macrilen will not wrongly diagnose an individual with GHD (per the ITT) as not having GHD.

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Figure 14: Study Design

Phase 3 Validation of Macimorelin as a Test of Adult Growth Hormone Deficiency	
Aim	Compare the level of agreement between Macrilen test results and insulin tolerance test (ITT) results in adult patients with different pre-test probabilities of AGHD, including with healthy control subjects.
Design	randomized, open-label, single-dose, cross-over. 4 groups of individuals A: Adults with high likelyhood of GHD. B: Adults with an intermediate likelihood of GHD. C: Adults with a low likelihood of GHD. D: Healthy adult controls. Healthy subjects matching Group A subjects by sex, age +/- 5 years, (BMI +/- 2kg/m2) and estrogen status.
Dosing	Experimental Sequence A: 1st: Macrilen, 2nd: ITT and inverse for sequence B
Endpoints	1) % positive and % neg agreement of Macrilen with ITT; 2) Overall agreements (positive/negative) for MAC and ITT, AE, ECG
Patients	n=157 underwent at least 1 of 2 tests. Data on both tests available for 140 subjects; 38 (27%) in Group A, 37 (26%) in Group B, 40 (29%) in Group C, ad 25 (18%) in Group D.
Safety	well tolerated vs ITT, AE: dysgeusia (4.5%); dizziness, fatigue, and headache (3.9%), nausea (3.25); no severe AE that led to failure to complete test; concomitant QT-prolongation drugs should be avoided, no need for ECG pre or post Macrilen; DDI: discontinue strong CYP3A4 inducers (avoids false-positive results).
Results	For both ITT and Macrilen test, serum concentrations of GH were measured @ 30, 45, 60 and 90 minutes post drug administration. Test was considered positive (AGHD diagnosed) if maximum serum GH level observed anytime after stimulation was less than the pre-specified cut point value of 2.8ng/mL for the Macrilen test or 5.1 ng/mL for the ITT. Results showed a high level of negative agreement, demonstrating that Macrilen will not wrongly diagnose an individual without GHD (per the ITT) as having GHD. Results showed high level of positive agreement, demonstrating Macrilen will not wrongly diagnose an individual with GHD (per the ITT) as not having GHD. Estimates for negative and positive agreement between Macrilen and ITT in overall study were 94% and 74% with lower 95% confidence interval bounds 85%and 63%, respectively. Negative and positive agreement between Macrilen and the ITT with intermediate or low risk (B,C) were 93% and 61% with lower 95% confidence interval bounds 80% and 43%, respectively. 1/154 Macrilen faile due to a technical error and 27/157 ITTs failed b/c induction of severe hypoglycemia.

Source: Company reports and Laidlaw estimates

In order to better illustrate the agreement between the two tests, here is a representation of these measures.

Figure 15: Definition of Agreement between ITT and Macrilen

		Insulin Tolerance Test		Total	
		+	-		
Macrilen	+	a	b	a+b	Positive Agreement (%)=100% x a/(a+c)
	-	c	d	c+d	Negative Agreement (%)=100% x d/(b+d)
Total		a+c	b+d	a+b+c+d	Overall Agreement (%)=100% x (a+d)/(a+b+c+d)

Source: 10K

The following tables represent the primary analysis results for the ITT and Macrilen test for all subjects together and each separately. In overall study, negative and positive agreement were 94% and 74% with lower 95% confidence interval bounds 85% and 63%, respectively. In intermediate or low risk subjects (B and C), negative and positive agreement between Macrilen and ITT were 93% and 61% with lower 95% confidence interval bounds 80% and 43%, respectively. These results were based on peak growth hormone values (maximum growth hormone concentrations across all measurement timepoints). Out of the 34

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subjects that took two Macrilen tests, 31 cases demonstrated agreement between tests (91.2%). Less than 1% of Macrilen tests weren't evaluable vs. 17% of ITTs.

Figure 16: Diagnostic Outcomes for Macrilen and the ITT in all Subjects and in Each Group Separately

All Subjects		Insulin Tolerance Test +	Insulin Tolerance Test -	Total
Macrilen	+	55	4	59
	-	19	62	81
Total		74	66	140

Agreement Between ITT and Macrilen	
Positive	74%
Negative	94%
Overall	84%

Group A High likelihood of AGHD		Insulin Tolerance Test +	Insulin Tolerance Test -	Total
Macrilen	+	33	0	33
	-	4	1	5
Total		37	1	38

Positive	89%
Negative	100%
Overall	89%

Group B Intermediate likelihood of AGHD		Insulin Tolerance Test +	Insulin Tolerance Test -	Total
Macrilen	+	20	1	21
	-	10	6	16
Total		30	7	37

Positive	67%
Negative	86%
Overall	70%

Group C Low likelihood of AGHD		Insulin Tolerance Test +	Insulin Tolerance Test -	Total
Macrilen	+	2	2	4
	-	4	32	36
Total		6	34	40

Positive	33%
Negative	94%
Overall	85%

Group D Healthy control		Insulin Tolerance Test +	Insulin Tolerance Test -	Total
Macrilen	+	0	1	1
	-	1	23	24
Total		1	24	25

Positive	0%
Negative	96%
Overall	92%

Source: 10K

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Keveyis for PPP

Keveyis (dichlorphenamide) is an oral carbonic anhydrase inhibitor and the only approved therapy in the US to treat hyperkalemic, hypokalemic and related variants of PPP, which is a rare genetic, neuromuscular disorder that can cause extreme muscle weakness and paralysis. Keveyis was approved by the FDA on 8/7/15, and has orphan drug exclusivity status in the US through 8/7/22. From May 2016 to December 2016, Taro Pharmaceuticals (TARO) and its affiliates, supplied Keveyis on a non-commercial basis to patients through a single specialty pharmacy in the US. SBBP then acquired the US marketing rights to Keveyis in December 2016 and launched it in the US in April 2017.

PPP is a rare, genetic, neuromuscular disorder related to a defect in muscle ion channels with multiple variants and subtypes. PPP may be localized or more widespread, and often goes underdiagnosed. Types of periodic paralysis are differentiated by criteria including underlying genetic mutations and changes in blood potassium during an episode. PPP seems to affect OR IS IT 4K-5K ~5,000-6,000 individuals in the US (AANEM, 2017).

While the exact MOA through which oral carbonic anhydrase inhibitors, and Keveyis in particular, decrease the frequency and severity of periodic paralysis attacks is unknown, their effects seem mediated locally and systemically. After its acquisition, the company continued to supply Keveyis to patients on a non-commercial basis until launching Keveyis in April 2017. Once US marketing rights for Keveyis were acquired, SBBP established sales, marketing, market access and patient service capabilities. They launched Keveyis using 12 sales representatives, and in the 4Q17, they expanded their sales force to 24 individuals consisting of three regional business directors and 21 sales representatives. Keveyis showed topline sales of $4.2M in 3Q18 and SBBP has guided to FY18 revenues of $16-$17M from their previous $18M-$20M due to patients stopping treatment.

In terms of clinical development, Keveyis was evaluated in two clinical studies as described below. Ultimately, treatment with Keveyis demonstrated fewer attacks/week vs. patients on placebo and fewer patients in the treatment arm reached acute worsening.

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Figure 17: Clinical Trial Design

Phase 3 (Study 1) Keveyis in Hypokalemic and Hyperkalemic periodic paralysis	
Aim	Evaluate efficacy of Keveyis in hypokalemic and hyperkalemic periodic paralysis patients
Design	9 week double-blind, randomized, placebo-controlled, multi-center. 2 substudies in patients with hypokalemic periodic paralysis (n=44) and a substudy in patients with hyperkalemic periodic paralysis (n=21).
Dosing	50mg bid for treatment-naïve patients. Patients already receiving dichlorphenamide prior to the study continued on the same dose if randomized to Keveyis during the study. In patients on acetazolamide prior to the study, the daily dose of Keveyis was set at 20% of the daily acetazolamide dose.
Endpoints	1) average number of self-reported attacks of muscle weakness/week over the final 8 weeks of trial. Withdrawal from the study for acute severe worsening was also assessed as an endpoint.
Patients	n=44 in patients with hypokalemic periodic paralysis and n=21 in patients with hyperkalemic periodic paralysis.
Results	Patients treated with Keveyis (n=24) had 2.2 fewer attacks/week than patients (n=20) treated with placebo (p=0.02).None of patients randomized to Keveyis reached the endpoint of acute worsening, vs 5 patients randomized to placebo. Mean dose of Keveyis at week 9 was 94 mg/day. In double-blind treatment period, patients treated with Keveyis (n=12) had 3.9 fewer attacks/week vs placebo (n=9) (p=0.08). 0 pateints randomized to Keveyis reached endpoint of acute worsening vs 2 patients randomized to placebo.

Source: Company Reports

Figure 18 Clinical Trial Design

Phase 3 (Study 2) Keveyis in Hypokalemic and Hyperkalemic Patients	
Aim	Evaluate efficacy of Keveyis in hypokalemic and hyperkalemic periodic paralysis patients
Design	35 week, double-blind, placebo-controlled, randomized, multi-center, 2-period crossover study. Also had 2 substudies: in patients with hypokalemic periodic paralysis (n=42), and in patients with hyperkalemic periodic paralysis (n=31).
Dosing	dosing determined similarly to study 1
Endpoints	1) in hyperkalemic periodic paralysis was the average number of self-reported attacks of muscle weakness/week
Patients	n=42 in hypokalemic and n=31 in hyperkalemic
Results	acute intolerable worsening was observed in 2 patients on Keveyis vs 11 on placebo (p=0.02). Patients treated had 2.3 fewer attacks/week on Keveyis than on placebo (p=0.006).

Source: Company Reports

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Veldoreotide for acromegaly and additional applications

Veldoreotide modified-release is a novel multi-receptor targeted somatostatin analog (SSA) that was previously in Phase 2 development as an IR formulation. Based on the differentiated activation pattern of somatostatin receptor subtypes (SSTRs) and the preclinical and clinical profile of IR veldoreotide, SBBP believes that modified-release veldoreotide may offer an improved efficacy and safety profile relative to existing drug therapies for acromegaly and other conditions that are modifiable through activation of somatostatin receptors, such as Cushing's disease and neuroendocrine tumors. Veldoreotide has been granted ODD by the FDA and the EMA for treatment of acromegaly. The lead formulation for veldoreotide modified-release is based upon PLGA microspheres, which is a well-known polymer that has been widely applied in modified-release formulations due to its biocompatibility, biodegradability, and favorable release kinetics. They expect to initiate a series of pre-clinical studies that seek to determine additional differentiating features of veldoreotide in both endocrine and nonendocrine conditions.

Acromegaly is a rare endocrine disorder that most commonly results from a benign tumor of the pituitary gland, leading to excess production of growth hormone and IGF1. The treatment goal is the normalization of growth hormone and IGF1, which is the main cause of the detrimental clinical signs and symptoms of acromegaly. SSAs are peptides that are administered as deep subcutaneous or intramuscular injections, typically as long-acting formulations for monthly injections. They are the most commonly used drug therapy for the treatment of acromegaly and work by binding to specific subtypes of SSTRs that are expressed by the tumor. Binding of SSAs to these SSTRs leads to the beneficial inhibition of growth hormone secretion but can also result in the unwanted inhibition of secretion of other endocrine hormones such as insulin and glucagon in the pancreas and elsewhere. Like other SSAs, veldoreotide is a peptide that SBBP is developing for subcutaneous injection, but in contrast to approved SSAs, veldoreotide activates a different subset of SSTRs. Veldoreotide does not bind to SSTR3 or the opiate receptor at pharmacological concentrations. Although the functional consequences of the binding of SSAs to the opiate receptor are not fully understood, it has been suggested as a mechanism contributing to inhibition of insulin secretion by SSAs and may also influence their effect on GI motility. Preclinical data from animal studies, and clinical data in healthy subjects and patients with acromegaly, showed that insulin secretion was less inhibited, potentially resulting in reduced side effects on blood glucose and an improved safety and tolerability profile.

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Competition

Figure 19: Competitive Landscape

Product/Disease	Competition
Keveyis	Acetazolamide (oral carbonic anhydrase inhibitor), is used off-label for prophylactic and treatment of PPP. Potassium supplements are also used. Other types of drugs like potassium-sparring diuretics, beta receptor agonists, mexelitine and other sodium channel blockers. Phase 2 clinical study of bumetanide, a loop diuretic, is ongoing in England for acute treatment of paralytic attacks.
Macrilen	Measurement of blood levels of IGF-1, typically used as the first test. The Insulin Tolerance Test (ITT) has considered the reference standard for the evaluation of AGHD (high sensitivity and specificity). However, the ITT inconvenient to both patients and physicians, IV, and contra-indicated in certain patients (coronary heart disease or seizure disorder). Additionally, administration of the ITT includes additional costs associated with the patient being closely monitored by a physician for the 2-4h duration of the test, and require emergency equipment available. The Glucagon Stimulation Test (GST) is considered relatively safe by endocrinologists. MOA is unclear. Also, takes at least 3-4h, intramuscular. Interpretation of the GST is complicated by variability of the peak growth hormone response.
Recorlev	Korlym (mifepristone) is a cortisol receptor blocker to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed surgery or are not candidates for surgery. Signifor (pasireotide) marketed by Novartis (NVS) in the US is indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been currative. Ketoconazole, metyrapone and mitotane are marketed by HRA Pharma in certain EU countries. Osilodrostat (LCI699), an 11-HSD2 inhibitor, is currently in Phase 3 clinical development by NVS in Cushing's disease. Corcept (CORT) is developing relacorilant (CORT125134), a selective glucocorticoid receptor antagonist, currently in Phase 2 for Cushing's syndrome. HRA Pharma is developing metyrapone for the EU market. Millendo is developing ATR- 101, a selective acyl-CoA:cholesterol acyltransferase 1 (ACAT) inhibitor, currently in Phase 2. The University of Oxford, in collaboration with AstraZeneca (AZN) is studying the selective 11‡HSD1 inhibitor, AZD4017, now in Phase 2. Cedars-Sinai is developing R-roscovitine in
Veldoreotide	There are currently 3 approved SSA therapies for acromegaly in the US: Sandostatin LAR (octreotide) marketed by NVS; Signifor LAR (pasireotide) marketed by NVS; and Somatuline Depot (lanreotide) marketed by Ipsen. There is 1 growth hormone receptor antagonist, Somavert (pegvisomant), marketed by Pfizer (PFE). Chiasma (CHMA) had filed an NDA for RG-3806 (Mycapssa), an oral octreotide formulation in 2015, and received a CRL. 4 additional therapies are in Phase 2 clinical development for acromegaly: octreotide longacting depot (CAM2029) developed by NVS and Camurus (CMX); ITF2984 developed by Italfarmaco; BIM-23B065 developed by Ipsen (IPSEF); and ATL-1103 developed by Antisense Therapeutics (ATHJF).

Source: Company reports and Laidlaw estimates

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Major Risks

Exogenous events could impact our outlook. We believe pharmaceutical companies have the least control over competitive, political, and regulatory risks. Although we have incorporated competitive assumptions into our forecasts, there may be other risks beyond the scope of our analysis. Changes in the drug reimbursement system, as well as any political or regulatory amendments, may significantly influence the earnings power of these companies.

Actual clinical results and the FDA's conclusions may deviate from expectations. Many of our assumptions are based on a review of incomplete clinical trial data available in the public domain. Often, our conclusions are drawn from early stage data, which may not be reflected by pivotal studies. Furthermore, the FDA's conclusions may not coincide with our own, materially changing our revenue and earnings assumptions.

Compliance issues, product recalls, and other mandates by regulatory authorities could materially change our expectations. Regulatory compliance issues, ranging from accounting irregularities to defective manufacturing practices, could materially change our assumptions and earnings outlook. Unanticipated product recalls and labeling changes could also have adverse consequences on our earnings assumptions.

Legal risks could lead to additional liabilities and revenue loss. In addition to the expenses incurred by patent challenges, product liability and other legal suits could occur and lead to additional liabilities and revenue loss, which could substantially change our financial assumptions.

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Management

Matthew Pauls, President and CEO. Matthew has more than 20 years of leadership experience in the pharmaceutical industry, with an emphasis on specialty pharma and rare disease. He brings extensive general management and commercial leadership experience to SBBP, including US and global product launches and brand management, business development, clinical development, and technical operations. Before joining Strongbridge, Matt was CMO at Insmed (INSM), a publicly traded biopharmaceutical company. Prior to that, he served as SVP, head of global commercial operations at Shire Pharmaceuticals (SHPG) and also held senior positions at Bristol-Myers Squibb (BMS) in brand management and payer marketing, and at Johnson & Johnson (JNJ) in various US and global commercial roles. Matt was previously a member of the board of directors at Mast Therapeutics, and currently serves on the board of directors of SBBP, Savara Pharmaceuticals, and is a volunteer board member of the Pennington School in Pennington, NJ. Matt holds an MBA and BS degree from Central Michigan University and earned his JD from Michigan State University College of Law.

Brian Davis, CFO. Brian has more than 20 years of experience in management and financial activities with life sciences companies, including equity and debt financings, restructuring activities, strategic transactions, and negotiations involving partnering, licensing, drug discovery, and clinical development. Most recently, he served as SVP and CFO at Tengion (TNGNQ). Earlier in his career, he held a series of positions of increasing responsibility during his 15 years at Neose Technologies, including SVP and CFO. Brian holds an MBA from The Wharton School at the University of Pennsylvania and a BS in accounting from Trenton State College

Fredric Cohen, CMO. Fred joined SBBP in 2015 and has held roles of increasing responsibility, including SVP, global R&D, and VP, clinical research and development. Fred is an endocrinologist by training with more than 20 years of drug and business development experience, most recently focused in development and commercialization of rare disease and specialty products. Prior to joining SBBP, Fred provided strategic and operational counsel to life science companies, actively supporting their development and licensing functions. Prior to that, he served as executive director, clinical pipeline, at Aptalis Pharma, where he was responsible for innovation strategy as well as building and advancing the company's specialty pharma pipeline. He has also held R&D positions with Johnson & Johnson and Eli Lilly & Company. Fred holds an MD from Pennsylvania State University College of Medicine and an AB in biology from Franklin and Marshall College.

Robert Lutz, Chief Business Officer. Rob leads the business development efforts and commercial strategy implementation at SBBP. He brings 25 years of experience in finance, business development, and product management to the team. Prior to joining, Rob worked at SHPG for 10 years in a number of diverse roles with increasing global responsibility. He also draws upon substantial experience in the financial and energy sectors. Rob holds an MBA from the Kellogg School of Management and a BA in economics and computer science from Amherst College.

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Figure 20: Quarterly Income Statement

Strongbridge Biopharma
Quarterly income statement

($000 except per share)	2017A 1QA	2017A 2QA	2017A 3QA	2017A 4QA	2017A Year	2018E 1QA	2018E 2QA	2018E 3QA	2018E 4QE	2018E Year
Revenues										
Keveyis		1,529	2,533	2,984	7,046	3,870	4,296	4,200	4,147	16,513
Macrilen								1,100	1,313	2,413
Recorlev										
Total Revenue		**$1,529**	**$2,533**	**$2,984**	**$7,046**	**$3,870**	**$4,296**	**$5,347**	**$5,460**	**18,973**
Expenses:										
COGS (% of US Revenue)		377	591	515	1,483	667	753	1,441	622	3,483
Gross Margin		**1,152**	**1,942**	**2,469**	**5,563**	**3,203**	**3,543**	**3,906**	**4,838**	**15,490**
SG&A	7,442	9,060	7,477	9,238	32,265	11,082	13,689	17,915	16,500	59,186
R&D	3,481	3,847	4,180	4,837	16,128	4,473	4,990	6,730	7,500	23,693
Impairment of intangible assets										
Total operating expenses	**10,923**	**12,907**	**11,657**	**14,075**	**48,393**	**15,555**	**18,679**	**24,645**	**24,000**	**82,879**
Operating income	**(10,923)**	**(11,755)**	**(9,715)**	**(11,606)**	**(42,830)**	**(12,352)**	**(15,136)**	**(20,739)**	**(19,162)**	**(67,389)**
Interest expense	(737)	(467)	137	(876)	(1,501)	(1,642)	(1,859)	(1,899)	(1,750)	(7,150)
Foreign exchange gain (loss)	(12)	(14)	(11)	(5)	(41)	(20)	13	(15)		
loss on extinguishment of debt			(3,545)	-	(3,545)	(500)				
Income tax (expense) benefit				128	(127)		(1)			
other income, net	(35)	60	82	41	147	180	329	445		
Net loss	**(11,707)**	**(12,176)**	**(13,052)**	**(12,318)**	**(47,897)**	**(14,334)**	**(16,654)**	**(22,208)**	**(20,912)**	**(74,539)**
Adj. NI/(loss)	**(11,707)**	**(12,176)**	**(13,052)**	**(12,318)**	**(47,897)**	**(14,334)**	**(16,654)**	**(22,208)**	**(20,912)**	**(74,539)**
unrealized gain (loss) on fair value of wari	(14,928)	(15,219)	1,953	(2,024)	(30,218)	(9,700)	19,017	7,131		
Income tax (expense) benefit	(1,594)	92	850	(1,247)	(1,644)					
Intangible asset amortization	(1,256)	(1,255)	(1,256)	(1,255)	(5,022)	(1,769)	(1,872)	(1,876)		
Impairment of intangible assets			(20,723)		(20,723)					
SG&A		(1,082)	(1,007)	(986)	(4,027)	(1,280)	(1,521)	(1,649)		
R&D		(281)	(324)	(318)	(1,140)	(408)	(463)	(468)		
non-cash interest expense		(270)	(1,501)	(599)	(2,812)	(1,232)	(1,430)	(1,488)		
NI/(loss) as reported	**(29,485)**	**(30,191)**	**(35,060)**	**(18,747)**	**(113,483)**	**(28,723)**	**(2,923)**	**(20,558)**		
Earning per Share (EPS)	**($0.83)**	**($0.85)**	**($0.98)**	**($0.47)**	**($3.11)**	**($0.66)**	**($0.06)**	**($0.44)**		
Adj EPS ex-1x & non-cash	**($0.33)**	**($0.34)**	**($0.37)**	**($0.31)**	**($1.31)**	**($0.33)**	**($0.36)**	**($0.47)**	**($0.40)**	**($1.58)**
Weighted avg. shares (000)	35,335	35,335	35,716	39,754	36,545	43,630	45,830	46,978	52,178	47,154
Fully diluted shares (000)	35,335	35,335	35,716	39,754	36,545	43,621	50,438	50,317	54,178	49,639

Source: Company Reports; Laidlaw & Company estimates

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Figure 21: Annual Income Statement

Strongbridge Biopharma
Annual income statement

($000's except per share)	2017A	2018E	2019E	2020E	Comments
Revenues					
Keveyis	$7,046	$16,513	$18,013	$22,747	Launched 2Q17
Macrilen	$0	$2,413	$2,514	$5,196	Launched July 2018
Recorlev	$0	$0	$0	$0	Launched 2021
Total sales	**$7,046**	**$18,926**	**$20,527**	**$27,944**	
COGS	1,483	3,483	2,423	2,730	
Gross margin	**5,563**	**15,443**	**18,104**	**25,214**	
R&D	16,128	23,693	30,500	33,000	
SG&A	32,265	59,186	48,500	54,000	
Adj. Net Income	**(47,897)**	**(74,539)**	**(67,896)**	**(68,786)**	
NI/(loss) as reported	**(113,483)**				
Adj-EPS ex-non-cash	**($1.31)**	**($1.58)**	**($1.20)**	**($1.06)**	
EPS as reported	**($3.11)**				
Shares out (000)	36,545	47,154	56,803	64,803	
Fully diluted shares (000)	36,545	49,639	58,803	67,803	

Source: Company Reports; Laidlaw & Company estimates

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Figure 22: Balance Sheet Statement

Strongbridge Biopharma
Balance sheet

($000's except per share)	2017	1Q18A	2Q18A	3Q18A	2018	2019	2020
ASSETS:							
Current assets							
Cash and cash equivalents + restric	$57,510	$92,405	$85,514	$67,383	$126,942	$63,545	$42,010
Accounts receivable	$1,584	$2,016	$2,376	$2,542			
Inventory	511	1,661	1,186	6,261			
Prepaid expenses and other current a	1,208	1,776	3,078	2,342			
Total current assets	**60,813**	**97,858**	**92,154**	**78,528**	**126,942**	**63,545**	**42,010**
PP&E	15	12	315	297	250	250	250
Deferred tax asset							
Intangible assets, net	35,155	58,041	56,169	54,463	55,000	60,000	65,000
Goodwill	7,256	7,256	7,256	7,256	7,500	7,500	7,500
Other assets	686	360	318	305			
Total Assets	**103,925**	**163,527**	**156,212**	**140,849**	**189,692**	**131,295**	**114,760**
LIABILITIES							
Current liabilities:							
accounts payable	1,247	2,168	2,411	3,227	2,500	2,750	3,000
accrued liabilities	11,232	8,837	11,856	19,985	12,000	12,500	13,000
Total current liabilities	**12,479**	**11,005**	**14,267**	**23,212**	**14,500**	**15,250**	**16,000**
LTD	37,794	76,142	77,572	79,061			
warrant liability	41,308	51,008	31,991	22,721	30,000	25,000	20,000
supply agreement liability, noncurrent	24,258	23,519	23,519	22,111	20,000	17,500	15,000
Total liabilities	**115,839**	**161,674**	**147,349**	**147,105**	**64,500**	**57,750**	**51,000**
Shareholder's equity							
deferred shares	44	44	44	44	40	40	40
ordinary shares	401	455	467	472	400	400	400
additional paid-in	230,524	272,960	282,881	288,316	442,174	458,424	517,424
accumulated deficit	(242,883)	(271,606)	(274,529)	(295,088)	(317,422)	(385,319)	(454,104)
Total shareholders' equity	**(11,914)**	**1,853**	**8,863**	**(6,256)**	**125,192**	**73,545**	**63,760**
Total liabilites & net worth	**103,925**	**163,527**	**156,212**	**140,849**	**189,692**	**131,295**	**114,760**

Source: Company Reports; Laidlaw & Company estimates

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Figure 23: Cash Flow Statement

Strongbridge Biopharma
Statement of cash flows

($000's except per share)	2017A	1Q18A	2Q18A	3Q18A	2018E	2019E	2020E
Operating Cash Flow							
Net loss	(113,483)	(28,723)	(31,646)	(52,205)	(74,539)	(67,896)	(68,786)
Adjustments to reconcile net loss to net cash							
change in fair value of warrant liability	30,218	9,700	(9,317)	(16,448)			
Impairment of intangible assets	20,723						
stock-based compensation	5,167	1,688	3,673	5,789	6,000	6,500	7,000
amortization of intangible assets	5,022	1,769	3,641	5,517	6,000	6,500	7,000
Interest and related guarantee fees paid in kind	896	766	1,813	2,890			
Amortization of debt discounts and debt issuance c	482	314	697	1,109			
Loss on extinguishment of debt	3,545	500	500	500	3,000	3,250	3,500
Deferred income tax expense	1,958						
Depreciation	10	3	10	28			
Changes in Assets & Liabilites	126	(4,036)	(1,919)	956	(18,229)	(5,000)	(5,000)
Cash from operations	**(45,336)**	**(18,019)**	**(32,548)**	**(51,864)**	**(77,768)**	**(56,646)**	**(56,286)**
Investing Activities							
Payment for acquisition	(7,500)	(24,655)	(24,655)	(24,655)	(25,000)	(30,000)	(35,000)
Payment for acquisition by Novo					57,000		
PPE			(310)	(310)			
Cash from investing	**(7,500)**	**(24,655)**	**(24,965)**	**(24,965)**	**32,000**	**(30,000)**	**(35,000)**
Financing Activities							
Proceeds from LTD	38,687	44,930	44,930	44,930	45,000		
Repayment on LTD	(22,261)						
Payment for loss on extinguishment of debt		(500)	(500)	(500)			
Proceeds from issuance of ordinary shares	26,384	33,508	33,508	33,508	70,200	23,250	69,750
Proceeds from issuance of ordinary shares in conne	73		7,961	7,951			
Payment related to tax withholding			(441)				
Proceeds from exercise of warrants				1,175			
Proceeds from exercise of stock options	626	59	59	79			
Payment for amendment of LTD		(428)		(441)			
Cash from financing	**43,509**	**77,569**	**85,517**	**86,702**	**115,200**	**23,250**	**69,750**
Change in cash	**(9,327)**	**34,895**	**28,004**	**9,873**	**69,432**	**(63,396)**	**(21,536)**
Cash, start of period	66,837	57,510	57,510	57,510	57,510	126,942	63,545
Cash, end of period	**57,510**	**92,405**	**85,514**	**67,383**	**126,942**	**63,545**	**42,010**

Source: Company Reports; Laidlaw & Company estimates

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DISCLOSURES:

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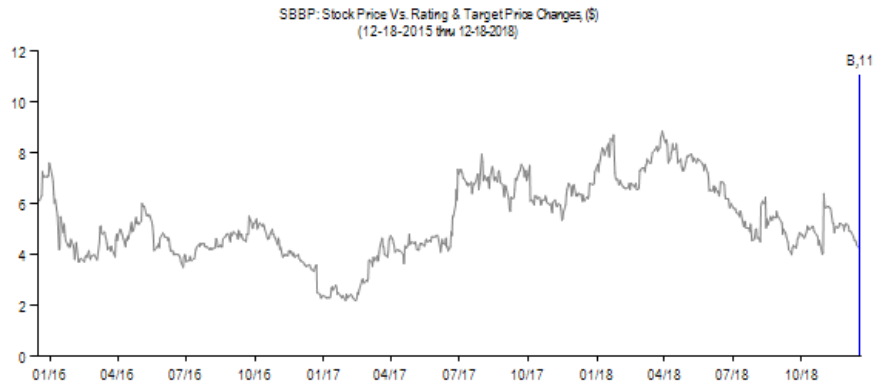
Additional information available upon request.

Laidlaw & Co (UK) Ltd. has not provided any investment banking services for the company (ies) mentioned in this report over the last 12 months.

RATINGS INFORMATION

Rating and Price Target Change History



3 Year Rating Change History

Date	Rating	Closing Price ($)
12/18/2018	Buy (B)	4.27*

3 Year Price Change History

Date	Target Price ($)	Closing Price, ($)
12/18/2018	11.00	4.27*

** Previous Close12/17/2018*

Source: Laidlaw & Company **Created by: Blue-Compass.net**

Laidlaw & Company Rating System*		% of Companies Under Coverage With This Rating	% of Companies for which Laidlaw & Company has performed services for in the last 12 months	
			Investment Banking	Brokerage
Strong Buy (SB)	Expected to significantly outperform the sector over 12 months.	0.00%	0.00%	0.00%
Buy (B)	Expected to outperform the sector average over 12 months.	61.67%	25.00%	3.33%
Hold (H)	Expected returns to be in line with the sector average over 12 months.	6.67%	1.67%	0.00%
Sell (S)	Returns expected to significantly underperform the sector average over 12 months.	0.00%	0.00%	0.00%

ADDITIONAL COMPANIES MENTIONED

Novartis (NVS – Not Rated)
Aeterna Zentaris (AEZS – Not Rated)
Novo Nordisk (NVO – Not Rated)
Taro Pharmaceuticals (TARO – Not Rated)
Corcept Therapeutics (CORT – Not Rated)
Millendo Therapeutics (MLND – Not Rated)
AstraZeneca (AZN – Not Rated)
Pfizer (PFE – Not Rated)
Chiasma (CHMA – Not Rated)
Ispen (IPSEF – Not Rated)
Camurus (CMX – Not Rated)
Antisense Therapeutics (ATHJF – Not Rated)

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ADDITIONAL DISCLOSURES

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