Strongbridge Biopharma plc

December 2018

STRONGBRIDGE BIOPHARMA

Forward-looking statements

This document contains forward-looking statements relating to the Company's strategy, objectives, business development plans and financial position. All statements other than statements of historical facts included in this document, including, without limitation, statements regarding the Company's future financial position, strategy, anticipated investments, costs and results, status and results of clinical trials, size of patient population, plans, outcomes of product development efforts, intellectual property portfolio and objectives of management for future operations, may be deemed to be forward-looking statements. You can identify forward-looking statements by words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of those terms, and similar expressions that convey uncertainty or future events or outcomes.

These forward-looking statements involve known and unknown risks, uncertainties, and other factors that may cause the Company's actual results, performance, or achievements or industry results to be materially different from those contemplated, projected, forecasted, estimated or budgeted, whether expressed or implied, by these forward-looking statements. Given these risks and uncertainties, investors should not place undue reliance on forward-looking statements as a prediction of actual results. A discussion of certain of these risks may be found in the filings the Company makes with the U.S. Securities and Exchange Commission. None of these forward-looking statements constitutes a guarantee of the future occurrence of such events or of actual results. These statements are based on data, assumptions, and estimates that the Company believes are reasonable.

The forward-looking statements contained in this document are made only as of the date hereof. Except as otherwise required by law, the Company expressly disclaims any obligation or undertaking to release publicly any updates of any forward-looking statements contained in this document to reflect any change in its actual results, assumptions, expectations or any change in events, factors, conditions, or circumstances on which any forward-looking statement contained in this document is based.

Investment highlights

Revenue-Generating Rare Disease Company

Rare Endocrinology

Macrilen – recently agreed to sell rights to Novo Nordisk for $145M and tiered royalties on future sales; transaction expected to close in December 2018

Recorlev – Positive data from first Phase 3 pivotal trial (SONICS) for Cushing's syndrome

veldoreotide – preclinical

Rare Neuromuscular

Keveyis – marketed in U.S. for Primary Periodic Paralysis

Proven Commercial Infrastructure

Field presence and operations in two therapy areas

Rare disease access, reimbursement and patient services expertise

Executing on Business Development

Proven ability to acquire and sell strategic assets

Well Capitalized

Pro forma 9/30/18 cash and debt
(assuming closing of Novo Nordisk transactions and repayment of outstanding debt)

- ~$148M in cash; no debt

Strongbridge and partnered product pipeline

		Indication/ Target Disease	Pre-clinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Lead
Rare Endocrinology	MACRILEN™ (macimorilen)	Adult Growth Hormone Deficiency diagnosis	Marketed					novo nordisk * US and Canada
	RECORLEV™ (levoketoconazole)	Endogenous Cushing's syndrome			Phase 3			STRONGBRIDGE BIOPHARMA Global
	veldoreotide modified-release	Acromegaly, other conditions modifiable through activation of somatostatin receptors, such as Cushing's disease and neuroendocrine tumors	Pre-clinical	Immediate Release Formulation Completed Phase 2				STRONGBRIDGE BIOPHARMA Global
Rare Neuro-muscular	KEVEYIS® (dichlorphenamide)	Primary Periodic Paralysis			Marketed			STRONGBRIDGE BIOPHARMA US

* Upon closing of transaction with Novo Nordisk (expected in December 2018)

Recorlev

(levoketoconazole)

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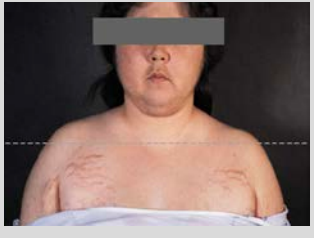
Cushing's syndrome complications and comorbidities

Cushing's syndrome symptoms

- Psychosis, impaired memory, sleep disturbance, depression, anxiety
- Heart attacks, stroke, high blood pressure, high cholesterol, vein clots
- Overweight/obesity, facial, neck and abdominal fat accumulation, diabetes
- Muscle and skin atrophy
- Osteoporosis



Unmet need and burden of illness

Per a 2017 study* of 224 patients, cortisol control was not achieved with any treatment modality—including surgery, radiation and medicines—in more than half of the subjects:

- **49.1%** control achieved
- **29.9%** control not achieved
- **21.0%** indeterminate

Cushing's disease patients have:[1*]

- **2-5x** higher incidence rates of comorbidities (eg, cardiovascular, endocrine, musculoskeletal, and mental health conditions)
- **7x** higher medical costs
- **4x** higher pharmacy costs

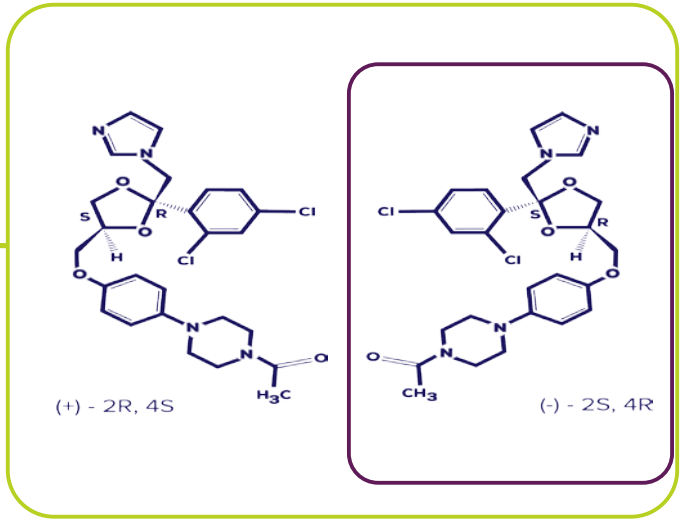
Source: Company sponsored research and published research including Feelders RA, Hofland LJ. (J Clin Endoc Metab. 2013;98(2):425-438) and Daly et al. (J Clin Endoc Metab 2006) *According to a retrospective analysis of claims from a large US commercial health plan (885 selected Cushing's disease cases and 2,655 matched controls without Cushing's disease) from 2007 to 2011. Burton T, et al. *Pituitary*. 2016;19:167–174. Geer et. al. (Endoc Pract 2017 Aug;23(8):962-970)

Recorlev (levoketoconazole) is the pure 2S,4R enantiomer of ketoconazole

KETOCONAZOLE

Two enantiomers combined

Not approved in the US to treat Cushing's syndrome



RECORLEV

Single enantiomer only (new chemical entity)

Single enantiomers often have significantly different clinical effects than their racemates

US/EU orphan designation for Cushing's syndrome

Development History and Regulatory Pathway

- Global phase 3 development program for Cushing's syndrome – SONICS topline results positive
  - Previously studied in two Phase 2 studies of diabetes (118 subjects received Recorlev)
- FDA 505(b)(2) regulatory approval pathway
  - Differentiated FDA 505(b)(2) drugs de-risk approval and have been successful in rare diseases (e.g., Korlym, Procysbi)

Ketoconazole labeled as last-line antifungal in U.S.
Warning against off label uses

Indications	Last-line anti-fungal, not indicated for Cushing's syndrome	NIZORAL® (ketoconazole) Tablets should be used only when other effective antifungal therapy is not available or tolerated...NIZORAL Tablets are indicated for the treatment of the following systemic fungal infections in patients who have failed or who are intolerant to other therapies.…
Dosage and administration	Limited 6-month course, 400-mg max dose, 200-mg strength, once daily	The recommended starting dose of NIZORAL Tablets is a single daily administration of 200 mg (one tablet). If clinical responsiveness is insufficient within the expected time, the dose of NIZORAL Tablets may be increased to 400 mg (two tablets) once daily…. The usual duration of therapy for systemic infection is 6 months.
Boxed warnings	Weekly ALT monitoring	During the course of treatment, serum ALT should be monitored weekly for the duration of treatment. If ALT values increase to a level above the upper limit of normal or 30 percent above baseline, or if the patient develops symptoms, ketoconazole treatment should be interrupted.
Adverse reactions to unapproved uses	FDA admonition of off-label use	Ketoconazole has been used in high doses for the treatment of advanced prostate cancer and for Cushing's syndrome when other treatment options have failed. The safety and effectiveness of ketoconazole have not been established in these settings and the use of ketoconazole for these indications is not approved by FDA.

FDA approved drugs for Cushing's disease/syndrome

Signifor®

Indication

Indicated for adults with Cushing disease for whom pituitary surgery is not an option or has not been curative

Adverse Reactions

Bradycardia, Hyperglycemia (40%), Cholelithiasis (30%), Diabetes Mellitus (18%) & Injection Site Reactions (17%)

Route of Administration

Self-administered injection 2-3 times daily

Korlym®

Indication

Indicated to control hyperglycemia secondary to hypercortisolism in adults with endogenous Cushing syndrome and diabetes

Disease Monitoring

Cannot measure UFC in Korlym patients

Efficacy on Secondary Outcome Measure

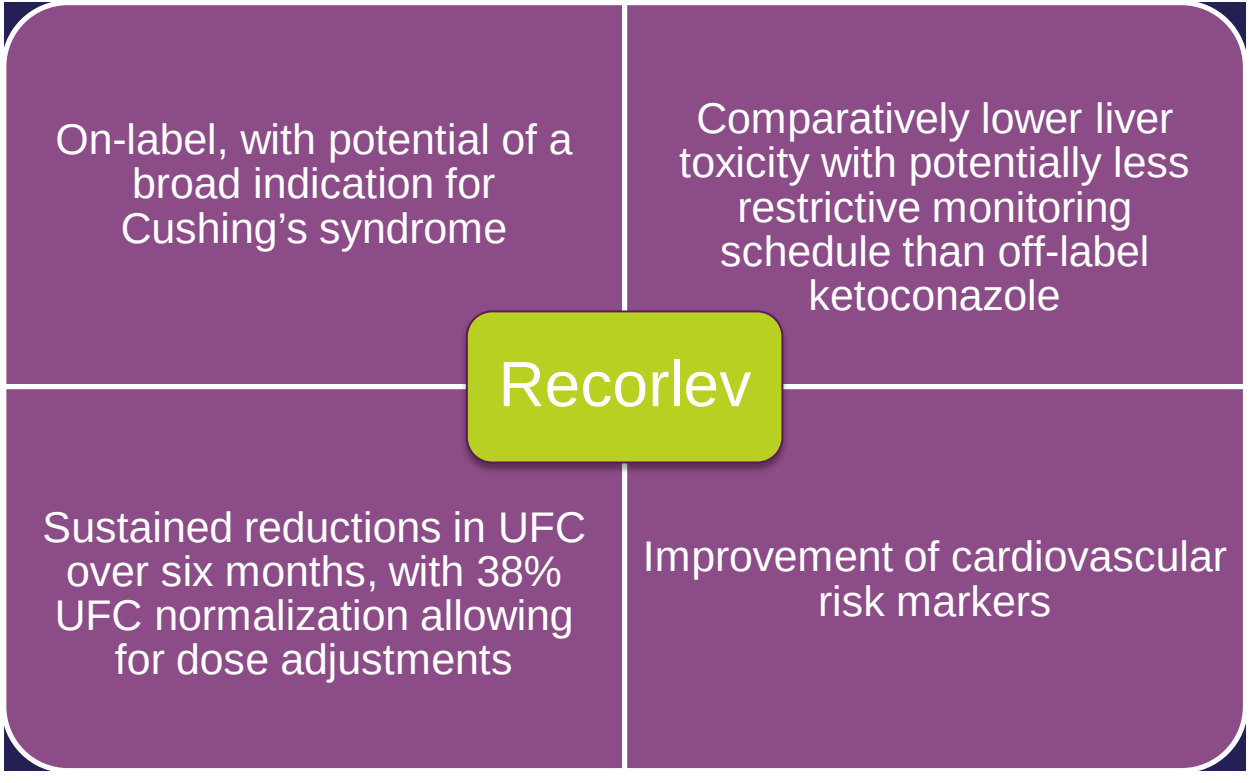
No effect on hypertension or cholesterol

Adverse Reactions

Vaginal bleeding, Adrenal Insufficiency, Hypokalemia

Black Box Warning

Recorlev: Potentially differentiated product profile



Phase 3 Recorlev clinical program

SONICS — Open label; 94 patients enrolled

DOSE TITRATION: 2 to 21 weeks → **MAINTENANCE:** 6 months → **EXTENDED EVALUATION:** 6 months

- Titrate in 150 mg increments up to max 600 mg 2x daily **until UFC normalization is achieved**
- Maintain UFC normalization with fixed therapeutic dose
- **Primary endpoint UFC level measured**

LOGICS — Randomized withdrawal; 54 randomized patient target

LEVOKETOCONAZOLE-NAÏVE-ONLY DOSE TITRATION: 14 to 19 weeks

- **SONICS-completers enter at Randomized Withdrawal**

RANDOMIZED WITHDRAWAL: (Active)

RANDOMIZED WITHDRAWAL: (Placebo)

RESTORATION PHASE

- **Primary endpoint responder rate**

Up to 19 weeks

Both are pivotal trials to support FDA regulatory submission for approval

OPTICS

Open-label extension *

* OPTICS is not intended as pivotal trial

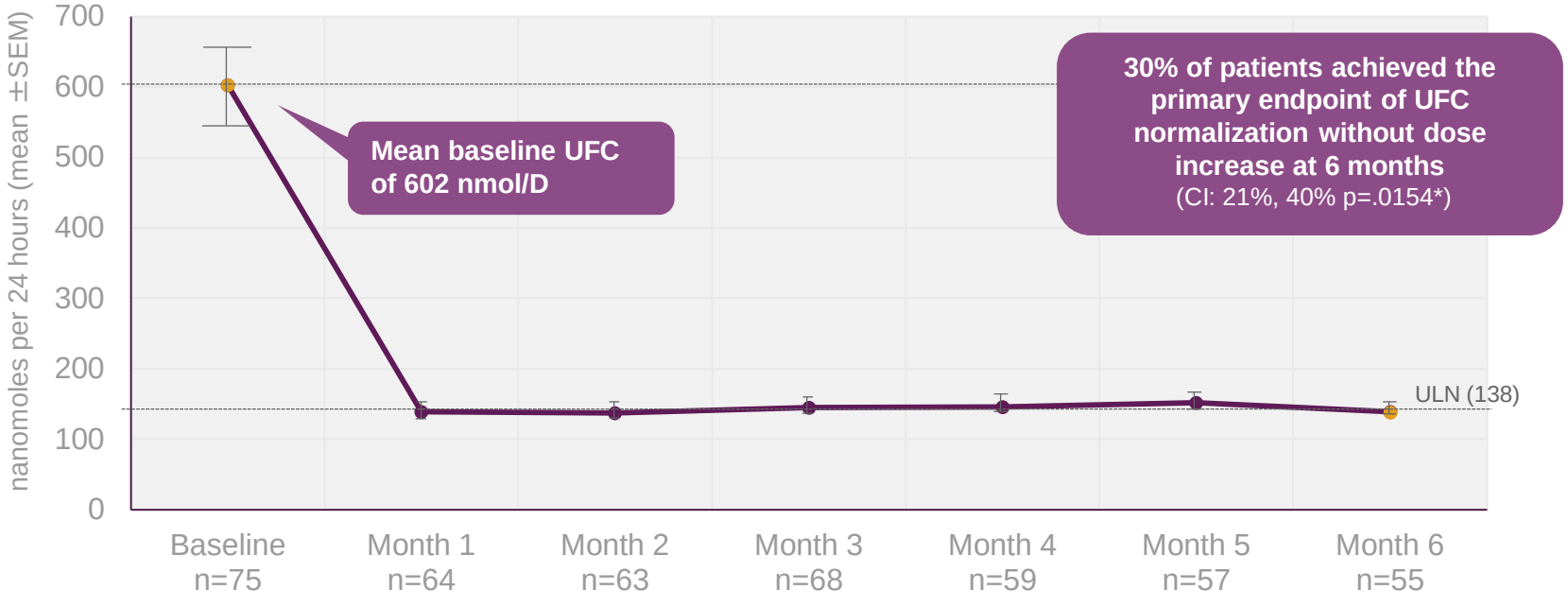
SONICS patient demographics & enrollment

Baseline Characteristic	(N=94)
Age	44 years (mean) 18-75 years (range)
Sex	82% female, 49% with childbearing potential
Body Mass Index	29 kg/m2 (median)
Pituitary source of Hypercortisolism	85%
Diagnosis of Diabetes	38%
Diagnosis of Hypertension	71%
Diagnosis of Hypercholesterolemia	36%
Baseline UFC (multiple of ULN)	Median 3.0; Mean 4.9

94 patients enrolled → **77 of 94 patients completed dose titration** → **61 of 94 patients completed maintenance**

SONICS trial achieved primary endpoint

Sustained reduction in mean UFC for six months after dose titration



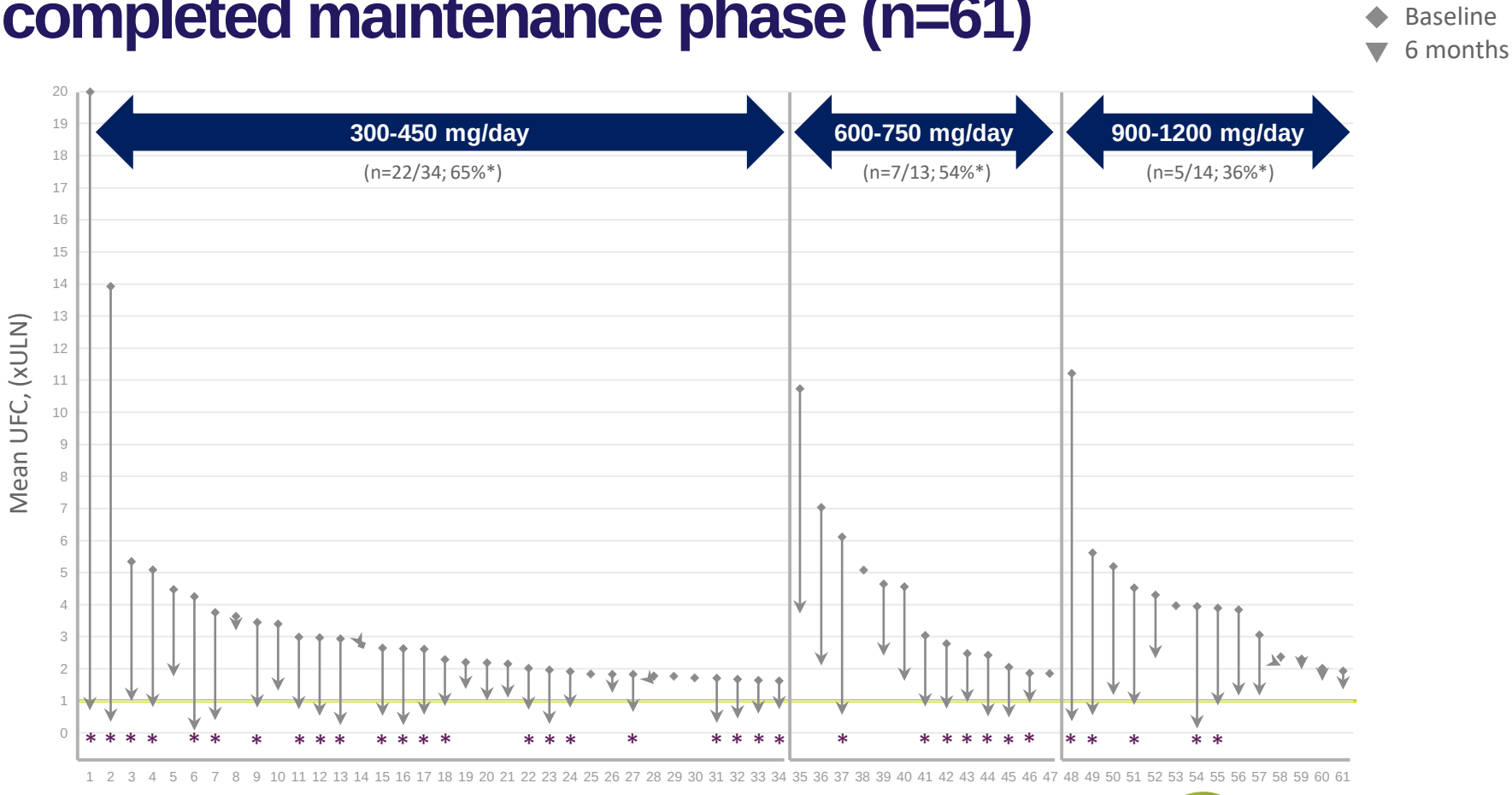
* 1-sided vs. null hypothesis of 20% or lower rate

UFC Responder Analysis At End Of Maintenance Phase

	N=94
Primary endpoint of UFC normalization without dose increase	**30%*, CI: 21%, 40% p=.0154**
Sensitivity analysis of the primary endpoint (UFC normalization regardless of dose increase)	38%*†, CI: 28%, 49%
Analysis of observed rate at month 6 with imputation for missing UFC after month 3	42%‡, CI: 32%, 53%
≥50% UFC decrease or normalization, regardless of dose increase	48%*†, CI: 37%, 58%
Maintenance completers with UFC data and ≥50% UFC reduction from baseline	76% (42/55) **

* Analyses were based on mixed-effects, repeated measures model with an underlying binomial distribution and a logit link function and adjusting for baseline covariates. Estimates of the response and the associated the 95% Confidence Intervals (CIs) and the one-sided p-value (for the primary analysis only) are presented.
† This analysis had the additional imputation step of imputing normalization for missing a missing value at end of maintenance phase, if the subject also had normalization at the preceding and following visits.
‡ The CI is from the Clopper-Pearson two-sided 95% CI for the one-sample binomial proportion.
** Data based on 55 maintenance phase completers with both baseline and month 6 UFC data available.

UFC response by patient for each patient who completed maintenance phase (n=61)



*Refers to proportion of subjects in each dose category achieving mUFC normalization in month 6 of maintenance phase regardless of need for dose increase.

SONICS achieved statistical significance in key secondary endpoints

Outcome Measure at End of Maintenance Phase	Baseline Mean, (n)	Mean Change From Baseline†, (n)	Adjusted* p-value of reductions from Baseline
Fasting Blood Glucose	5.8 mmol/L, (76)	-0.7, (50)	<0.0001
Hemoglobin A1c	6.0%, (77)	-0.4, (55)	<0.0001
Total cholesterol	5.7 mmol/L, (77)	-1.1, (53)	<0.0001
LDL-cholesterol	3.3 mmol/L, (77)	-1.0, (53)	<0.0001
HDL-cholesterol	1.6 mmol/L, (77)	-0.2, (53)	<0.0001
Body Weight	82.1 kg, (77)	-5.1, (54)	<0.0001

*Hochberg adjustment applied to p-values to control type 1 error; reductions from baseline based on least squares mean changes from repeated measures model.

No statistically significant mean changes observed in blood pressure or c-reactive protein; small but statistically significant mean decrease observed in HDL-c.

Most common reported AEs (>=15%, both phases combined)

Adverse Event	Subjects ≥ 1 AE	% of enrolled (N=94)
Nausea	30	32%
Headache	26	28%
Peripheral edema	18	19%
Hypertension	16	17%
Fatigue	15	16%
Diarrhea	14	15%
ALT increased*	14	15%

Adverse Events of Special Interest
Liver-related (7%)
QTc prolongation (5%)
Adrenal insufficiency (3%)

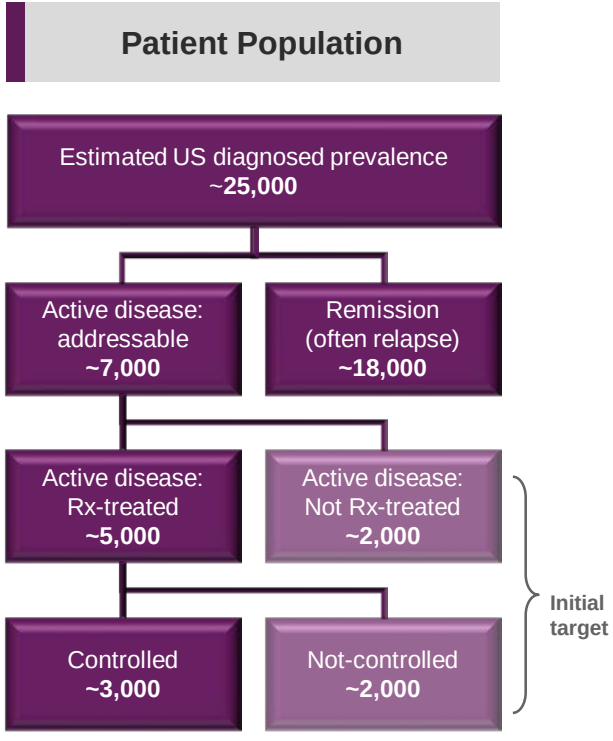
*Includes all alanine aminotransferase (ALT) increases reported as an adverse event regardless of level or relationship to drug. A subset of these ALT increased events was also reported as adverse events of special interest.

Liver data and anticipated labelling

	Recorlev	Signifor LAR*
ALT >3X ULN (includes those > 5x ULN)	10.6%	14%
ALT >5x ULN	3.2%	5%
Total bilirubin values > 1.5x ULN	0%	NA
Liver warning & precautions	TBD	Yes (but no black box)
Known or expected monitoring	Monitoring at least once every two weeks during dose titration. Monthly monitoring for six months after the therapeutic dose is established; then every three months thereafter.	At least once prior to treatment and again after the first two-to-three weeks of treatment; then monthly for three months.

* Signifor LAR Prescribing Information

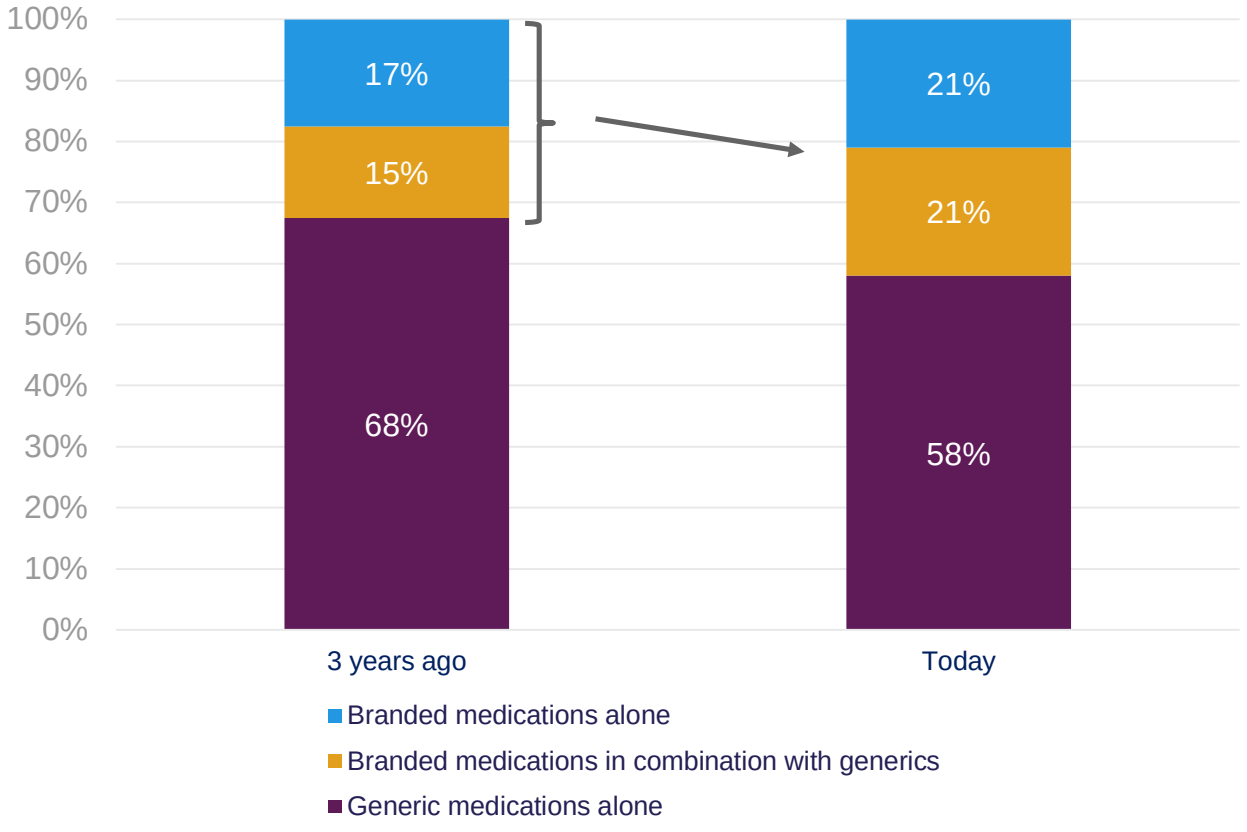
Recorlev U.S. Commercial Opportunity



- SONICS data may support Recorlev launch strategy of positioning for both:
  - Drug-naïve patients, as first-line drug treatment
  - Patients on other drugs, including approximately 2,000 off-label ketoconazole patients
- Recorlev profile supports pricing in the currently established Cushing's syndrome drug pricing corridor of ~$200K-$400K annually
  - Current FDA-approved drugs for Cushing's syndrome are not managed by payers – little-to-no use of fail first / step edits
- Ongoing Macrilen / endocrinology presence may accelerate Recorlev time to peak penetration

Source: Company-sponsored research

Use of branded options gaining momentum in Cushing's syndrome



Based on Strongbridge Biopharma survey of 144 Endocrinologists in the U.S. who manage Cushing's syndrome patients

Recorlev upcoming milestones

- Type C meeting to discuss NDA filing strategy by end of Q1 2019

- Additional SONICS data to be reported at upcoming medical meetings
  - ICE – December 1-4, 2018
  - Pituitary Society – March 20-22, 2019
  - Endocrine Society – March 23-26, 2019
  - AACE – April 24-28, 2019

- SONICS top-line, one-year open label safety and tolerability data expected H1 2019

- LOGICS top-line data expected Q4 2019

Macrilen

(macimorelin)

The first and only FDA-approved oral drug for diagnosing adult growth hormone deficiency

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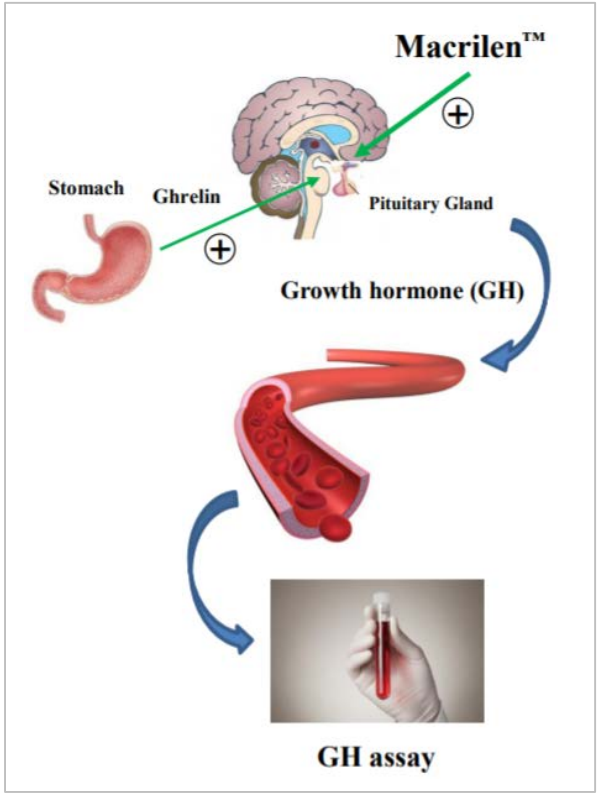
Macrilen

Macrilen is an oral ghrelin receptor agonist (secretagogue) administered to stimulate growth hormone production

FDA approval in December 2017 for use in the diagnosis of patients with AGHD

Strongbridge acquired U.S. and Canadian rights in January 2018 and launched Macrilen in the United States in July 2018

Strongbridge announced sale of US and Canadian rights to Novo Nordisk for $145M upfront and tiered royalties. Transaction expected to close in December 2018.



Novo Nordisk transactions
Acquisition of Macrilen and investment in Strongbridge equity

DEAL TERMS*	
Upfront Cash Payment	$145 million from Novo Nordisk for U.S. and Canadian rights to MACRILEN
Royalty	Strongbridge will receive tiered royalties related to sales of MACRILEN through 2027
Strongbridge Endocrine Field Force	Novo Nordisk will leverage and fund Strongbridge's 23-person rare endocrine commercial field organization for up to three years
Equity Investment	Novo Nordisk will purchase approximately 5.2 million ordinary shares of Strongbridge at a purchase price of $7.00 per share.

*Closing of transactions with Novo Nordisk expected in December 2018

Veldoreotide Extended Release

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Veldoreotide History and Next Steps

2015-2018	2019-2020
Created long-acting formulation, generated IP resulting in new U.S. patent issuance in Aug 2018, and confirmed somatostatin receptor (SST) differentiation	Exploratory non-clinical work aimed at proving the potential clinical value of the SST profile

PLGA microspheres

SST	Inhibition of	Octreotide	Lanreotide	Pasireotide	veldoreotide
1		Low / No	Low / No	High	Low / No
2	GH, Glucagon, Gastric acid	Very High	Very High	High	High
3		High	Medium	High	Low / No
4	GH	Low / No	Low / No	Low / No	High
5	GH, Insulin, Amylase	High	High	Very High	High

IC50 Range (nmol/l)	Very High	High	Medium	Low/No
	< 1	1 - 10	10 - 100	100 +

Adapted from data in M Afargan et al, Endocrinology Vo. 142 (2000); Y Patel, Frontiers in Neuroendocrinology 20, 157-198 (1999); I Shimon et al, J. Clin. Invest. Vol. 100, No. 9 (Nov. 1997); H Schmid et al., J. Endocrinology (2012) 212, 413-20

Keveyis

(dichlorphenamide)

The first and only FDA-approved therapy for primary periodic paralysis*

* FDA-approved treatment for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis

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Primary periodic paralysis: a spectrum of rare, chronic, genetic, neuromuscular disorders

PPP	Symptoms/triggers	Impact of attacks	Frequency
Causes recurrent, progressive, and debilitating episodes of muscle weakness and temporary paralysis[2-4]	Symptoms: clumsiness, extreme fatigue, weakness, palpitations, pain Triggers: may include potassium, carbohydrates, rest after exercise, cold exposure, stress	Paralytic attacks are acute episodes that can be debilitating[4] Attacks may last from one hour to several days[1] As patients age, muscle weakness can become permanent[3]	**59%** have **weekly** attacks **28%** have **daily** attacks

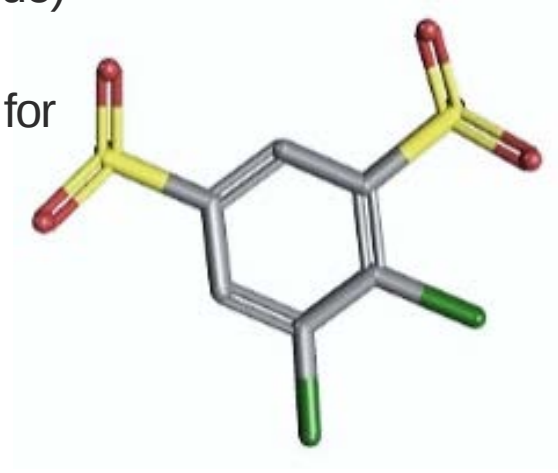
Sources: 1. Charles G, Zheng C, Lehmann-Horn F, Jurkatt-Rott, Levitt J. Characterization of hyperkalemic periodic paralysis: a survey of genetically diagnosed individuals. *J Neurol*. 2013;260:2606-2613. 2. Cannon SC. Channelopathies of skeletal muscle excitability. *Compr Physiol.* 2015;5:761-790. 3. Cavel-Greant D, Lehmann-Horn F, Jurkat-Rott K. The impact of permanent muscle weakness on quality of life in periodic paralysis: a survey of 66 patients. *Acta Myol.* 2012;31:126-133. 4. Sansone V, Meola G, Links TP, Panzeri M, Rose MR. Treatment for periodic paralysis. *Cochrane Database Syst Rev.* 2008; Jan 23;(1):CD005045.

Estimated 4,000 – 5,000 diagnosed U.S. patients

* Based on Strongbridge analysis of medical claims database. Identified patients were required to have medical activity of any type in the last 12-36 months.

Keveyis Overview

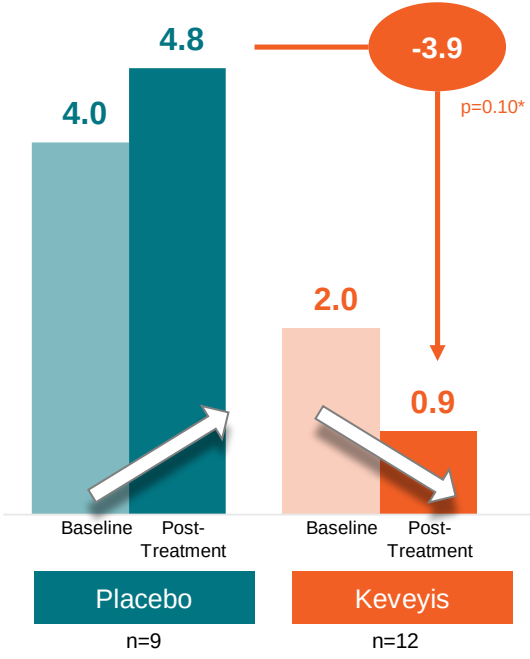
- Strongbridge acquired U.S. rights to Keveyis® (dichlorphenamide) in December 2016 and launched in April 2017
- Keveyis is the **first and only** FDA-approved therapy indicated for the treatment of:
  - Primary hyperkalemic periodic paralysis
  - Primary hypokalemic periodic paralysis
  - Related variants
- Twice-daily dosing in an oral tablet formulation
  - Starting dose is 50 mg 2X daily-- can be titrated up to 100 mg 2X daily
- From 2002 to 2015, dichlorphenamide was not available the U.S.
  - Taro bought the rights in 2007, developed it, received Fast Track designation, and received FDA approval in August 2015 with Orphan Drug regulatory exclusivity through August 2022



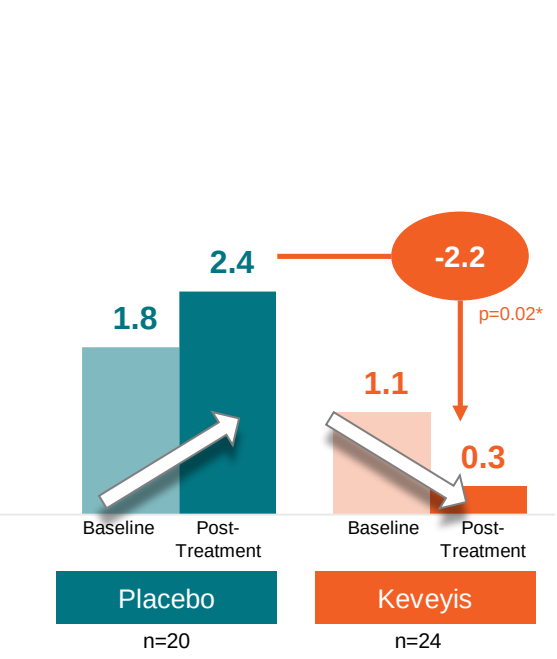
Treatment With Keveyis Decreased Weekly Attack Rates

Study 1: decreased weekly attack rates from baseline to week 9

Hyperkalemic



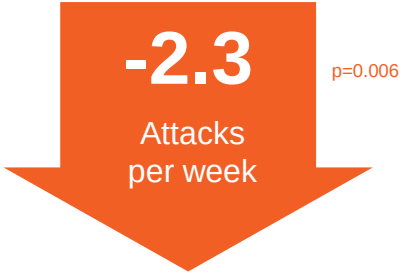
Hypokalemic



Study 2

Hyperkalemic

Mean decrease in attack rates relative to placebo



Mean weekly attack rate at baseline was 3.8 (n=31)

Study 1: Sansone VA, et al. Neurology 2016;86:1408-1416
Study 2: Tawil R, et al. Ann Nuerol. 2000; 47:46-53.

*Treatment effects (DCP-placebo) are computed as the median of the bootstrap distribution of the treatment group difference in median response

Safety and tolerability

Adverse reactions (≥5% and more common than in patients treated with placebo in Study 1)

	Adverse Reaction	Keveyis n=36 (%)	Placebo n=29 (%)
Nervous system disorders	Paresthesia	44	14
	Cognitive disorder	14	7
	Dysgeusia	14	0
	Confusional state	11	0
	Headache	8	7
	Hypoesthesia	8	0
	Lethargy	8	0
	Dizziness	6	0
Gastrointestinal disorders	Diarrhea	6	3
	Nausea	6	0
General disorders and administration site conditions	Fatigue	8	0
	Malaise	6	0
Investigations	Weight decreased	6	0
Musculoskeletal and connective tissue disorders	Muscle spasms	8	0
	Arthralgia	6	3
	Muscle twitching	6	0
Respiratory	Dyspnea	6	0
	Pharyngolaryngeal pain	6	0
Skin	Rash	8	0
	Pruritus	6	0

KEVEYIS prescribing information.

Strategic priorities & revenue guidance

- Continue to organize and construct the market
- Focus commercial investment to accelerate pathway to profitability
- Pursue life cycle opportunities to extend exclusivity runway beyond 2022
- 2018 revenue guidance: $16-17M

Drivers and enablers for revenue growth

Patient Identification	Convert to Therapy	Maintain on Therapy
Refine data analytics and physician targeting	Educate physicians / patients on clinical value and treatment expectations	
Leverage social media across multiple channels	Leverage CareConnections by increasing patient / physician communication during first 30 days of therapy	
Ongoing Patient Advocacy Support	Connect patients to helpful resources such as our PPP MentorConnect program	

About Strongbridge

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Intellectual property and orphan exclusivity

	IP		Orphan exclusivity	
	US	EU	US	EU
Macrilen	2022 Composition of Matter 2027 Method of use	US and Canadian rights only	Dec 2024	US and Canadian rights only
Recorlev	2030 Method of use: reducing CRP levels and systemic inflammation 2026 Method of use: treating Cushing's syndrome	2026 Method of use: treating Cushing's syndrome	7 years	10 years
Veldoreotide	2037 Formulation	Filed patent application for novel formulation	7 years	10 years
Keveyis	Exploring options	US rights only	Aug 2022	US rights only

Key Objectives Driving Value

Recorlev	• FDA Type C meeting (Q1 2019) • LOGICS topline data (Q4 2019) • SONICS data presentations (through H1 2019)
Keveyis	• Grow revenue-- continue to organize and construct the market • Focus commercial investment • Continue exploring life cycle opportunities
Macrilen	• Seamless transition of Macrilen to Novo Nordisk • Collaborate commercially to accelerate growth
Corporate	• Evaluate additional late-stage or commercial rare disease assets