Strongbridge Biopharma plc

May 2018

STRONGBRIDGE BIOPHARMA

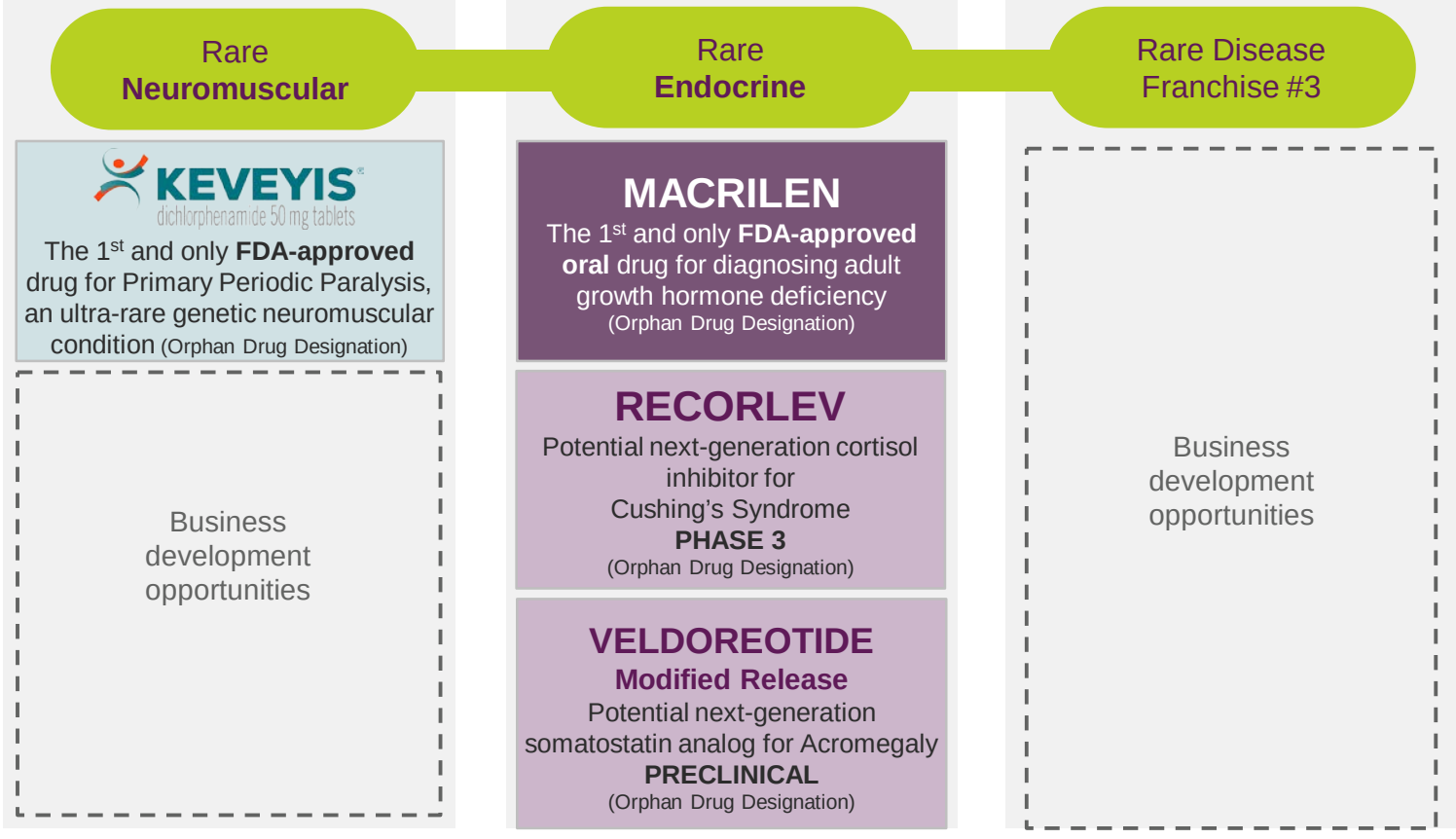
Forward-looking statements

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, 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.

Strongbridge Biopharma plc: Building a portfolio of therapeutically-aligned vertical franchises in rare diseases



The management team is highly experienced in managing orphan and ultra-rare disease assets

Matthew Pauls President, CEO, Director	Shire, Johnson & Johnson, Bristol-Myers Squibb, Insmed
Fred Cohen, M.D. Chief Medical Officer	Aptalis, Johnson & Johnson, Eurand, Lilly
Brian Davis Chief Financial Officer	tengion, NEOSE
Stephen Long Chief Legal Officer	ReedSmith, BARD, Warner Lambert
Robert Lutz Chief Business Officer	Shire, medgenics, Goldman Sachs
Dave Bonnell SVP Sales & Marketing	Shire, AstraZeneca, Schering-Plough
Peter Valentinsson SVP, Global Technical Operations	NPS Pharma, Schering-Plough
Scott L. Wilhoit SVP, Global Market Access & Patient Services	NPS Pharma, Johnson & Johnson, PTC, Marathon, Auxilium

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

Causes recurrent, progressive, and debilitating episodes of muscle weakness and temporary paralysis[2-4]

~4-5k
patients in the U.S. [5]

Symptoms/triggers

Symptoms: clumsiness, extreme fatigue, weakness, palpitations, pain

Triggers: may include potassium, carbohydrates, rest after exercise, cold exposure, stress

Impact of attacks

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]

Frequency

59%
have **weekly** attacks

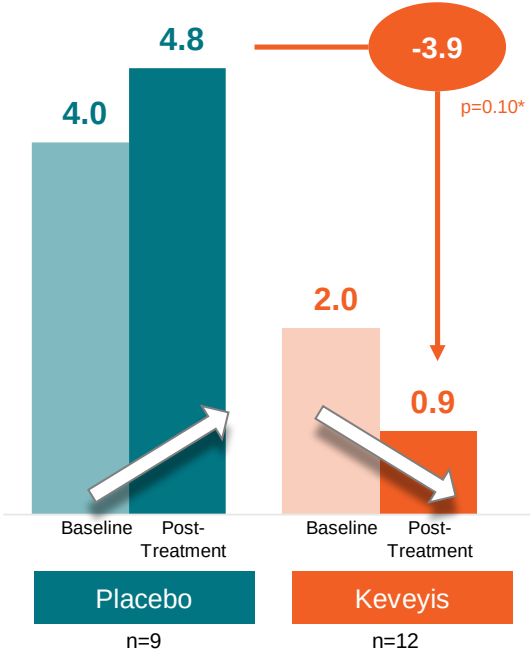
28%
have **daily** attacks

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. 5. Based on Strongbridge Biopharma analysis of medical claims database

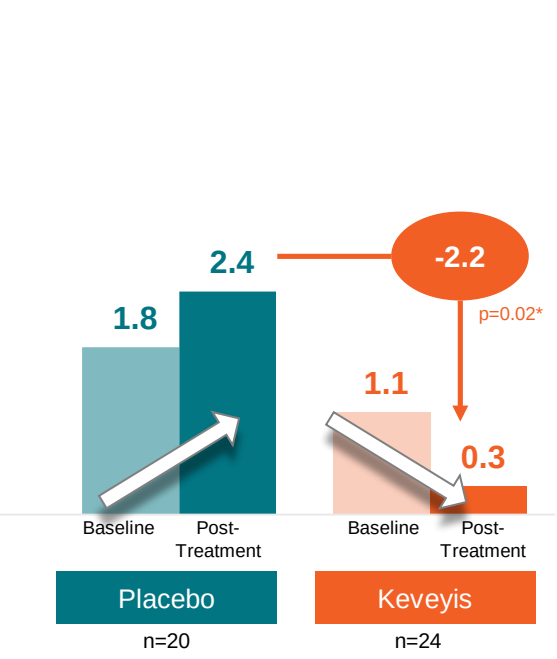
Treatment with Keveyis decreased weekly attack rates

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

Hyperkalemic



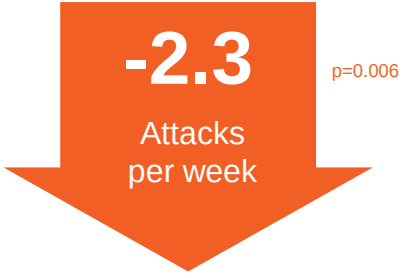
Hypokalemic



Study 2

Hyperkalemic

Mean decrease in attack rates relative to placebo



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

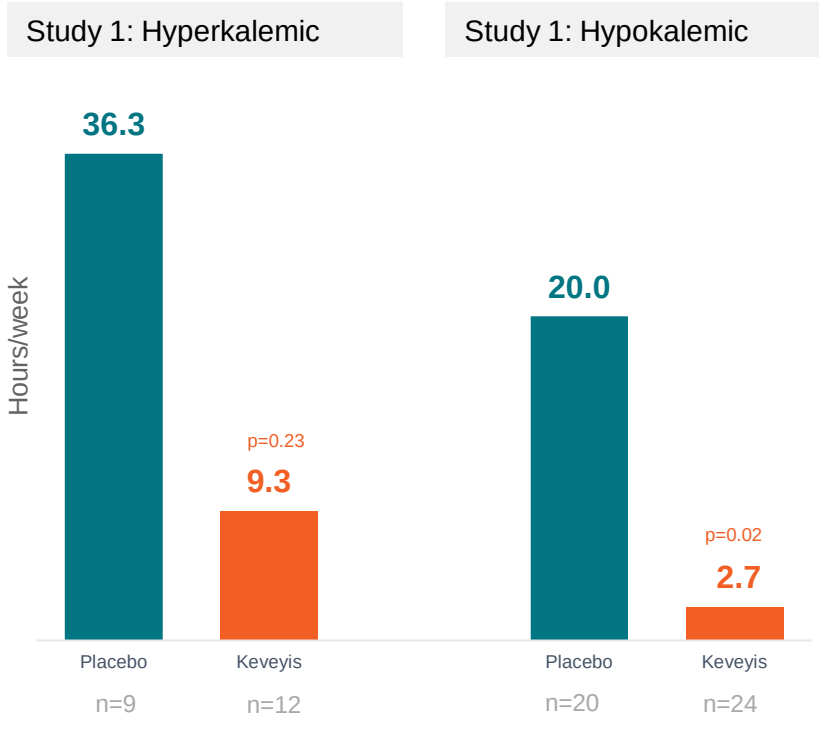
Study 1: Sansone VA, et al. Neurology 2016;86:1408-1416
Study 2: Tawil R, et al. Ann Nuerol. 2000; 47:46-53.

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

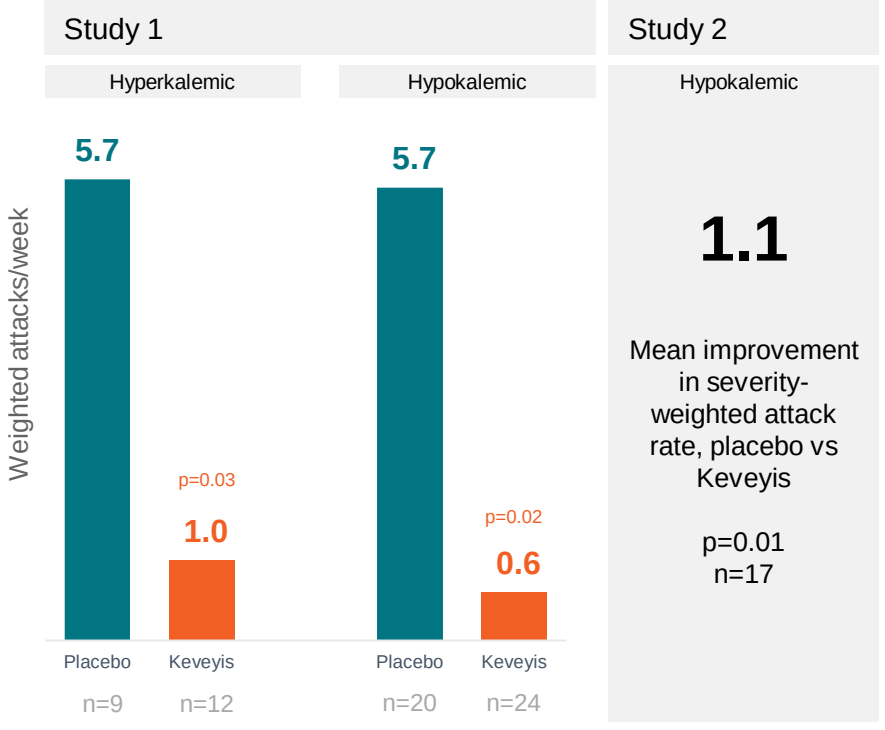
Reduced duration of weekly attacks and decreased attack severity

Average values for each group over weeks 2-9

Decreased weekly attack duration



Decreased severity-weighted attack rate



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

Secondary EPs in Study 1

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.

Keveyis 2017 performance highlights & 2018 revenue guidance

2017 FY actual	**2018 Q1** actual	**2018 FY** guidance
$7m	$3.9m	$18-20m

Macrilen

(macimorelin)

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

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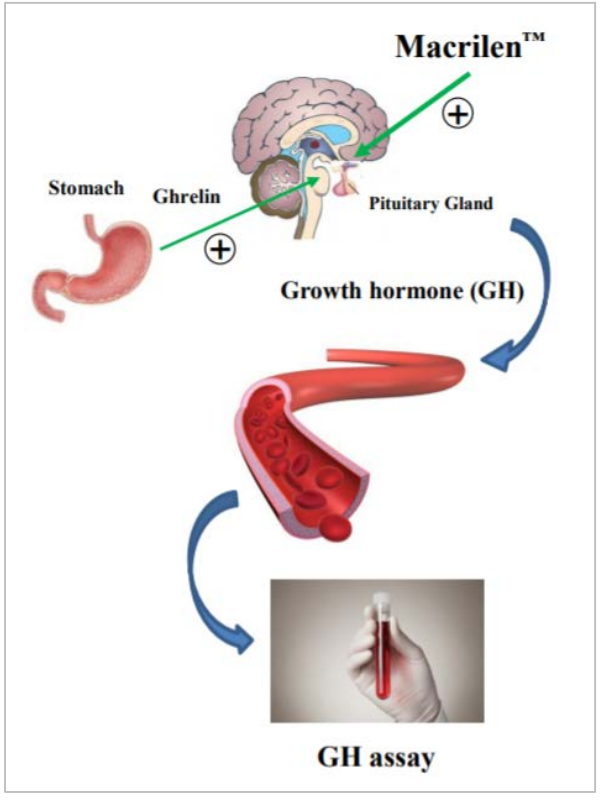
Macrilen summary

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

Significant convenience and tolerability advantage when compared to current assessments

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

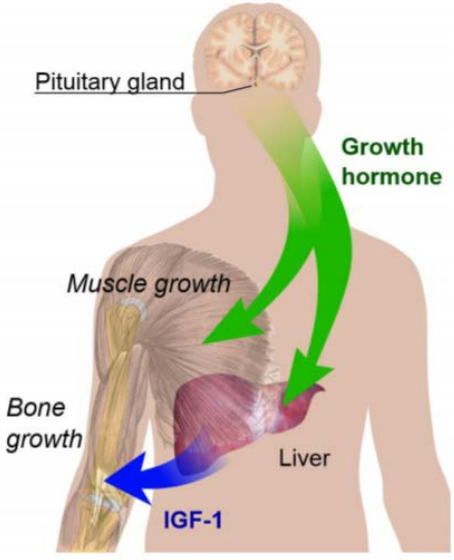
Strongbridge acquired U.S. and Canadian rights in January 2018 with U.S. launch anticipated in July-2018



Adult growth hormone deficiency (AGHD)

Symptoms

- **Body composition altered:**
  - Increased fat mass
  - Decreased lean body mass
  - Reduced skeletal muscle strength
- **Cardiovascular (CV) issues**:
  - Increased risk of CV death
  - Abnormal lipids, other risk markers
- **Bone mineral density**
  Increased fracture rate
- **Overall:**
  - Decrease quality of life
  - Low physical/mental energy



Häggström, Mikael.
"Medical gallery of Mikael Häggström 2014". *Wikiversity Journal of Medicine* **1** (2).

Causes

- **Tumors**
- **Surgery**
- **Cranial radiation**
- **Infectious / inflammatory**
- **Trauma / vascular injury**
- **Childhood onset**

Growth hormone treatment has been shown in clinical trials to improve health for adults with GHD

Macrilen: The 1st and only FDA-approved oral drug for diagnosing adult growth hormone deficiency (AGHD)

Preferred route of administration	✓	Oral (Macrilen) versus IV (ITT) and IM (GST)
Less time for patient and office	✓	Macrilen assessment takes on average 1.5 hours as compared to 3-4 hours for GST and 2 hours for ITT
Fewer blood draws	✓	4 for Macrilen versus 6 for ITT and 9 for GST
Better safety profile	✓	ITT has been shown to induce hypoglycemia and therefore requires direct physician oversight and proximity to a crash cart
Improved tolerability	✓	Macrilen had far fewer adverse events than ITT in the Phase III study
No contraindications	✓	None in the label for Macrilen
Greater evaluability	✓	Macrilen showed improved evaluability compared to ITT
FDA-approved	✓	ITT and GST are not FDA-approved

Macrilen accurately diagnoses AGHD: comparison to ITT

Results from an open-label, ITT-controlled, 2-way , randomized crossover study

Insulin Tolerance Test (ITT)
(GH cutoff 5.1 ng/mL)

Macrilen (GH cutoff 2.8 ng/mL)	Positive	Negative	Total Tests
Positive	55	4	59
Negative	19	62	81
Total	74	66	140
AGREEMENT	74%*	94%*	84%

- Positive agreement higher (89%) for high-risk AGHD category
- Negative agreement 86-94%
- Labeling reflective of overall and risk-stratified agreements
- <1% of Macrilen tests were not evaluable vs. 17% of ITTs
- Macrilen was highly reproducible (91%) in the same patient

Negative Agreement: 93.94% (CI: 85.20%, 98.32%)- Met pre-defined performance criterion (i.e. excluded negative agreement with ITT of less than 75% with 95% confidence), Positive Agreement: 74.32% (CI: 62.84%, 83.78%)- Did not meet pre-defined performance criterion (i.e. could not exclude positive agreement with ITT of less than 70% with 95% confidence)

* Co-Primary efficacy endpoints; a positive test is one that fails to reach the respective test's GH cutoff

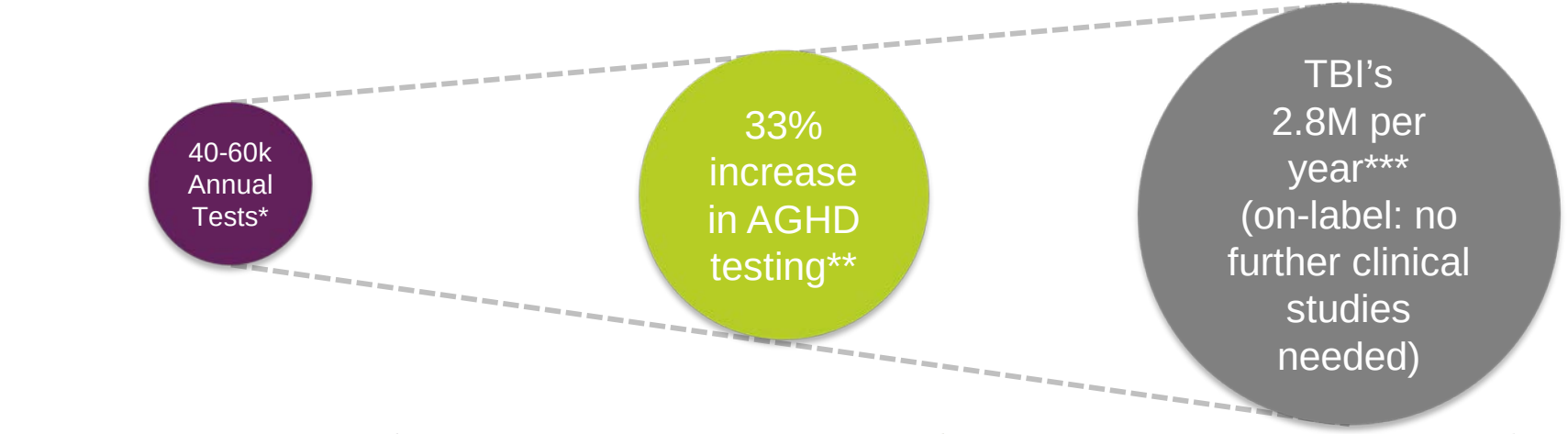
Macrilen Safety Summary

- Macrilen well tolerated as compared to ITT (see table)
- Most common adverse reactions with Macrilen:
  - Dysgeusia (4.5%); dizziness, fatigue, and headache (3.9% each); nausea (3.2%)
  - Most adverse reactions were mild; none severe or led to failure to complete test
- QTc_F upper 90% confidence limit about 11 ms at doses 2x-4x higher than used for GH stimulation (NO hERG inhibition)
  - Concomitant QT-prolonging drugs should be avoided
  - NO need to perform ECG before or after use of Macrilen
- DDI potential: Discontinue strong CYP3A4 inducers (avoids false-positive results)

GHST-emergent adverse events (TEAE)	**Macimorelin** (N=154)			**ITT** (N=157)		
	Frequency[1]	%[2]	N AEs[3]	Frequency[1]	%[2]	N AEs[3]
Any TEAE	39	25.3	77	151	96.2	761
Any likely or possible TEAE	22	14.3	37	149	94.9	710
Any **severe** TEAE	1	0.6	1	11	7	25

[1]: Number of subjects with any GHST-emergent AE, each subject was counted only once within each category
[2]: Number of subjects with any AE / number of all subjects; [3]: Number of all AEs

Macrilen Market Opportunity



- Expected increase in testing for AGHD because of Macrilen

- All patients with moderate to severe traumatic brain injury (TBI) require evaluation of pituitary function.
- Does not include potential 40K pediatric population, which requires clinical studies

*Oppenheimer 2011—manufacturer-sponsored research; Navigant, 2009—manufacturer-sponsored research; Symphony, 2017—manufacturer-sponsored research; TVG Research—manufacturer-sponsored research, 2017; Lumelian, 2017—manufacturer-sponsored research.
**Results of quantitative (n=40 endocrinologists) and qualitative (n=5) market research conducted by a 3rd party sponsored by Strongbridge (2017).
***https://www.cdc.gov/traumaticbraininjury/severe.html.

Many patients are not screened for AGHD due to the complexity, tolerability and safety issues of the current tests

NOT FDA APPROVED

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]

1. Yuen KCJ. South Dartmouth, MA; Endotext [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK395585/. Accessed February 19, 2018.
2. Agrawal V, Garcia JM. The macimorelin-stimulated growth hormone test for adult growth hormone deficiency diagnosis. *Expert Rev Mol Diag.* 2014;14(6):647-654.
3. Leong KS, et al. *Clin Endocrinol.* 2001;54: 463-468.
4. Post-Traumatic Hypopituitarism – Who Should be Screened, When, and How, Mark Quinn and Amar Agha

Both physicians and payers have a positive opinion of Macrilen

Summary Feedback - Prescribers

83%	Somewhat/extremely likely to use Macrilen (based on draft profile)
33%	Expected increase of testing for AGHD because of Macrilen
>50%	Physicians indicated Macrilen would be the majority of 1st line AGHD assessments
>40%	Macrilen share of AGHD assessments

"It would allow me to start testing in my office" - Endocrinologist

Results of quantitative (n=40 endocrinologists) and qualitative (n=5) market research conducted by a third party sponsored by Strongbridge

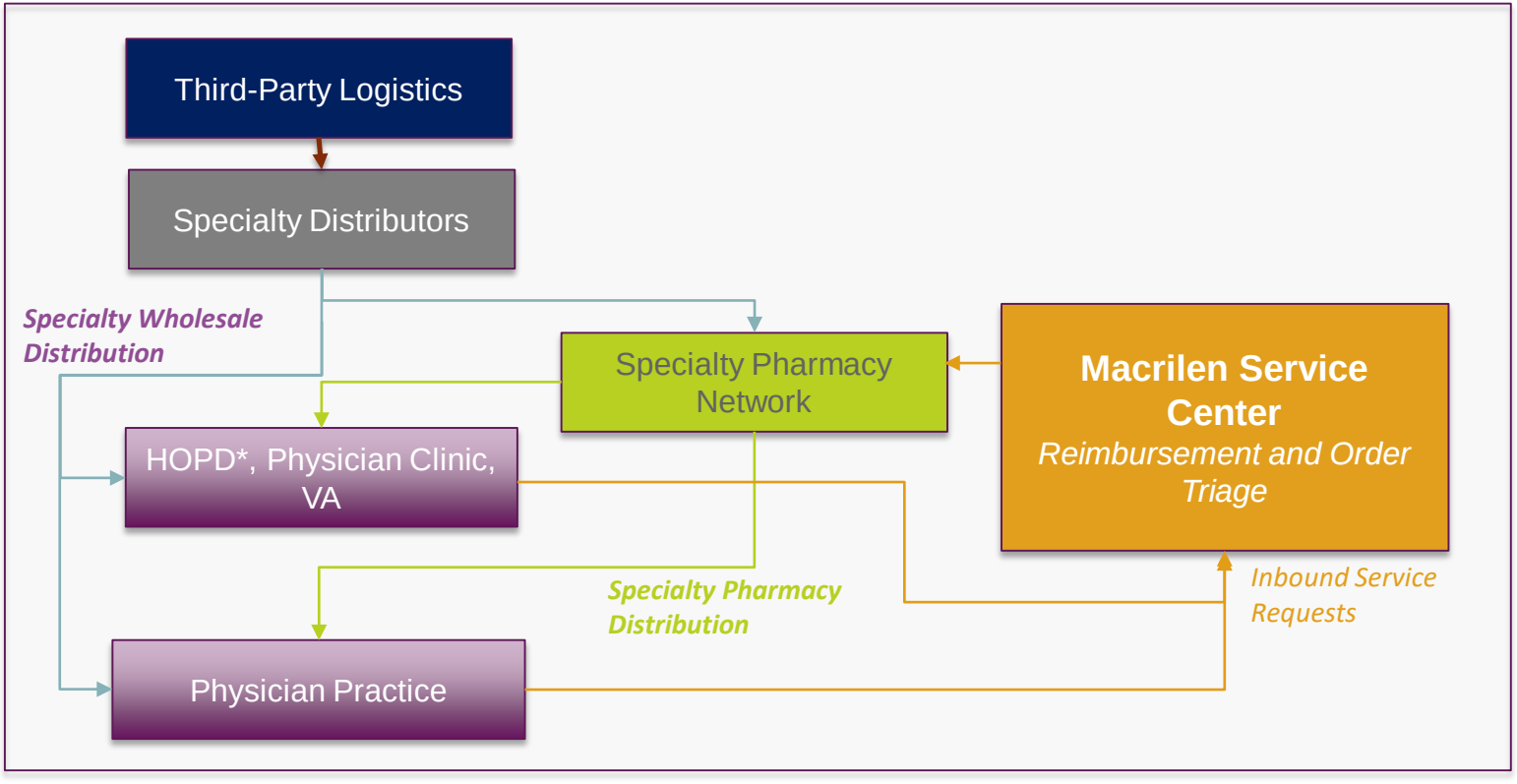
Summary Feedback - Payers

- Macrilen likely to be incorporated into medical policy to help protect payers from paying for costly human growth hormone treatments
- If Macrilen is supported by the Endocrinology/KOL community it would help to support Macrilen inclusion in updated GH testing policies
- Payers suggest that Macrilen may end up on the medical benefit and would be accessible to physicians through a buy and bill model or through specialty pharmacy distribution

"It is well differentiated and could change the practice for GH testing" – Commercial Payer

Results of qualitative (n=10 payers) market research conducted by Strongbridge

Flexible and Scalable Distribution & Services Model



*Hospital Outpatient Department

Recorlev

(levoketoconazole)

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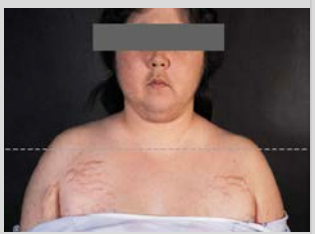
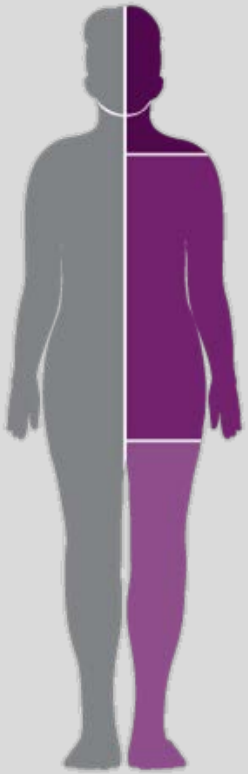
Cushing's syndrome complications and comorbidities





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

Compared to those without Cushing's disease, young patients have:[1*]

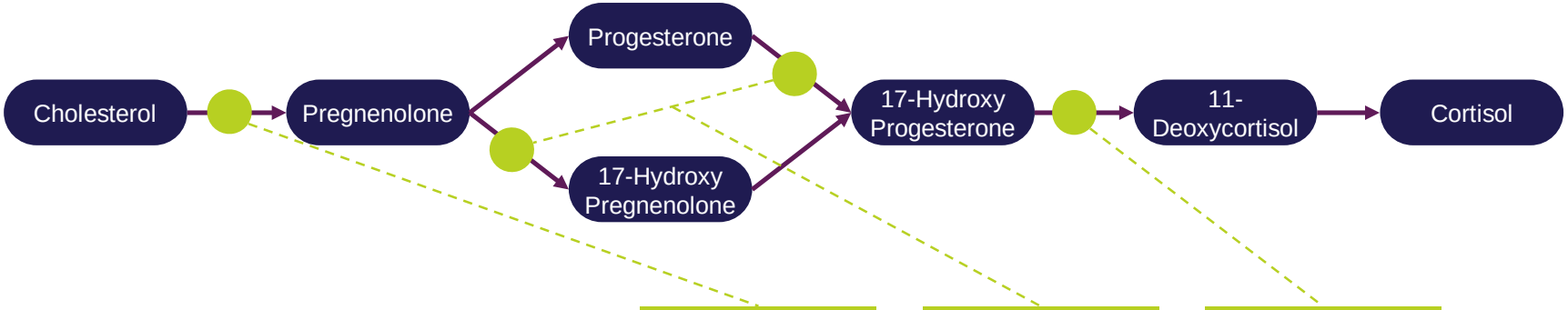
2-5x higher incidence rates of comorbidities (eg, cardiovascular, endocrine, musculoskeletal, and mental health conditions)

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.

Recorlev (levoketoconazole) is the active half of ketoconazole responsible for cortisol synthesis inhibition



	CYP11A1	CYP17A1	CYP11B1	
2R,4S-ketoconazole enantiomer	25,080	596	1,365	10-26x
Ketoconazole, racemate	2,267	58	139	1.6-2.7x
Levoketoconazole*	**1,447**	**28**	**52**	

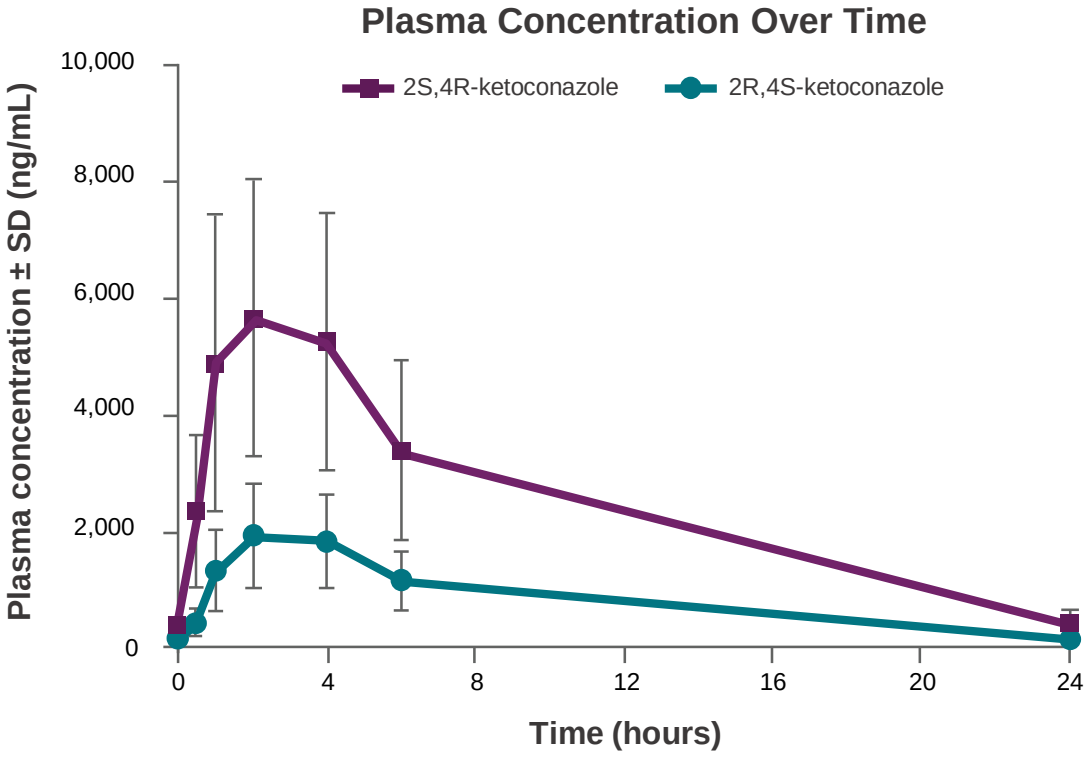
50% inhibitory concentration, nmol/L; lower number indicates greater inhibition potency

Auchus RJ, Wu JL, Peng HM "2S,4R-Ketoconazole is the Relevant Enantiomer of Ketoconazole for Cortisol Synthesis Inhibition: Steroidogenic P450s Inhibition Involves Multiple Mechanisms" Endocrine Society's Annual Meeting. University of Michigan, Chicago, IL. 18, March 2018. Poster presentation.

Recorlev has potential for reduced liver toxicity

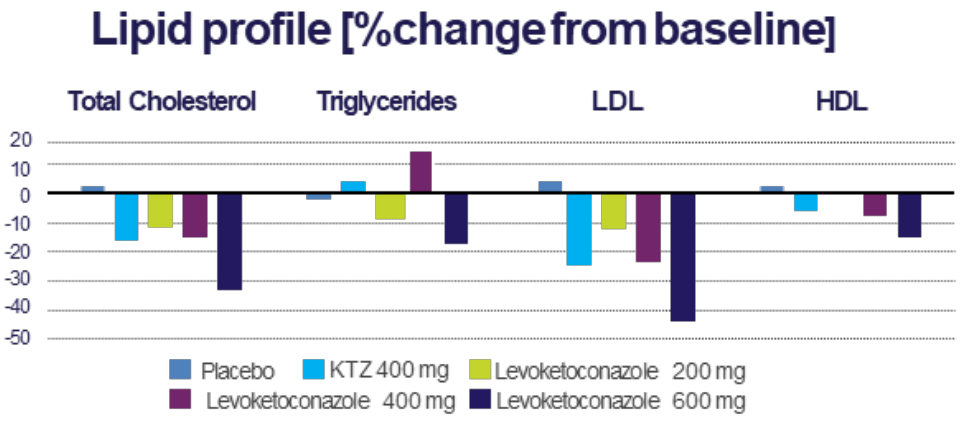
12 times less potent inhibitor of CYP7A, the rate-limiting enzyme for bile acid synthesis

~3 times greater plasma concentration*



*Day 5 data from 24 healthy patients dosed with 400mg KTZ Days 1-4 plus 80mg atorvastatin on Day 5.
Source: Rotstein DM, Kertesz DJ, Keith A. M. Walker, and David C. Swinney. Stereoisomers of ketoconazole: preparation and biological activity. *J Med Chem.* 1992;35(15):2818–2825.

Recorlev rapidly reduces serum lipids in patients with type 2 diabetes



- Cardiovascular disease drives increased mortality in CS and type 2 diabetes and contributes to substantial morbidity in both
- Hyperlipidemia is responsible for some of this increase in cardiovascular risk
- 14 days' treatment with levoketoconazole dose-dependently reduced total cholesterol, LDL-cholesterol and LDL-C/HDL-C ratio in patients without CS who had type 2 diabetes

Data from Study DIO-501: A Phase 1/2a, Randomized, Placebo-Controlled, Double-Blind, Parallel-Group Study of Safety, Tolerability, Pharmacokinetics and Activity of 14 Days of Oral Dosing with [Levoketoconazole] in Subjects with Type 2 Diabetes Mellitus, Clinical Study Report.

Phase 3 Cushing's syndrome clinical program

SONICS 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 Target 35 Patients

SONICS-completers enter at Randomized Withdrawal

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

- **RANDOMIZED WITHDRAWAL: (Active)**
- **RANDOMIZED WITHDRAWAL: (Placebo)**

→ **RESTORATION PHASE**

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.

Sample size & power

- SONICS sample size of 90 subjects yields 90% power, based on excluding a 20% or lower UFC response with 95% confidence
- We estimate that at least 25% of subjects achieving the primary endpoint would likely result in statistical significance at the 5% level
- We believe ~25% UFC response would be considered clinically important if other improvements in signs, symptoms, or comorbidities of Cushing's syndrome are seen

Newly published data: LFT abnormalities with ketoconazole (KTZ)

Castinetti study (2018)[1]

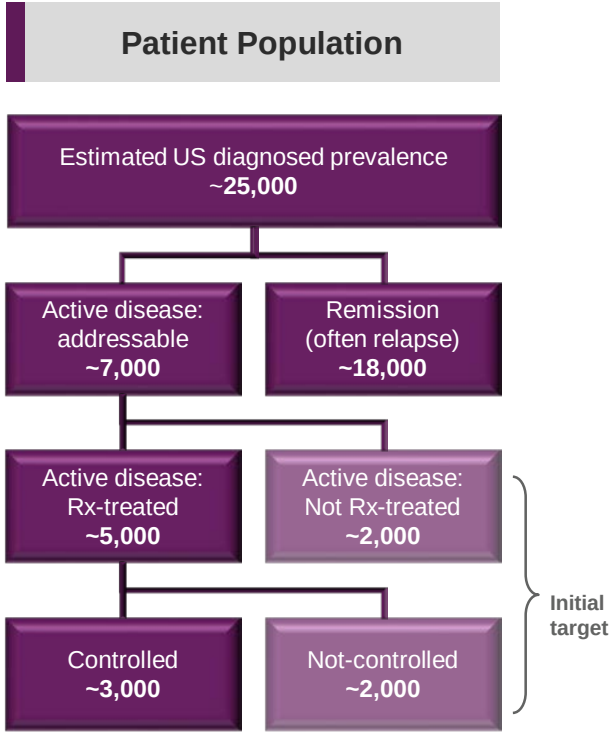
- Based on observational prospective French cohort study (compassionate use program)
  - » 108 treated (47 KTZ-naïve and 61 KTZ continuation)
  - » ~10% of screened population excluded due to liver disease and abnormal liver function tests
- Not a clinical study: did not include protocol, site monitoring, CRFs, etc.

	Naïve to KTZ*	KTZ Continuation†
	32% **at least 1 ALT elevation**	23% **at least 1 ALT elevation**
	19% **<5X ULN**	23% **<5X ULN**
	13% **≥5x ULN**	0% **≥5x ULN**

- Methodological limitations hamper accurate estimation of liver injury risk with KTZ
- We believe that a properly designed and monitored clinical trial of KTZ would yield higher rates of LFT abnormalities than observed thus far

Abbreviations: ALT, alanine aminotransferase; CRF, case report forms; ULN, upper limits of normal.
*No KTZ use in prior 4 weeks; ALT n=31. †Previously using KTZ>6 mos.; ALT n=35.
Source: 1. Young et al. Eur J Endocrinol. 2018 Feb 22. pii: EJE-17-0886. doi: 10.1530/EJE-17-0886. [Epub ahead of print]

Recorlev Commercial Opportunity



- No FDA-approved product with broad Cushing's syndrome indication
- If approved, position Recorlev as first-line, first-choice therapy
- Currently approved therapies priced at ~$200K-500K/patient/year
- Recorlev time to peak sales is potentially earlier due to Macrilen strong strategic fit

Source: Company-sponsored research

Veldoreotide

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Veldoreotide modified release: a novel, multi-receptor somatostatin analog

BACKGROUND

Acquired immediate-release formulation of veldoreotide in 2015 and focused initial R&D on long-acting reformulation

10/2016: Successfully formulated for convenient, at-home, subcutaneous administration using PLGA microspheres

Unique formulation may provide additional IP

Data through Phase IIa: potential differentiated benefits from currently approved somatostatin analogues

- Comparable maximal GH suppression to octreotide
- Reduced impact on gallbladder function, bile acid production, and GI motility in rodents
- Reduced impact on hormonal responses to mixed meals in healthy subjects

SSAs: Somatostatin Analogs

About Strongbridge

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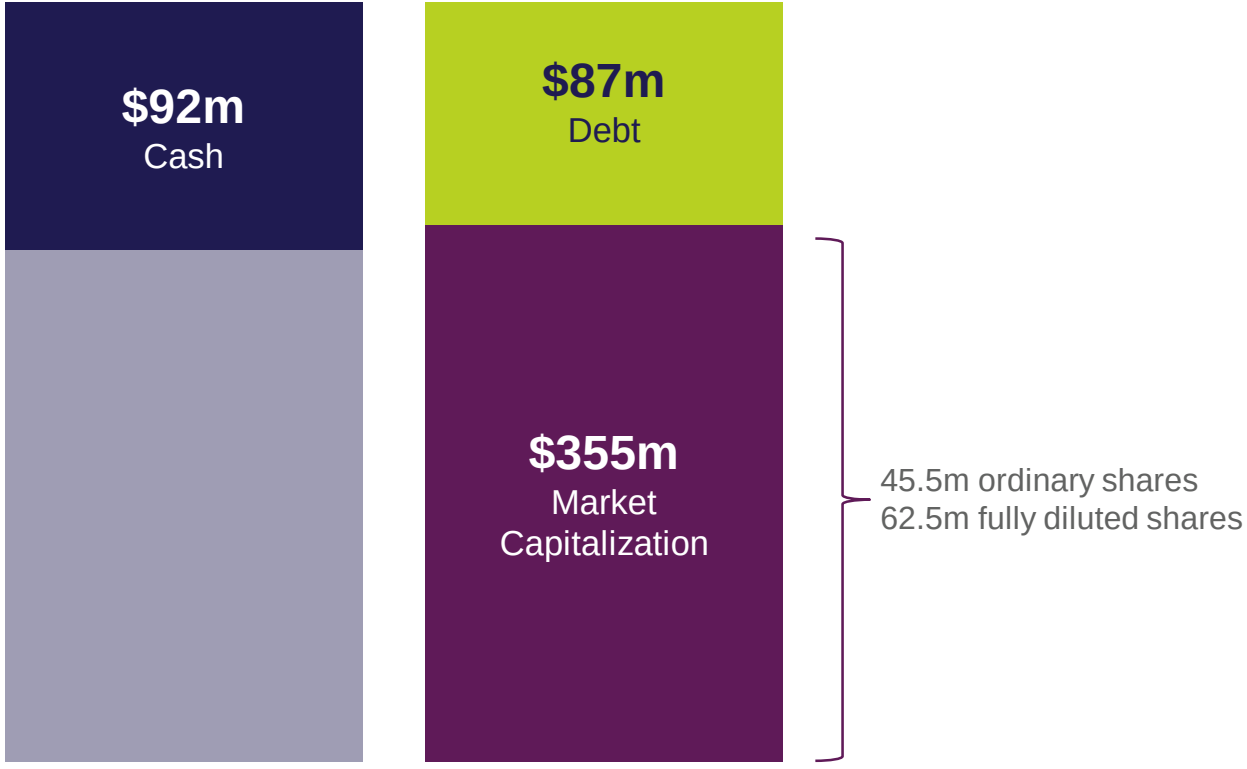
Intellectual property and orphan exclusivity

	IP		Orphan exclusivity	
	US	EU	US	EU
Keveyis	Exploring options	US rights only	Aug 2022	US rights only
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	Filed patent application for novel formulation		7 years	10 years

Strong Balance Sheet to Support Growth Objectives



Sufficiently capitalized with cash and potential additional borrowings to fund operations through Recorlev approval and launch to cash flow positive

Cash, debt and shares as of March 31, 2018. Market capitalization as of May 10, 2018

Anticipated milestones – 2018

	H1	H2
Corporate	Q4 2017 & Q1 2018 earnings	Q2 2018 & Q3 2018 earnings
Keveyis	Quarterly sales updates	Quarterly sales updates
Macrilen	Commercial launch (July 2018)	Quarterly sales updates
Recorlev	**LOGICS** Initiate enrollment (Q1) **SONICS** Topline data (mid-2018)	

Strongbridge Biopharma plc: Building a portfolio of therapeutically-aligned vertical franchises in rare diseases