

Strongbridge Biopharma plc

March 2018

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: A Global Rare Disease Biopharmaceutical Company with a Commercial and Late-Stage Portfolio



FDA-APPROVED

The 1st and only FDA-approved drug for ultra-rare Primary Periodic Paralysis*

ORPHAN

MACRILEN
macimorelin

FDA-APPROVED

The 1st and only FDA-approved oral drug for assessing adult growth hormone deficiency

ORPHAN

Acquired Jan 2018

RECORLEV™
levoketoconazole

PHASE 3

Potential next-generation cortisol inhibitor for Cushing's Syndrome

ORPHAN

Veldoreotide modified-release

PRECLINICAL

Potential next-generation somatostatin analog, Acromegaly

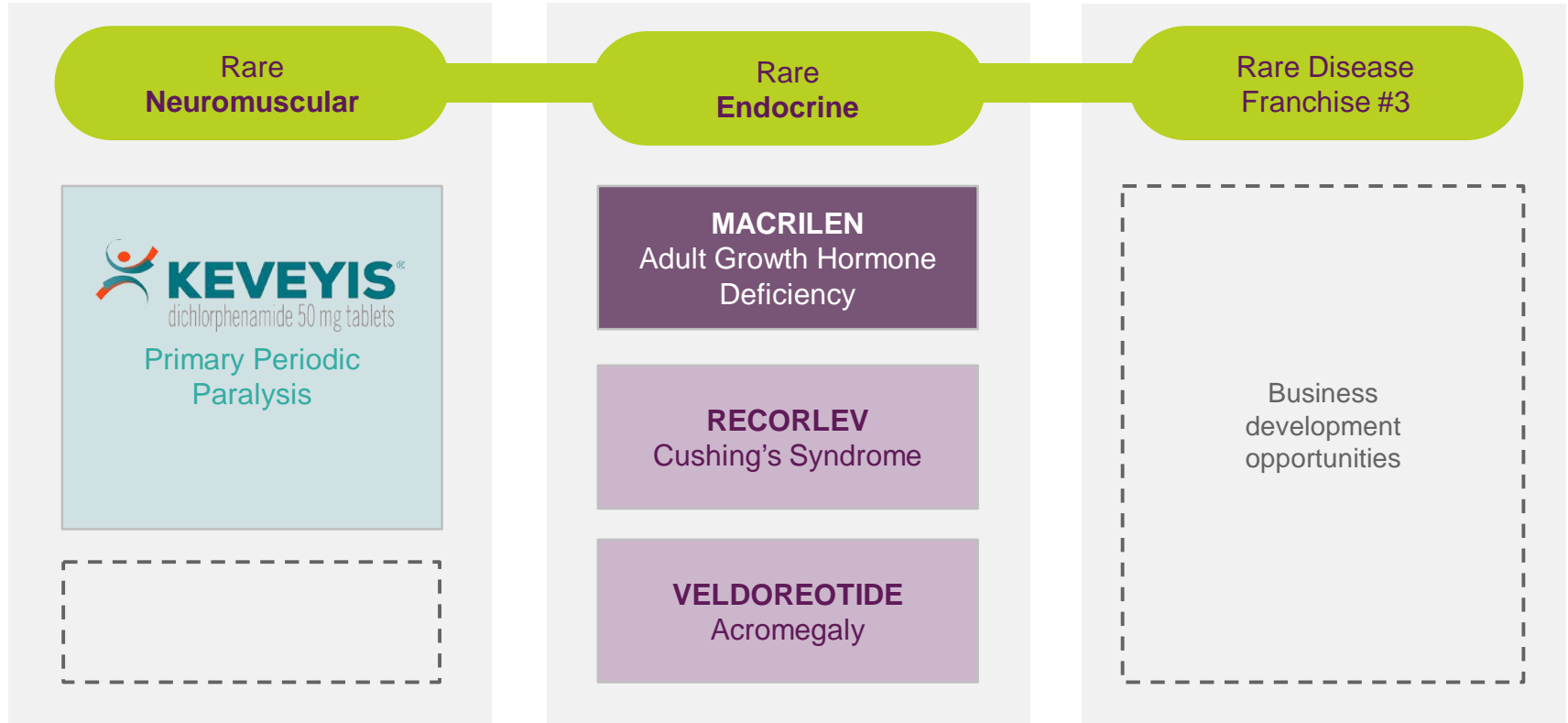
ORPHAN

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

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

<p>Matthew Pauls President, CEO, Director</p>	
<p>Fred Cohen, M.D. Chief Medical Officer</p>	
<p>Brian Davis Chief Financial Officer</p>	
<p>Stephen Long Chief Legal Officer</p>	
<p>Robert Lutz Chief Business Officer</p>	
<p>Dave Bonnell SVP Sales & Marketing</p>	
<p>Peter Valentinsson SVP, Global Technical Operations</p>	
<p>Scott L. Wilhoit SVP, Global Market Access & Patient Services</p>	

Building a portfolio of therapeutically-aligned vertical franchises in rare diseases



Anticipated milestones – 2018



Keveyis

dichlorphenamide

Keveyis: the first and only FDA-approved therapy for primary periodic paralysis



2017 Net Product
Revenues: \$7M

2018 Revenue Guidance:
\$16M - \$19M

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

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

Causes recurrent, progressive, and debilitating episodes of muscle weakness and temporary paralysis

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

Symptoms: clumsiness, extreme fatigue, weakness, palpitations, pain. As patients age, muscle weakness can become permanent

59%

have **weekly** attacks

28%

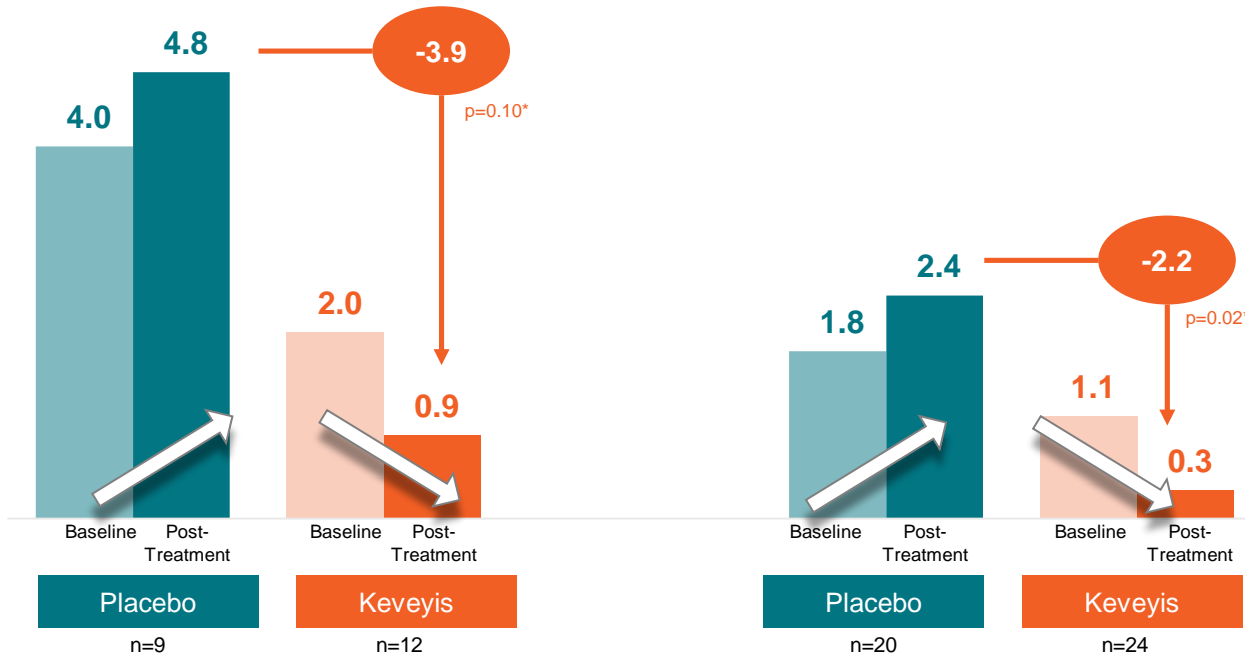
have **daily** attacks

Treatment with Keveyis decreased weekly attack rates

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

Hyperkalemic

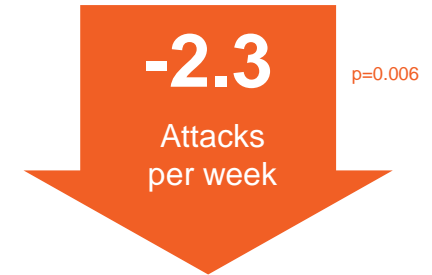
Hypokalemic



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

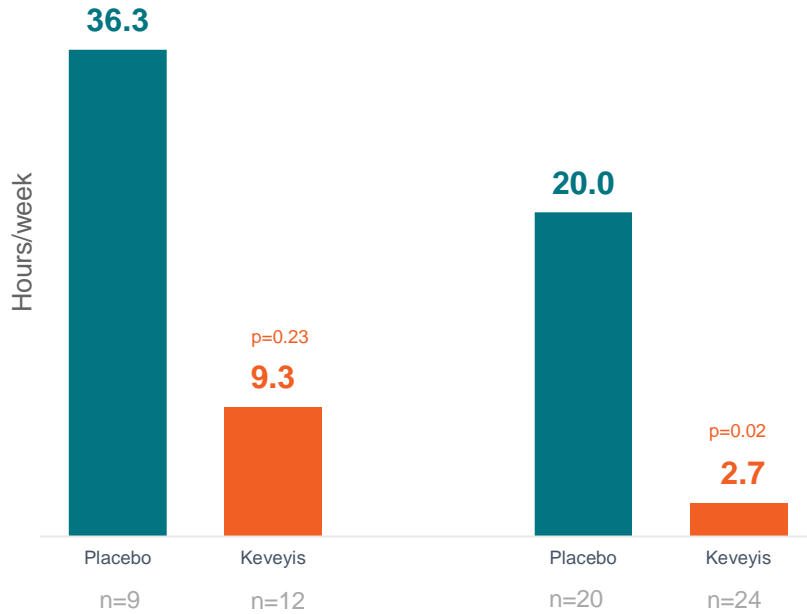
Reduced duration of weekly attacks and decreased attack severity

Average values for each group over weeks 2-9

Decreased weekly attack duration

Study 1: Hyperkalemic

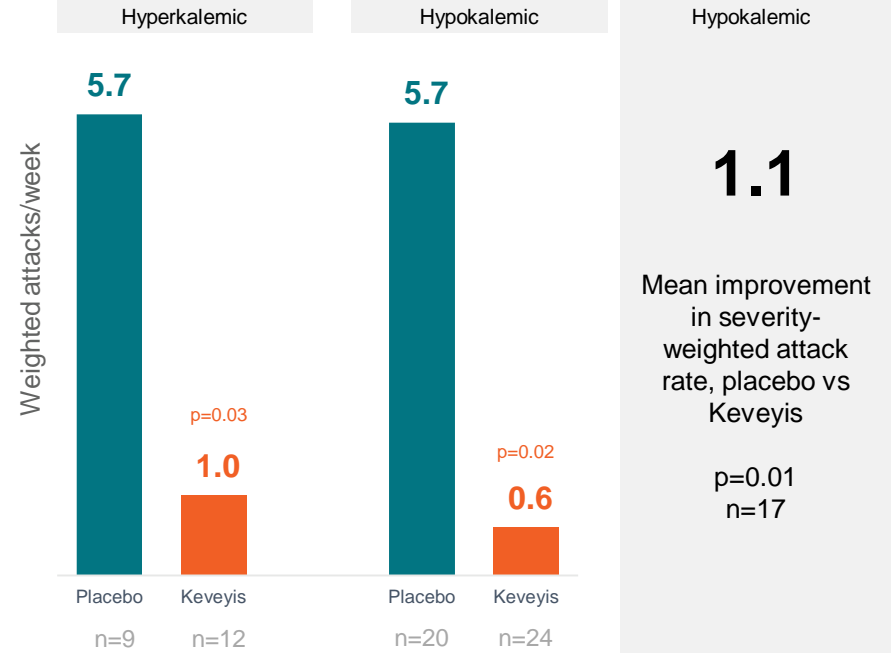
Study 1: Hypokalemic



Decreased severity-weighted attack rate

Study 1

Study 2



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

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

PPP market opportunity

Patient population

Approximately 4,000 – 5,000 diagnosed patients*
(2x previous estimate)

Diagnosis can be challenging, often takes 20+ years from symptom onset

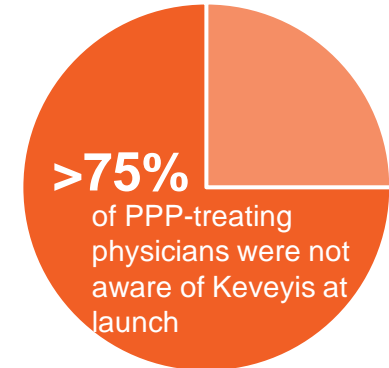
Underdeveloped market

Limited historical investment in disease awareness / education

No other FDA-approved treatment options**

Low Keveyis awareness

Unaided awareness



* Based on Strongbridge Biopharma analysis of medical claims database

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

Keveyis: the formula for early launch success

SALES FORCE



Expanded to 24-person team

- 21 representatives
- 3 regional directors

Significant experience across multiple orphan drug launches

ADVANCED ANALYTICS



Multiple data sources

Predictive modeling

Identify diagnosed

Identify undiagnosed

PATIENT SERVICES/ADVOCACY



Expanded team

- Patient Access Managers
- Program Operations Lead
- Case Managers

Increased focus on
Adherence/Compliance
Genetic Testing Program

HCP EDUCATION



Conference presence

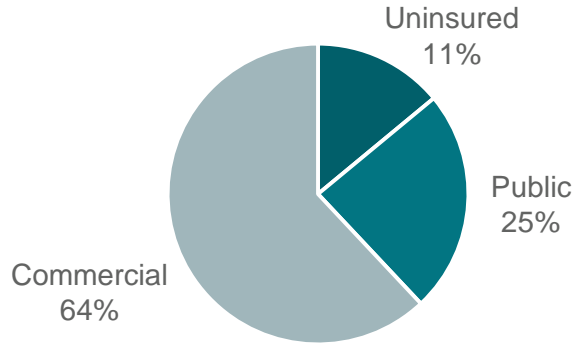
Speaker bureau

Branded webinars

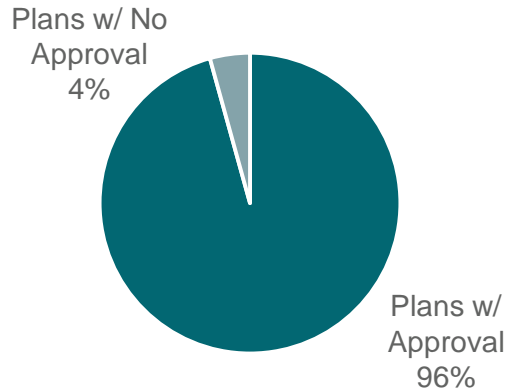
Disease education tools

Keveyis market access status: current patients

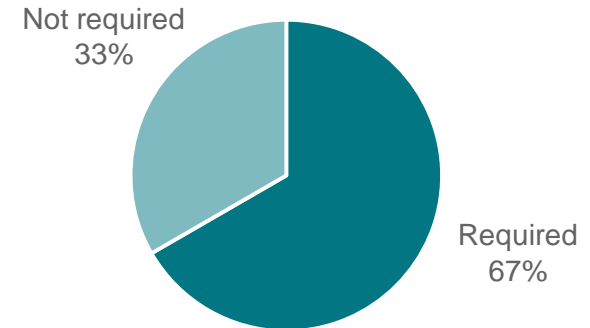
Payer Mix



Broad Payer Coverage



Payer Prior Authorization Requirements



Dosing

AVERAGE
126 mg/day
2.52 tabs/day

Average Age of Patients

42 Years

Annualized Price

Starting dose:
100 mg per day

\$109,500

Max dose:
200 mg per day

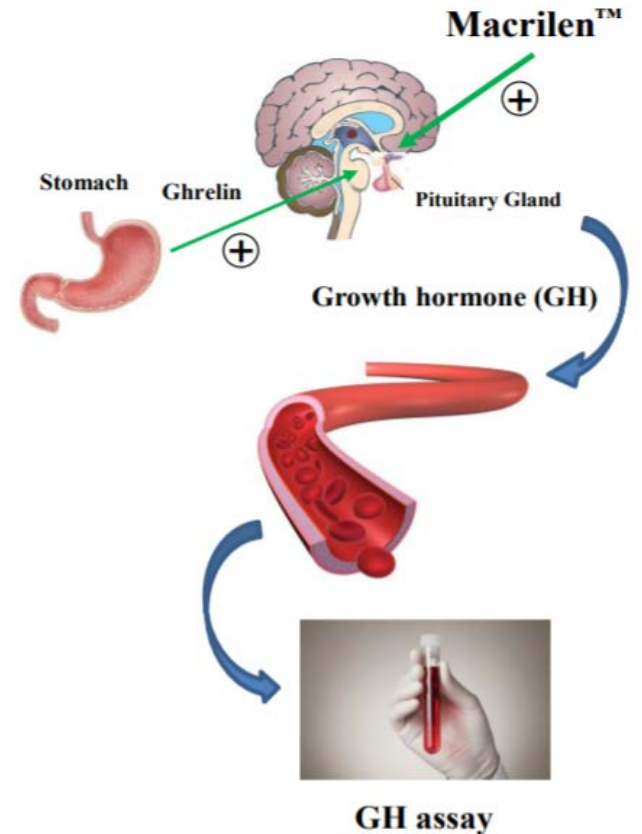
\$219,000



Macrilen

Macrilen Overview

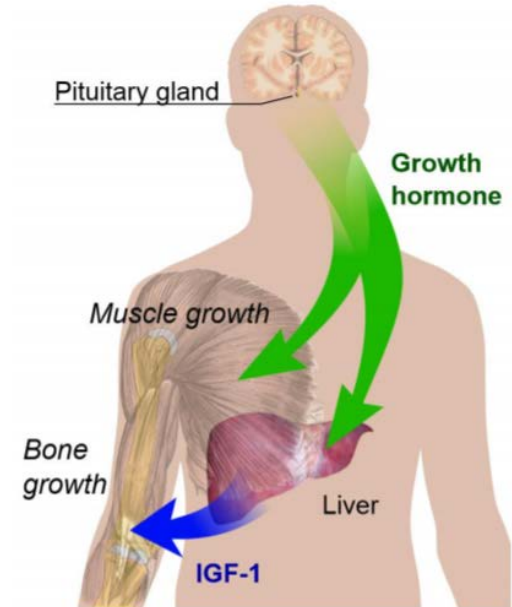
- Oral ghrelin receptor agonist (secretagogue) for assessing Adult Growth Hormone Deficiency (AGHD)
 - Macrilen administered to stimulate production of growth hormone
 - Blood will be taken at 30, 45, 60, and 90 minutes to measure growth hormone production
- AGHD is typically caused by injury/insult to the pituitary and leads to metabolic, bone, and mental health issues
- Endo guidelines recommend AGHD is treated with growth hormone
- Represents a potential significant convenience and tolerability advance to current AGHD assessments



Source: Aeterna Zentaris website, June 2017 IR deck

Implications and Treatment of AGHD

- AGHD symptoms are diverse and non-specific but significant:
 - **Overall:** Decrease quality of life, low physical and mental energy, reduced muscle strength and decreased ability to exercise
 - **Metabolic/CV:** Increased abdominal visceral fat mass, overweight, reduced skeletal and lean body mass, increase in atherosclerotic risk factors, decrease ventricular function
 - **Psychiatric:** Depression, sleep issues, poor memory
- For AGHD patients, growth hormone therapy can reverse or ameliorate many of the symptoms
- Treatment guidelines support testing for and treatment of AGHD with growth hormone replacement



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

Macrilen Test Accurately Diagnoses AGHD vs. ITT

Results from an ITT-Controlled, Two-way, Randomized Crossover Study

All Subjects		Insulin Tolerance Test (ITT) (GH cutoff 5.1 ng/mL)		Total Tests	Percent Agreement MACRILEN and ITT*
		Positive	Negative		
MACRILEN (GH cutoff 2.8 ng/mL)	Positive	55	4	59	Positive Agreement* 74%
	Negative	19	62	81	Negative Agreement* 94%
Total Tests		74	66	140	Overall Agreement 84%

- Agreement between MACRILEN and the ITT overall shown
- Positive agreement higher (89%) for high-risk AGHD and lower among lower-risk categories
- Negative agreement 86-100%
- Labeling reflective of overall and risk-stratified agreements
- <1% of Macrilen tests were not evaluable vs. 17% of ITTs
- Macrilen was highly reproducible 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
- QT_{cF} 95% confidence interval extended to 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: Avoid strong CYP3A4 inducers (avoids false-negative 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

Current AGHD US Market Assessment

**~40-60K
Annual Adult
AGHD
Assessments**

Estimated Market Size for AGHD Assessments	<ul style="list-style-type: none">• ~40-60K annual assessments of adult patients with a pituitary tumor or in adult patients due to pituitary surgery, radiation, chemo as well as patients transitioning into adulthood• Does not include potential LCM opportunity in pediatric GHD (annual 40K); in addition opportunity exists with traumatic brain injury patients, with over 2.5M Emergency Department encounters with TBI per year in the US (on-label: no further clinical studies needed)
Available Assessments	<ul style="list-style-type: none">• The two most commonly used stimulation tests to diagnose AGHD in the US are ITT and GST. Neither is FDA-approved, and they each have unique challenges
Prescribing Physicians	<ul style="list-style-type: none">• Assessments are largely conducted by Endocrinologists• Significant overlap with potential Recorlev prescribers, particularly at Pituitary Centers

Market Research Results

- Results of quantitative (n=40 endocrinologists) and qualitative (n=5) market research*:
 - 83% of endocrinologists are somewhat likely or extremely likely to use Macrilen (based on draft profile)
 - They indicated they would increase their testing for AGHD by 33% because of Macrilen
 - Physicians indicated Macrilen would be the majority of first-line assessments for AGHD for them
 - Physicians also thought that Macrilen would be more than 40% of their overall use of assessments

“It would allow me to start testing in my office” – Community-Based Endocrinologist

* Third-party research sponsored by Strongbridge

Feedback from KOLs and Market Research Results*

	Macrilen	Comments
Preferred route of administration	✓	Physicians prefer oral (Macrilen) versus intravenous injection (GST) and intramuscular injection (ITT)
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 than ITT	✓	ITT has been shown to induce hypoglycemia and therefore requires direct physician oversight and proximity to a crash cart
Improved Tolerability as Compared to ITT	✓	Macrilen had 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

* Third-party research sponsored by Strongbridge

Macrilen Go-To-Market Strategy

FIELD FORCE



Sales force of ~15
Field reimbursement personnel of ~5
Cover $\geq 80\%$ of the target audience

ADVANCED ANALYTICS



Multiple data sources
Predictive modeling
Identify key AGHD treaters

COVERAGE & ACCESS



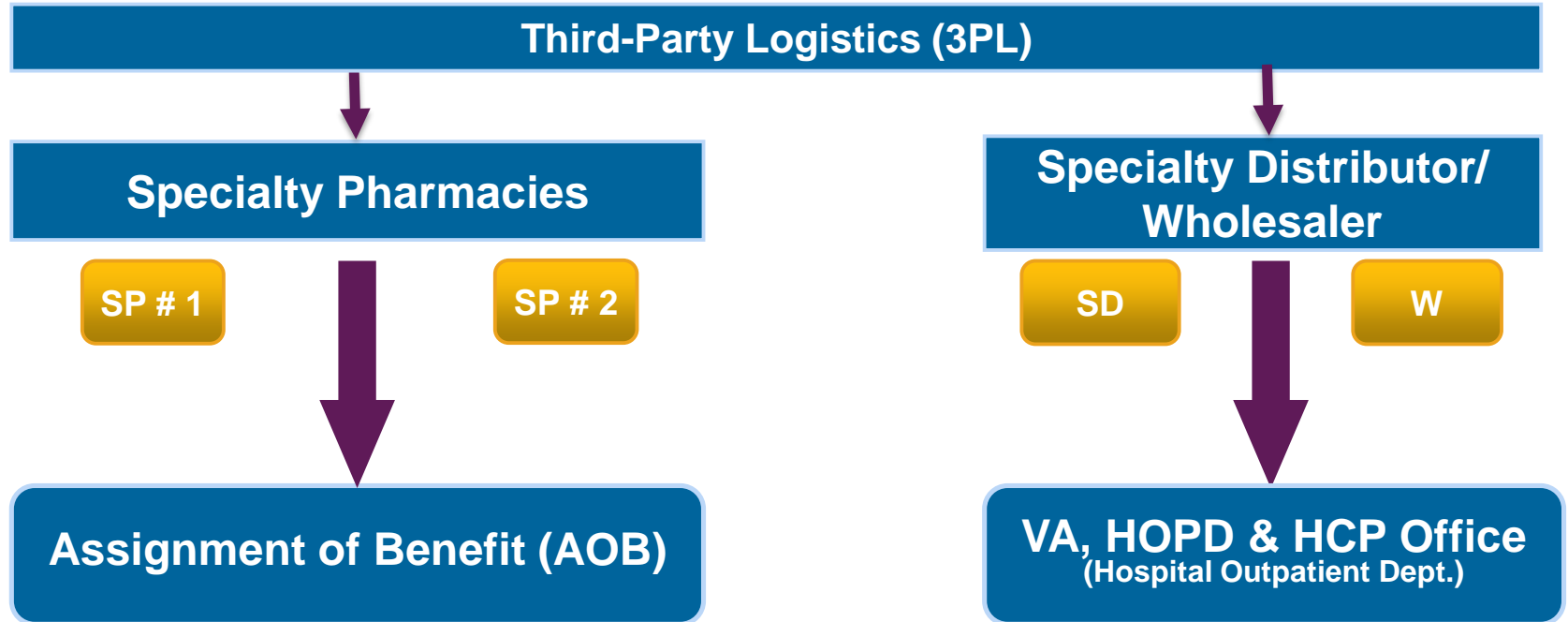
Leverages current structure
Compelling product + services model
Educate top commercial & government payers

HCP and PATIENT EDUCATION



Conference presence
Speaker bureau
Advocacy webinars
Disease education tools

Planned Distribution Approach Leverages Current Model



- Dispensed from SP to “preferred” site of care
- Pharmacy bills 3rd party payer
- Physician bills for services

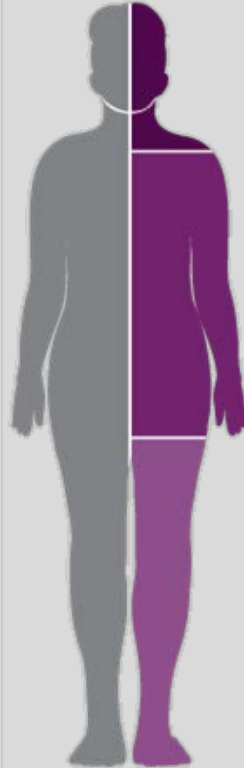
- Shipped directly to institution
- VA Purchases under Federal Supply Schedule
- Institution bills insurers

Recorlev

levoketoconazole

Cushing's syndrome: a rare endocrine disease defined by elevated cortisol

Typically caused by pituitary adenomas



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



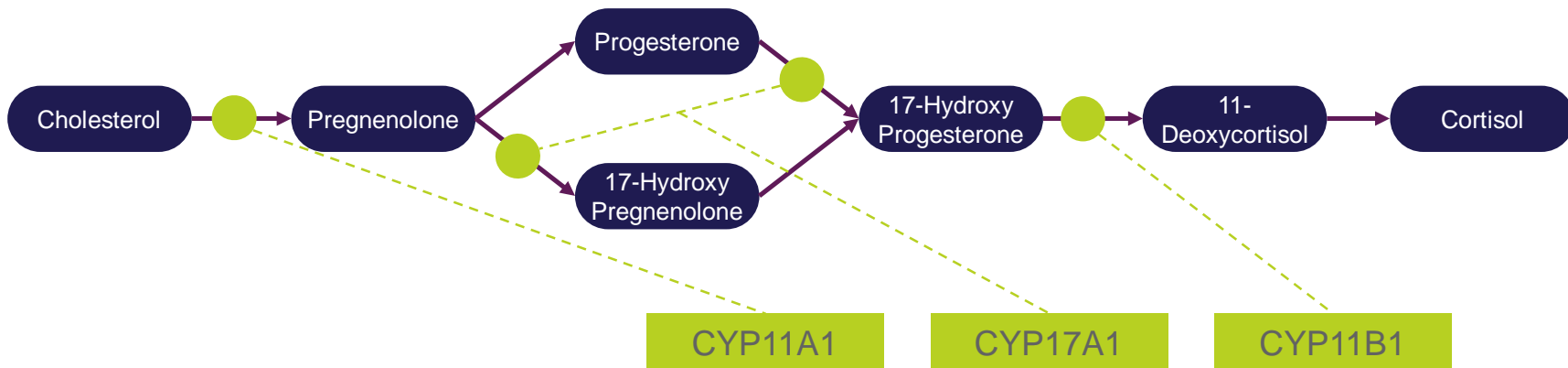
Muscle and skin atrophy



Osteoporosis

2-4X
increased mortality rate

Levoketoconazole is the active half of ketoconazole responsible for cortisol synthesis inhibition



	CYP11A1	CYP17A1	CYP11B1
2R,4S-ketoconazole enantiomer	25,080	595.7	1,365
Ketoconazole, racemate	2,267	57.77	138.6
Levoketoconazole*	1,447	27.94	51.65

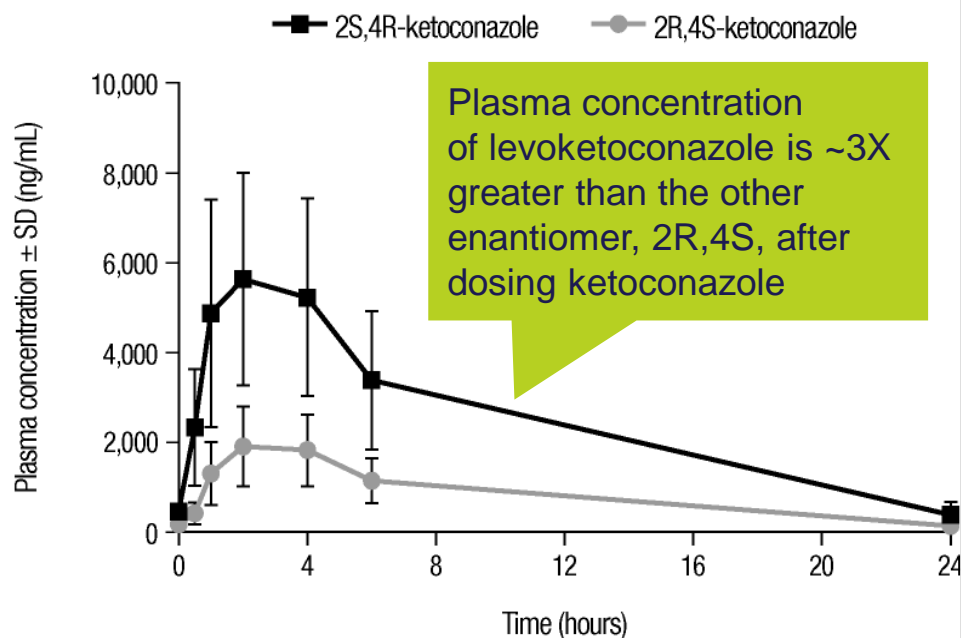
10-26x (comparing Levoketoconazole to Ketoconazole, racemate for CYP11B1)
1.6-2.7x (comparing Levoketoconazole to Ketoconazole, racemate for CYP17A1)

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

Source: Auchus RJ, U. of Michigan, data on file; *The active ingredient in RECORLEV

Recorlev has potential for reduced liver toxicity

PK implies less liver extraction of levoketoconazole



Less potent inhibition of CYP7A

50% inhibition concentration, nmol/L

Levo-KTZ

2,400

2R,4S-KTZ

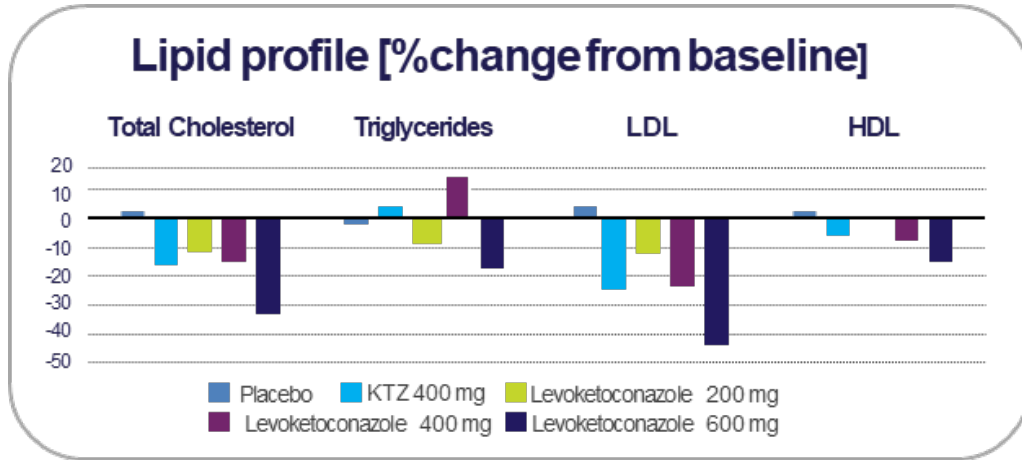
195

12x

Levoketoconazole is a 12-fold **less potent** inhibitor of CYP7A, the rate-limiting enzyme for bile acid synthesis.

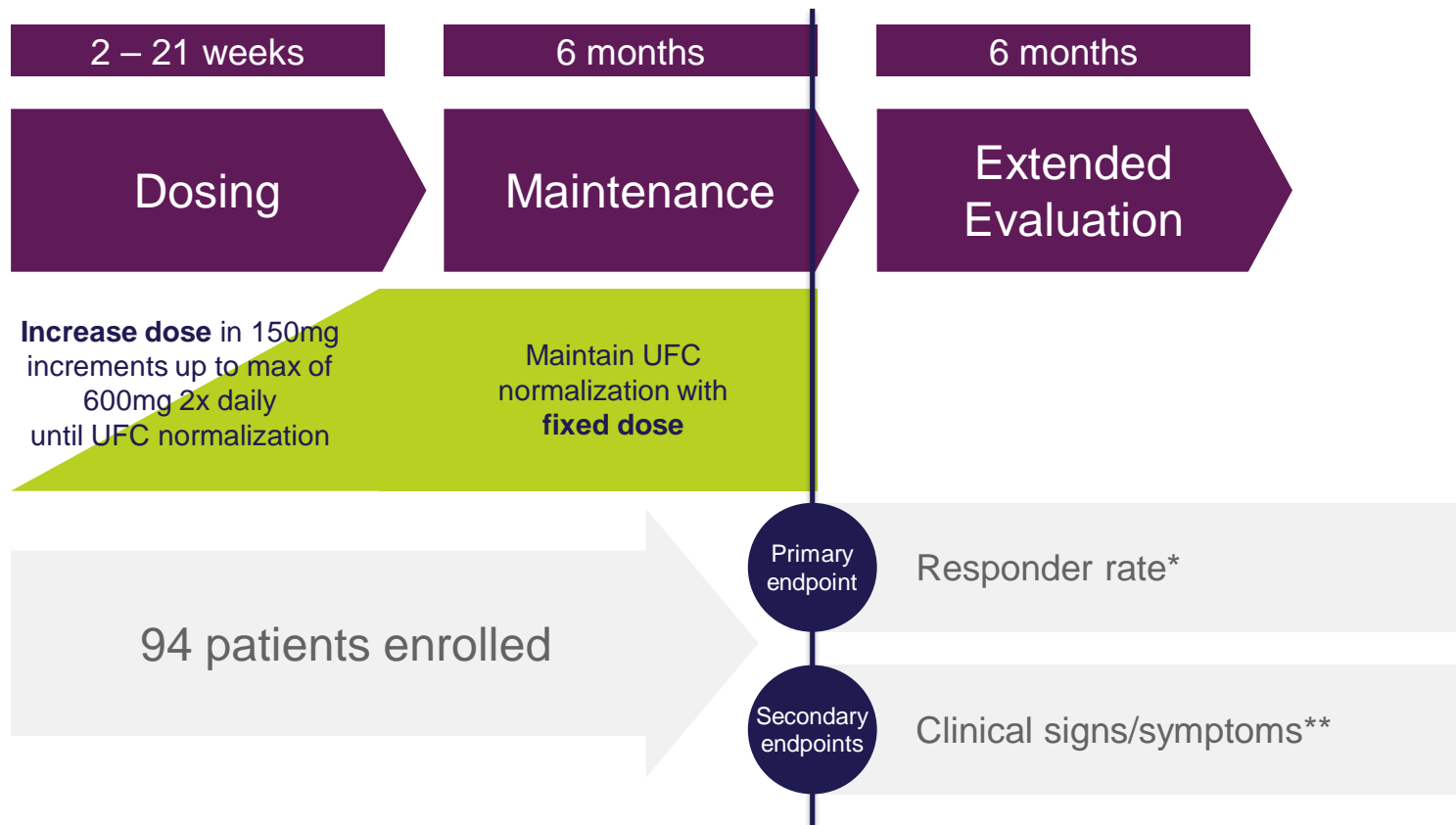
Bile acids aid fat and vitamin absorption and help eliminate toxins and drugs, including Recorlev.

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.

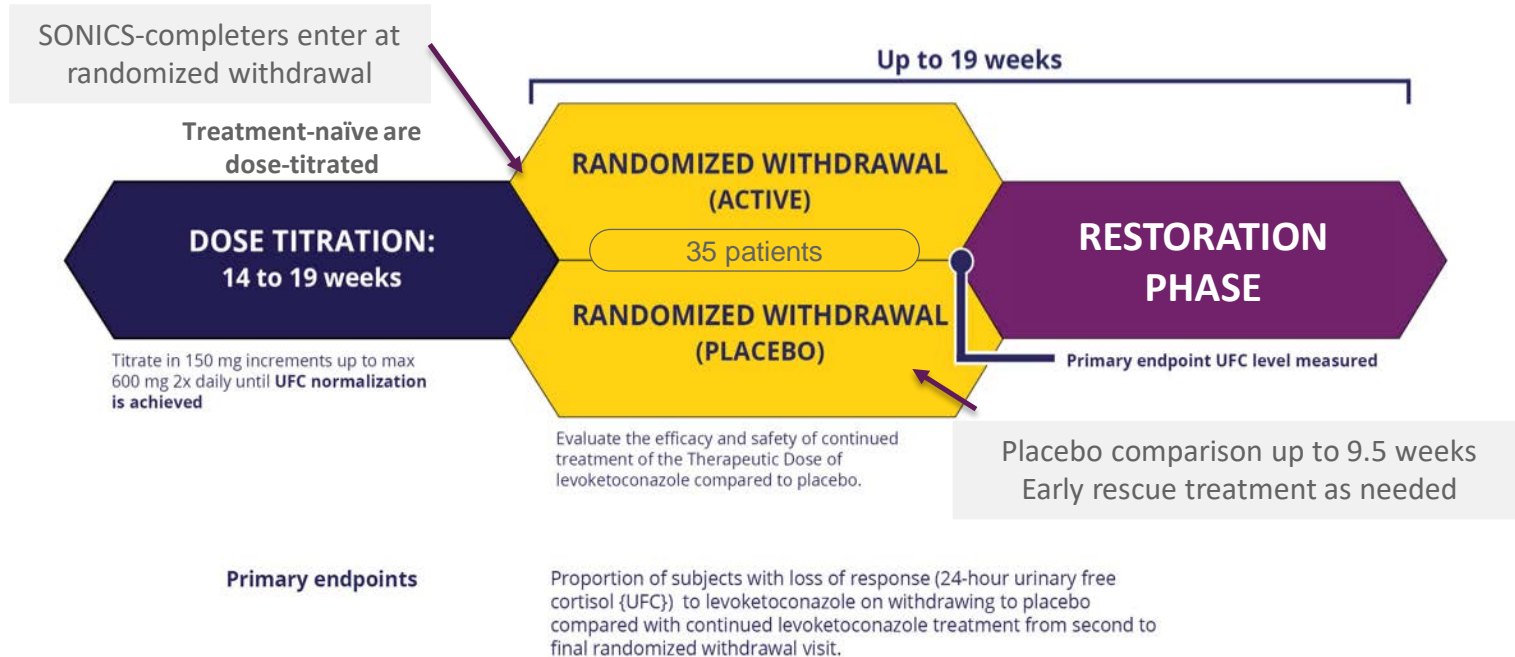
Recorlev phase 3 clinical trials: SONICS – single-arm, open-label study in 94 patients



* Normalized 24-hour urinary free cortisol (UFC) after 6 months of maintenance without dose increase

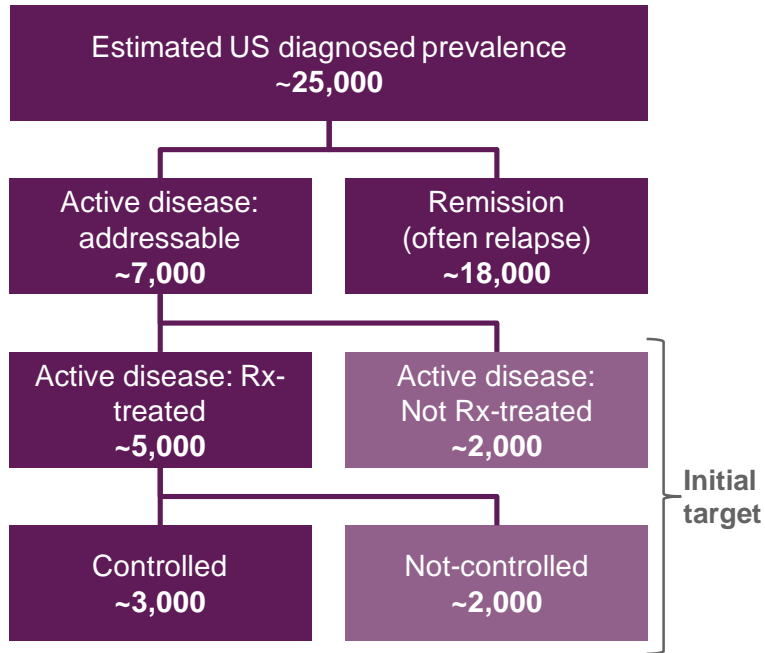
** HbA1c, glucose, blood pressure, lipid profile, CRP, weight, quality of life measures

Recorlev phase 3 clinical trials: LOGICS – double-blind, randomized, placebo-controlled study in 35 patients



Cushing's syndrome US market opportunity

Patient population



Current suboptimal treatments

Highly fragmented market,
significant off-label use

No FDA-approved product with
broad CS indication

Risks of hyperglycemia or
abortion/uterine bleeding with FDA-
approved drugs

Frequent subcutaneous dosing or
difficulty titrating dose and
monitoring drug effect of oral tablets

RECORLEV

Pure single enantiomer of
ketoconazole, which is subject of
significant off-label use in CS

Seeking global registrations for
broad CS indication as first-line drug
treatment

No risks for hyperglycemia or
uterine bleeding identified; potential
for CV risk reduction

Oral tablets allow precise titration
and monitoring of CS control via
blood or urine cortisol levels

Early engagement with Cushing's syndrome community & market development initiatives

Patient advocacy



Multi-language patient education brochures



Sponsor of the Annual Patient Summit

Disease awareness



Cushing Syndrome on "The Balancing Act"

Attend major endocrine conferences

Create/implement market development initiatives for Cushing's Syndrome

KOL engagement

Scientific Advisory Board

Richard Auchus MD PhD University of Michigan	Beverly Biller MD Massachusetts General Hospital	Thierry Brue MD PhD University of Marseille
Frederic Castinetti MD PhD University of Marseille	Maria Fleseriu MD Oregon Health & Science University	Eliza Geer MD Memorial Sloan-Kettering Cancer Center
Anthony Heaney MD PhD University of California, Los Angeles	Aart Jan van der Lely MD PhD Erasmus University	Shlomo Melmed MBChB Cedars-Sinai Medical Center
Richard Feelders MD PhD Erasmus University	Christian Strasburger MD Charite University, Berlin	Susan Webb MD PhD University of Barcelona

Veldoreotide

Veldoreotide LAR: 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

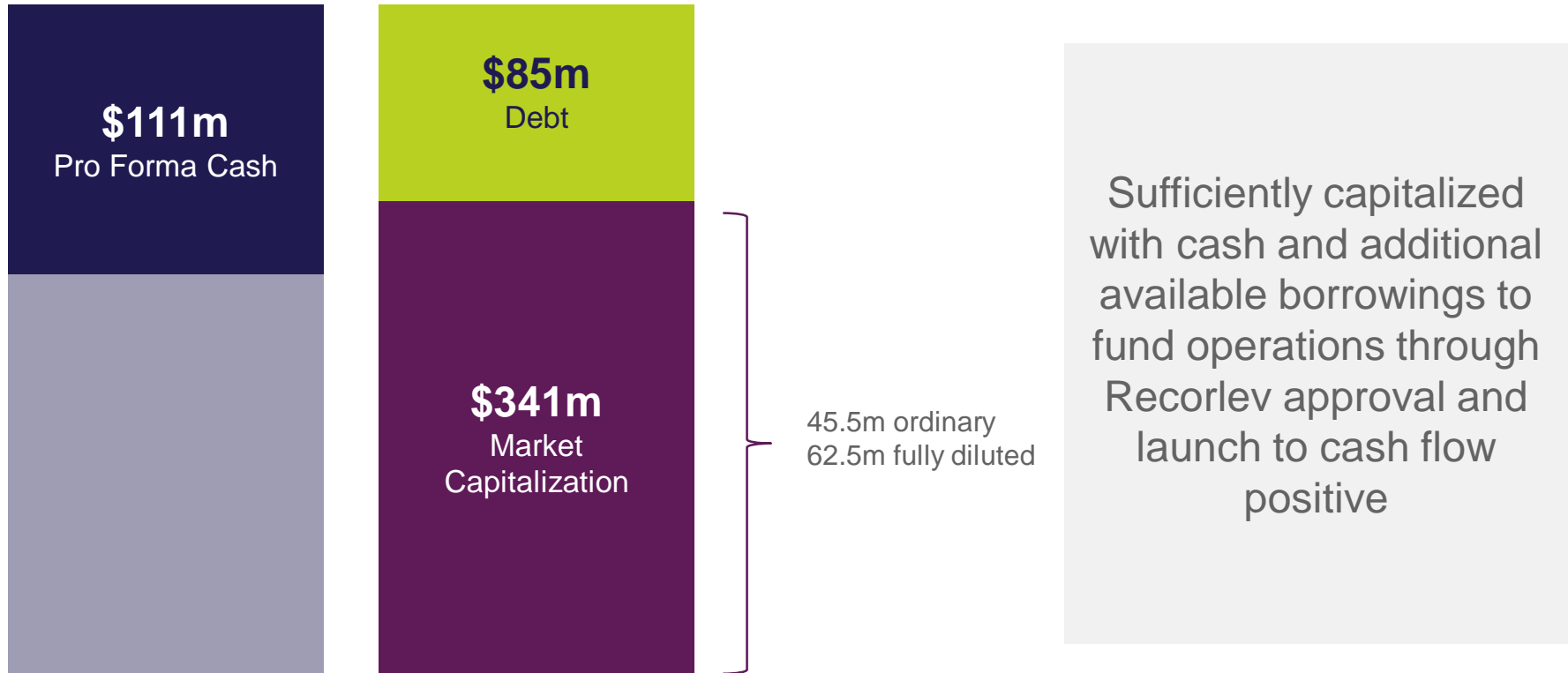
Reduced impact on hormonal responses to mixed meals in healthy subjects

About Strongbridge

Intellectual property and orphan exclusivity

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

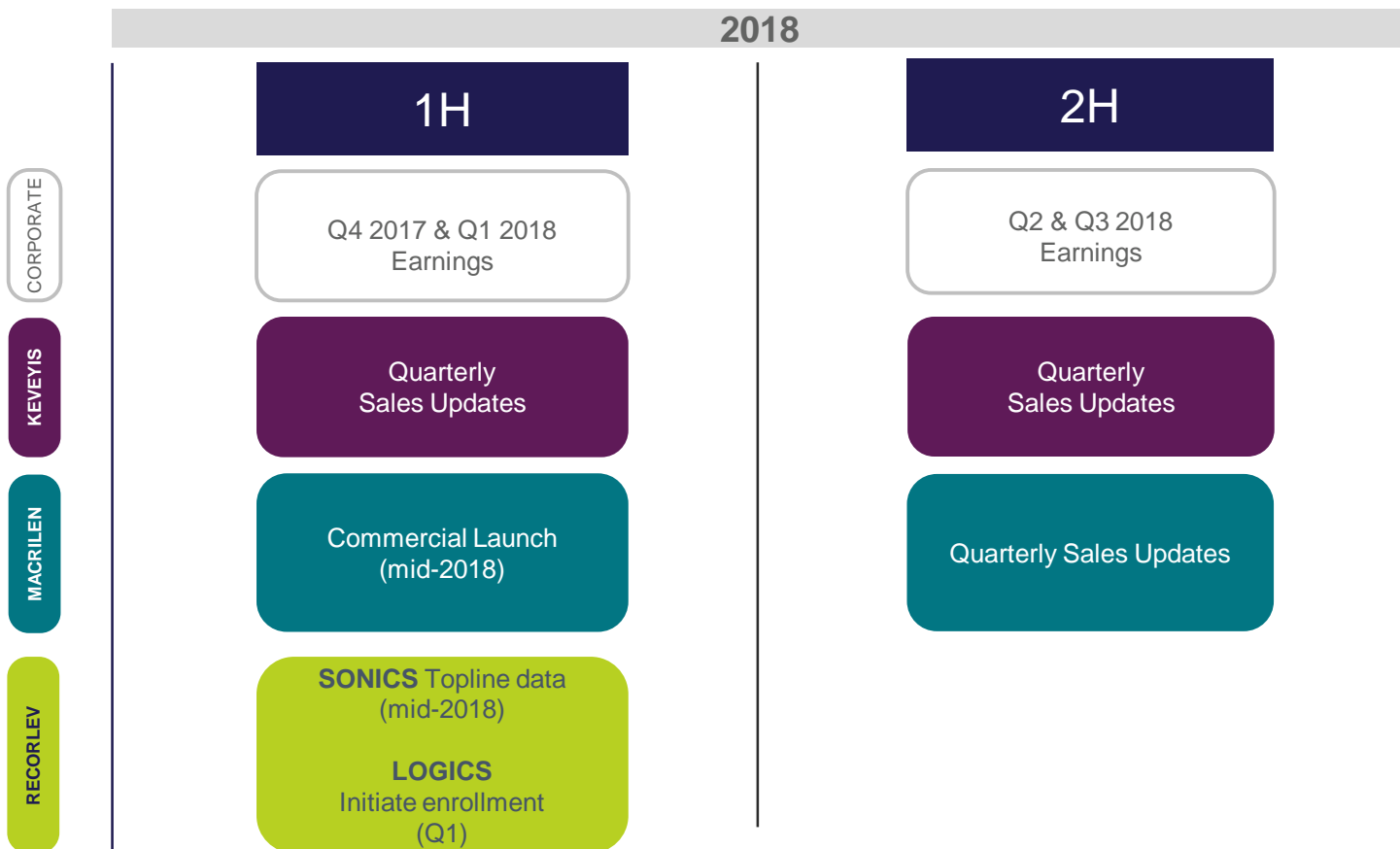
Strong Balance Sheet to Support Growth Objectives



Market capitalization and shares outstanding as of March 8, 2018

Pro forma cash as of December 31, 2017 includes net incremental proceeds in January 2018 from follow-on equity offering, new borrowing under expanded credit facility and the acquisition of rights to Macrilen

Anticipated milestones – 2018



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ORPHAN

MACRILEN
macimorelin

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The 1st and only FDA-approved oral drug for assessing adult growth hormone deficiency

ORPHAN

Acquired Jan 2018

RECORLEV™
levoketoconazole

PHASE 3

Potential next-generation cortisol inhibitor for Cushing's Syndrome

ORPHAN

Veldoreotide modified-release

PRECLINICAL

Potential next-generation somatostatin analog, Acromegaly

ORPHAN

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