



STRONGBRIDGE BIOPHARMA PLC

JANUARY 2021



Forward-looking statements

This document contains forward-looking statements relating to the Company's strategy, objectives, business development plans, financial position, clinical development, regulatory plans and revenue guidance. 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, anticipated timing of release of results from clinical trials, size of patient population potential, advantages of a product or product candidate, anticipated timing of activities related to the regulatory approval process for a product candidate, results of company-sponsored market research, plans, outcomes of product development efforts, intellectual property portfolio, revenue guidance 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. These risks and uncertainties include those associated with clinical development and the regulatory approval process, the reproducibility of any reported results showing the benefits of RECORLEV, the adoption of RECORLEV by physicians, if approved, as treatment for any disease and the emergence of unexpected adverse events following regulatory approval and use of the product by patients. Additional risks and uncertainties relating to Strongbridge and its business can be found under the heading "Risk Factors" in Strongbridge's Annual Report on Form 10-K for the year ended December 31, 2019 and its subsequent Quarterly Reports on Form 10-Q, as well as its other filings with the SEC. These forward-looking statements are based on current expectations, estimates, forecasts and projections and are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors. The forward-looking statements contained in this presentation are made as of the date hereof, and Strongbridge Biopharma does not assume any obligation to update any forward-looking statements except as required by applicable law.

Strongbridge has a three-product, rare-disease portfolio

		Indication/Target Disease	Preclinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Rights
Rare Neuromuscular	KEVEYIS® (dichlorphenamide)	Primary Periodic Paralysis	Marketed					U.S.
Rare Endocrinology Investigational Agents	RECORLEV® (levoketoconazole)	Endogenous Cushing's syndrome	Phase 3					Global
	veldoreotide modified release	Conditions modifiable through activation of somatostatin receptors, such as Cushing's disease and neuroendocrine tumors	Preclinical	Immediate Release Formulation Completed Phase 2				Global

RECORLEV® (levoketoconazole)

Positive results from two Phase 3 studies

NDA submission anticipated Q1 2021

10-month PDUFA review expected

Launch Q1 2022 if approved



2020 revenue of approximately \$30.7M up 41.5% from 2020 despite COVID-19

2021 revenue guidance: \$34M-\$36M

Provides established and leverageable rare disease commercial infrastructure

VELDOREOTIDE modified-release

Novel, patented, extended-release formulation is **under evaluation** in nonclinical disease models potentially amenable to SST modulation



RECORLEV

(levoketoconazole)

In Phase 3 development for Cushing's syndrome

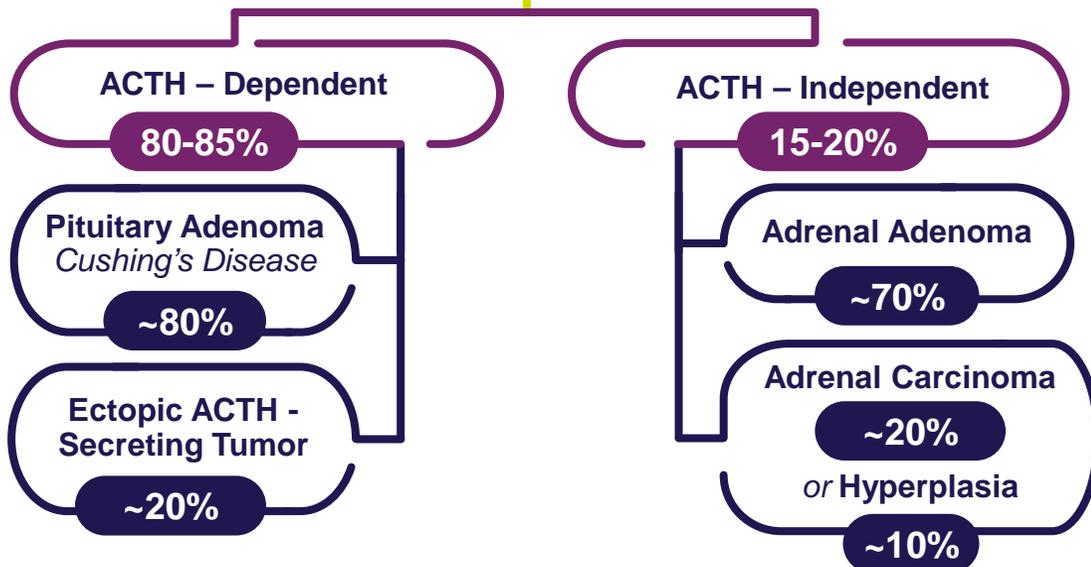


Endogenous Cushing's syndrome is a serious rare disease



Underlying cause is chronic exposure to
EXCESS SERUM CORTISOL
due to any of several etiologies

Endogenous Cushing's syndrome (CS)



Abbreviation: ACTH, adrenocorticotrophic hormone. Source: Sharma TS, et al. Clin Epidemiol. 2015;7:281–293.

Affects the whole body



Heart attacks,
stroke, high blood
pressure, high
cholesterol,
vein clots

Overweight/obesity,
facial, neck and
abdominal fat
accumulation,
diabetes

Psychosis,
impaired memory,
sleep disturbance,
depression,
anxiety

Muscle and
skin atrophy

Osteoporosis



Patients have*



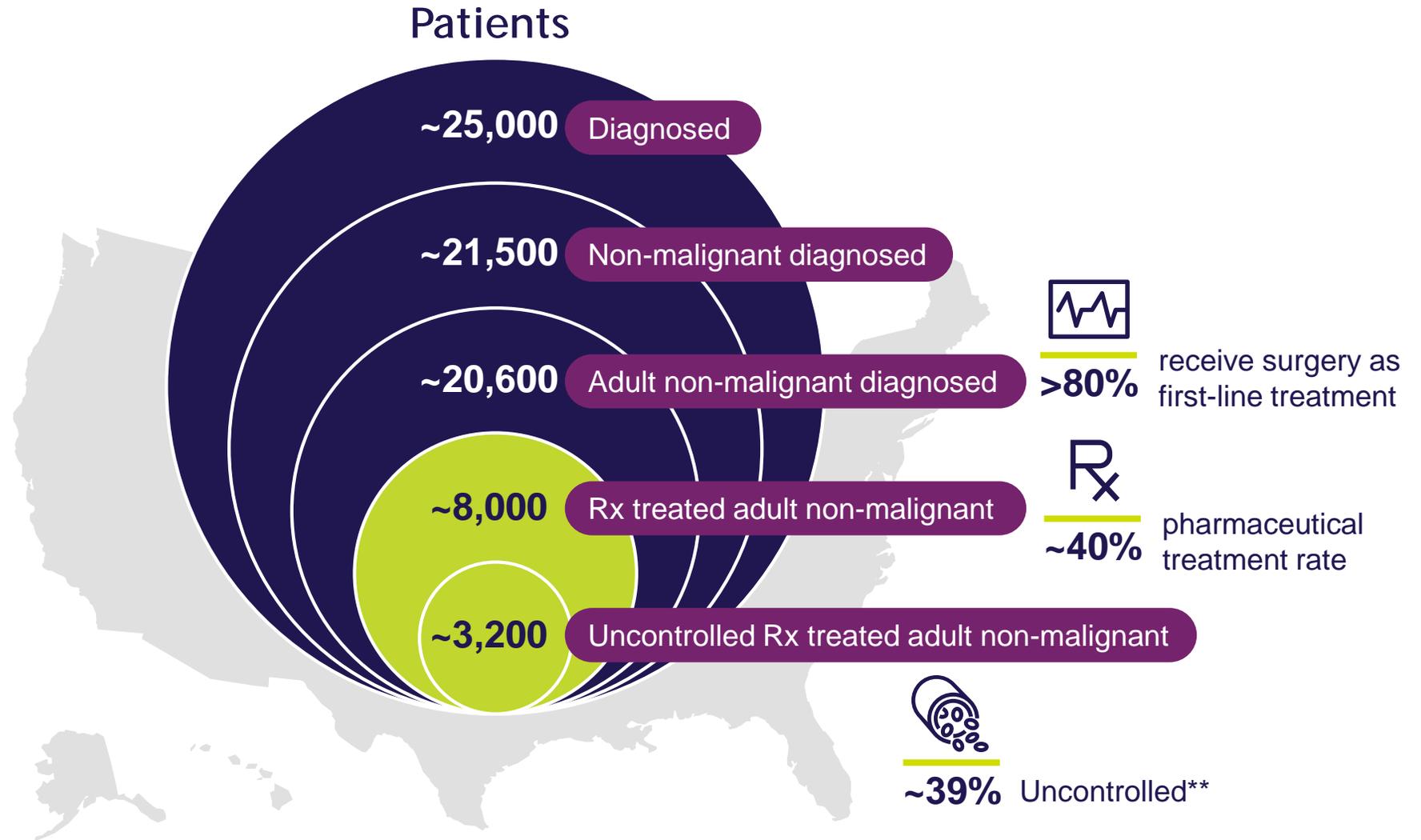
2-5x 
higher incidence
rates of
comorbidities

7x 
higher
medical
costs

4x 
higher
pharmacy
costs

*According to a retrospective analysis of claims from a large U.S. commercial health plan (885 selected Cushing's disease cases and 2,655 matched controls without Cushing's disease) from 2007 to 2011.

An estimated
 ~8,000 CS
 patients in
 the U.S. are
 Rx-treated*
 ~3,200 of whom are
 not well controlled**



Abbreviation: Rx= prescription drug

* Source: Secondary literature and company sponsored research

** A07. Of your endogenous Cushing's patients currently receiving pharmacological therapy, what percent would you consider have their symptoms controlled vs. uncontrolled by their medication(s) for CS?



The safety and efficacy of Recorlev (levoketoconazole) for treatment of endogenous Cushing's syndrome has not been established.

Levoketoconazole, an enantiomer of ketoconazole, comprises virtually all the cortisol inhibition activity of ketoconazole*

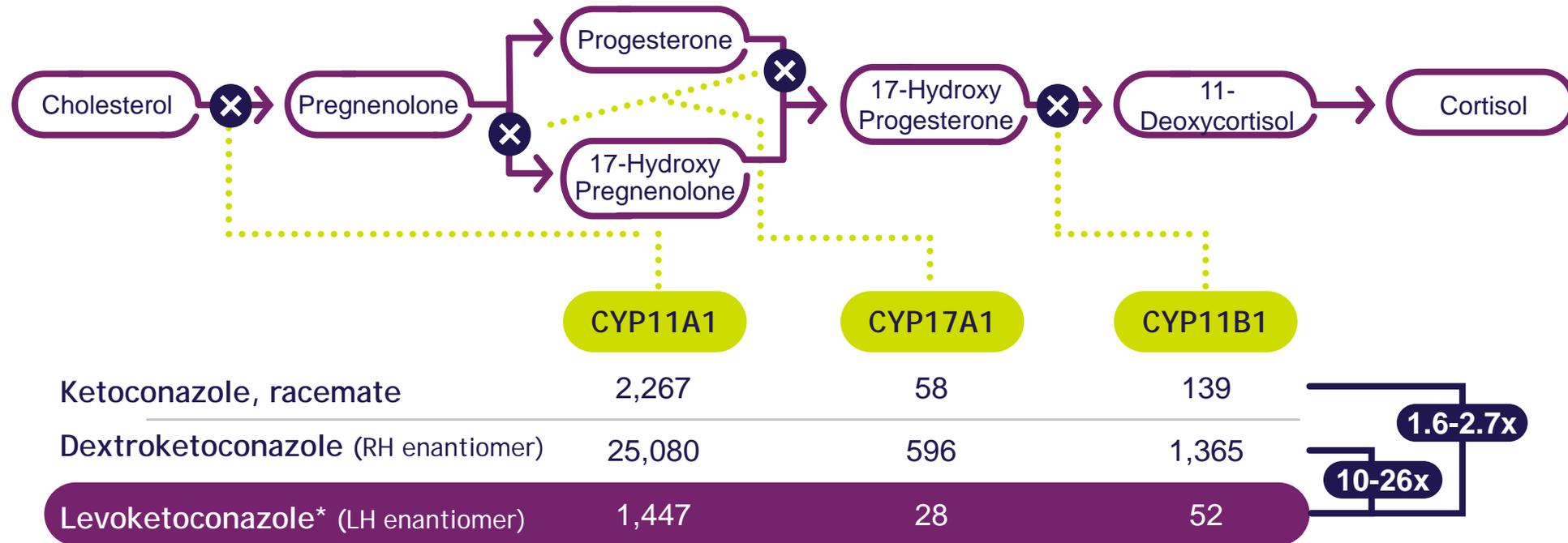
Ketoconazole is a flawed “standard of care” in CS:

Not indicated for CS outside of Europe

Limited data in CS: efficacy and safety poorly characterized

U.S. label limits top dose to 400mg daily, 6 months therapy

Weekly monitoring for liver injury recommended by FDA



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.

The safety and efficacy of Recorlev (levoketoconazole) for treatment of endogenous Cushing’s syndrome has not been established.

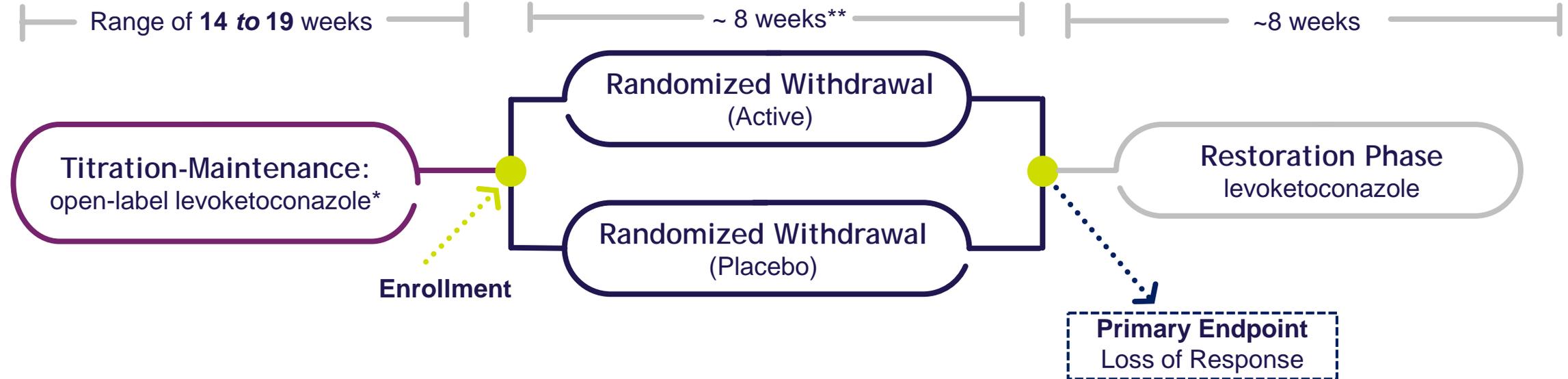
Phase 3 program for Recorlev: includes two phase 3 studies with positive results

Phase 3 Study	Study Design	Patients	Status
SONICS¹	Single-arm, open-label, dose-titration study in adults with Cushing's syndrome (CS)	94 patients enrolled in dose-titration phase	<ul style="list-style-type: none"> Completed with statistically significant result on primary endpoint Full results published in <i>The Lancet Diabetes and Endocrinology</i>
LOGICS²	Double-blind, placebo-controlled, randomized withdrawal following open-label treatment in adults with CS	<p>84 total patients (12 participated after completing SONICS)</p> <p>44 entered and 43 completed the randomized-withdrawal phase</p>	<ul style="list-style-type: none"> Statistically significant result on primary endpoint
OPTICS	Long-term, open-label extension study in adults with CS	Project 45-50 to be enrolled	<ul style="list-style-type: none"> Last patient last visit for the study expected to be in 2023 Preliminary safety data to be included in NDA

1. Fleseriu M, et al. *Lancet Diab Endocrinol*. 2019;7(11):855-865.

2. Zacharieva S, et al. *Journal of the Endocrine Society*, Volume 4, Issue Supplement_1, April-May 2020, MON-332, <https://doi.org/10.1210/jendso/bvaa046.1129>.

LOGICS: a phase 3, double-blind, placebo-controlled, randomized-withdrawal trial



- Phase 3, multinational, double-blind, placebo-controlled, randomized-withdrawal study of CS patients with study baseline mUFC at least 1.5 times the upper limit of normal (ULN) for patients naive to levoketoconazole
- Levoketoconazole individually titrated open-label according to mUFC response with maintenance at therapeutic dose for at least 4 weeks and with at least 14 weeks total therapy
- Completers of SONICS study were potentially allowed entry into LOGICS, but required re-titration if not on a stable therapeutic dose for at least 12 weeks prior to screening for LOGICS
- Randomization 1:1 active:placebo
- The study population was similar to SONICS and representative of the CS population

* Subjects who directly rolled over into LOGICS from SONICS and were on a stable therapeutic dose for 12 weeks prior to screening did not require titration-maintenance

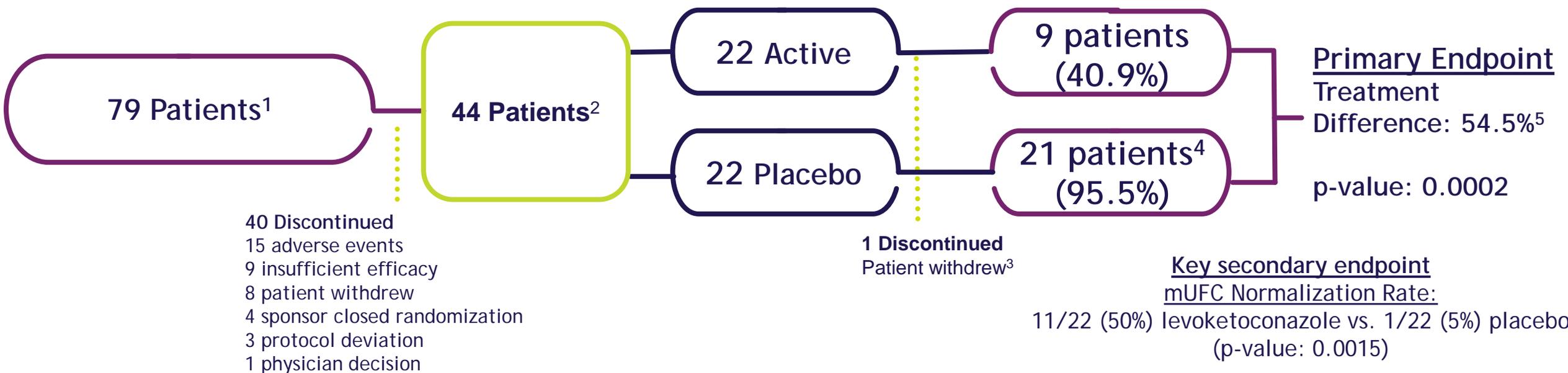
** Early rescue can happen at any time during randomized withdrawal

LOGICS showed that 54.5% more patients lost response on placebo than on levoketoconazole (p-value: 0.0002)

Titration Maintenance

Randomized Withdrawal

Loss of Response (ITT)



The enrolled study population had baseline characteristics comparable to those in the SONICS study, representative of a medically treated CS population with moderate to severe hypercortisolemia

1) 7 former SONICS patients entered TM; 2). 5 former SONICS patients enrolled directly into randomized-withdrawal; 3) 1 patient discontinued during RW from active arm; 4) Patients on placebo were rescued after a median 22 days, mean 28 days; 5) 95% Conf. Interval (27.4-75.7);



Adverse events during levoketoconazole treatment in LOGICS were generally comparable to those seen in SONICS

Treatment-Emergent Adverse Events During Levoketoconazole Use (Phases combined)

N=80*

Nausea	29%
Hypokalemia	28%
Headache	21%
Hypertension	19%
Diarrhea	15%

Treatment-emergent events with incidence ≥15%

Treatment-Emergent Adverse Events (Randomized-Withdrawal)

N=44

	L-KTZ n=22	Placebo n=22
Nausea	2 (9%)	1 (5%)
Fatigue	2 (9%)	1 (5%)
Headache	2 (9%)	2 (9%)
Dizziness	0%	2 (9%)
Hypertension	3 (14%)	1 (5%)
Insomnia	0%	2 (9%)

Treatment-emergent events with incidence ≥5%



*Includes 79 patients who entered the titration maintenance phase plus one patient who joined the randomized-withdrawal phase directly from SONICS and was randomized to the active arm

Safety measures in LOGICS were generally comparable to those seen in SONICS

Liver Test Results During Levoketoconazole Use (Phases combined) (Worst observed value for ALT)

N=79*

ALT > 3x ULN (includes those > 5x ULN)	11.4%
ALT > 5x ULN	3.8%
Total bilirubin values > 1.5x ULN	0.0%

No Hy's Law, no transaminases >20x ULN; no clinical sequelae; 7 patients discontinued due to a liver-related abnormality (6 were AESIs); all liver abnormalities >3x ULN resolved without clinical sequelae (with medication cessation in some cases)

QTc Results (Phases combined) (Worst observed values for QTcF)

N=80

> 500msec **2.5%**

No clinical sequelae related to QTcF; all cases resolved with medication interruption; 2 patients discontinued due to QTc prolongation

Adrenal Insufficiency (Phases combined)

N=80

Adverse Events **10%**



The safety and efficacy of Recorlev (levoketoconazole) for treatment of endogenous Cushing's syndrome has not been established.

*One patient of the 80 who were treated with levoketoconazole did not have post-baseline liver test result data because they dropped out of the study

Recorlev
could be
launched in
U.S. Q1
2022 if
approved



NDA submission ~Q1 2021
~10-month PDUFA review



PDUFA date ~Q4 2021 or Q1 2022



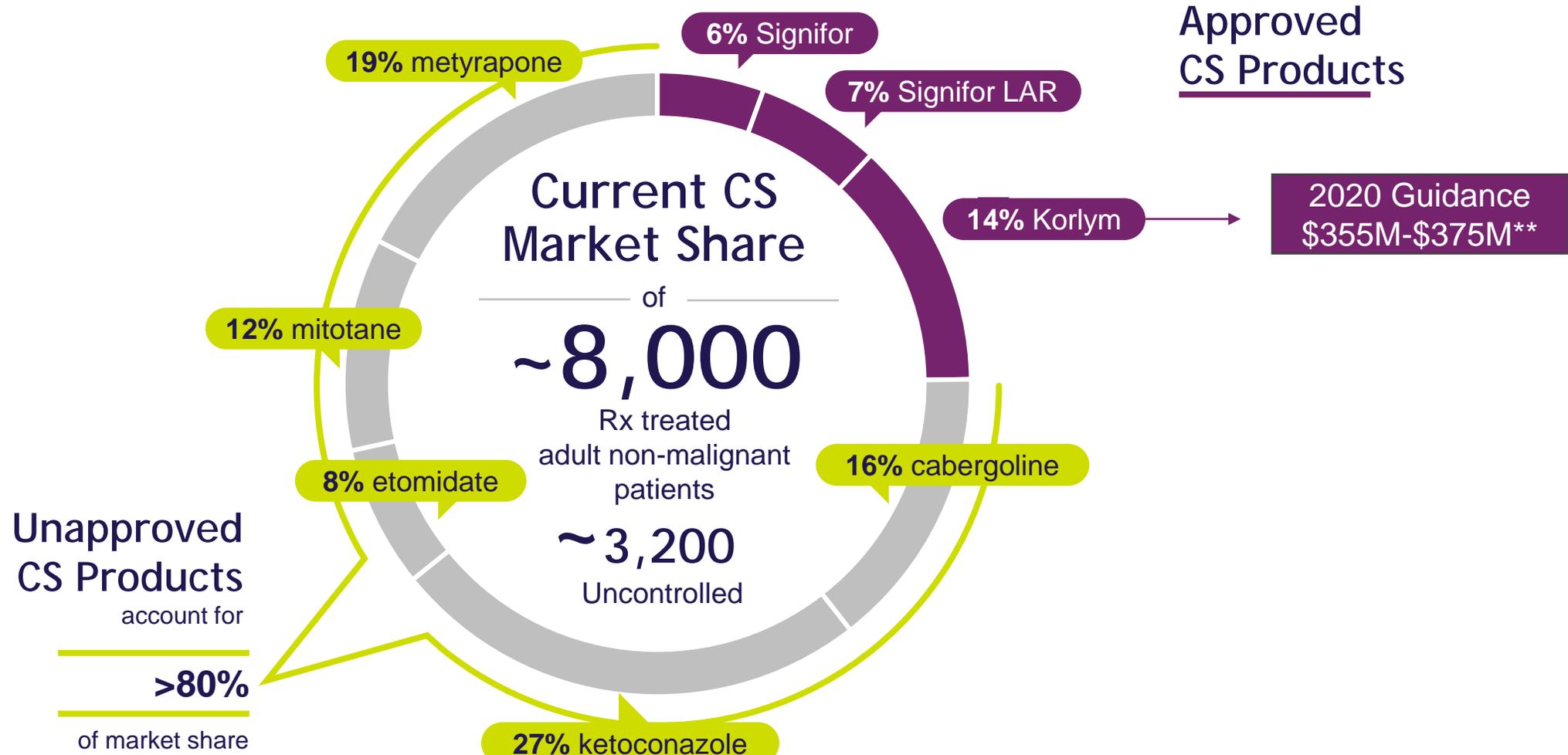
U.S. Launch ~Q1 2022

RECORLEV COMMERCIAL OPPORTUNITY



The safety and efficacy of Recorlev (levoketoconazole) for treatment of endogenous Cushing's syndrome has not been established.

Fragmented CS prescribing market - dominated by unapproved CS products*



Source: Company sponsored research

Signifor and Signifor LAR are owned by Recordati; Korlym is owned by Corcept

* Isturisa was approved on March 9th 2020, after the market research was conducted

**2020 Corcept guidance

B08. Of your endogenous Cushing's syndrome patients currently receiving a pharmacological therapy pre-surgery, what percent are receiving each pharmacological therapy listed below?

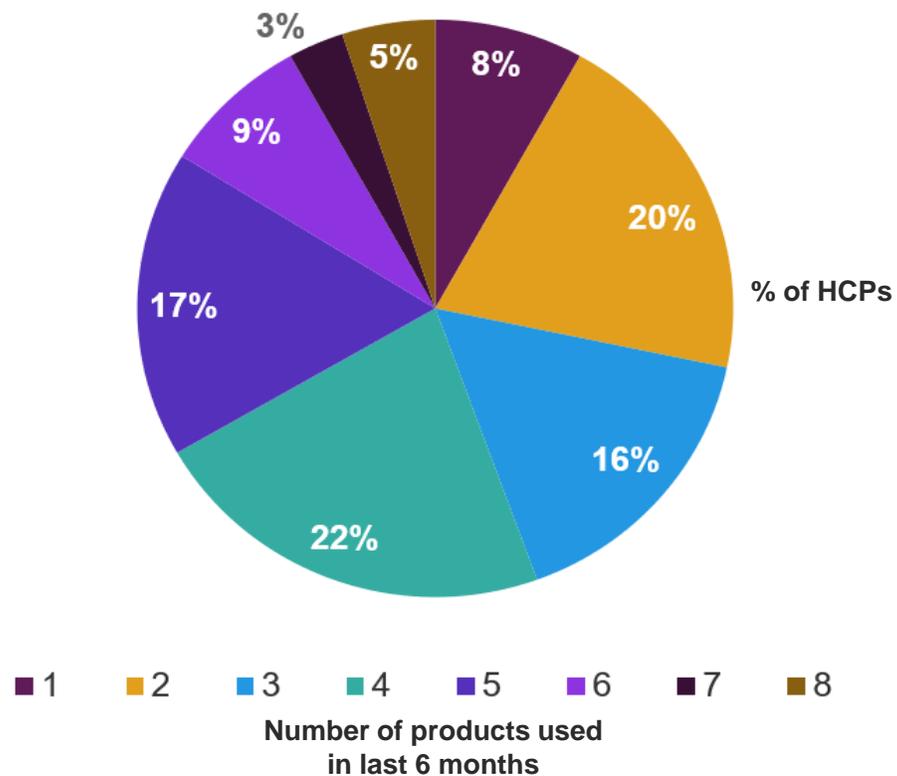
B09. Of your endogenous Cushing's syndrome patients currently receiving a pharmacological therapy post-surgery – 1st line, what percent are receiving each pharmacological therapy listed below?

B10. Of your endogenous Cushing's syndrome patients currently receiving a pharmacological therapy post-surgery – 2nd line or later, what percent are currently receiving each pharmacological therapy listed below?

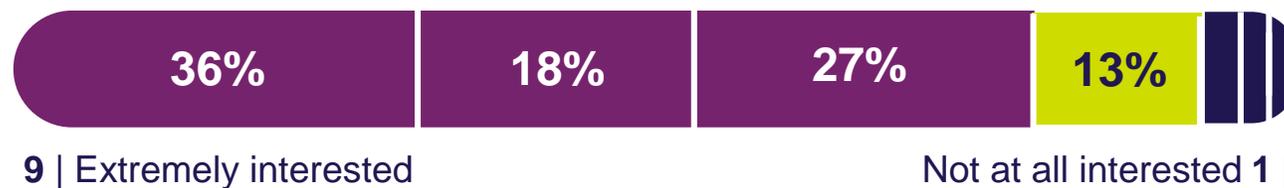


A need for new treatment options exists

72% of Endocrinologists have used 3 or more products in the past 6 months



 **81%** of endocrinologists have moderate to high interest in new treatments for CS



 **Controlled vs. Uncontrolled** on Pharmacological Therapy



Source: Company sponsored research

B02. When thinking of your endogenous Cushing's syndrome patients that you have personally managed in the past six months, please indicate which of the following pharmacological therapies your patients have received.

A07. Of your endogenous Cushing's patients currently receiving pharmacological therapy, what percent would you consider have their symptoms controlled vs. uncontrolled by their medication(s) for CS?

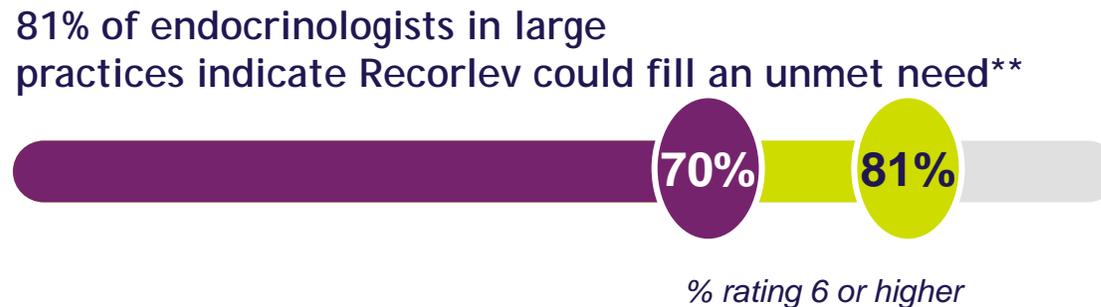
B15. In general, how interested are you in new treatments for endogenous Cushing's syndrome? Please rate on a 9-point scale, where 1 is "Not at all interested" and 9 is "Extremely interested".

Endocrinologists had a positive reaction to the Recorlev clinical profile and indicated a likelihood to prescribe if approved

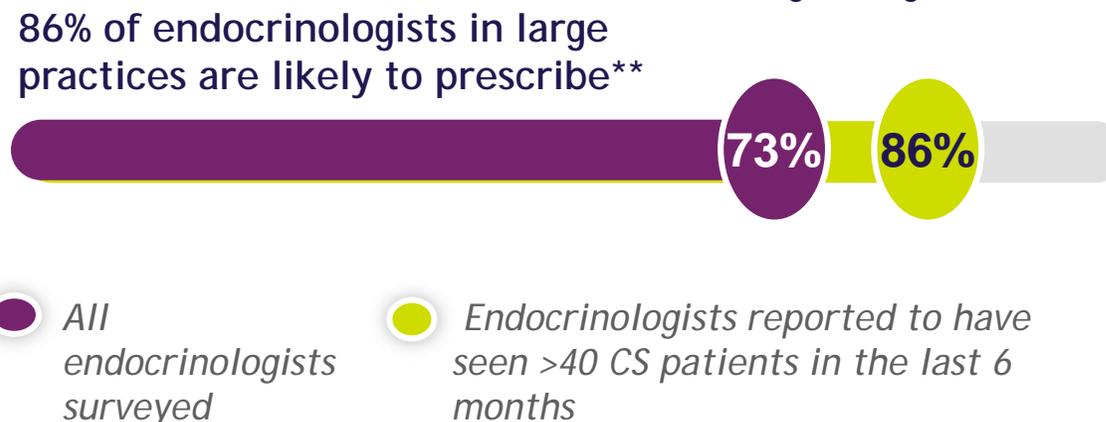
Recorlev Has Potential to Fill Key Unmet Needs as Described by Endocrinologists

- Patient-reported improvements in QoL
- Reduction in UFC / Ability to monitor therapeutic response
- CV Profile (e.g., progressive weight loss)
- Safety (e.g., hepatotoxicity, hyperandrogenism, adrenal insufficiency)

Fills an Unmet Need



Likelihood to Prescribe



Source: Company sponsored research

D03. Based on this profile, what is your likelihood to prescribe Product Y? Please rate on scale from 1-9, with 1 being "Not at all likely" and 9 being "Very likely".

D02. To what extent does Product Y fill an unmet need in the treatment and management of endogenous Cushing's syndrome? Please rate on scale from 1-9, with 1 being "Not at all" and 9 being "Very much".

**Not statistically significant



The safety and efficacy of Recorlev (levoketoconazole) for treatment of endogenous Cushing's syndrome has not been established.

Although Ketoconazole is currently the most prescribed treatment, there is a significant opportunity for Recorlev

40% of HCPs surveyed do not use ketoconazole

- Reluctant to use Keto due to safety concerns
- CS label primary driver of product selection
- More willing to try a new therapy coming to market given efficacy and safety data from clinical trials

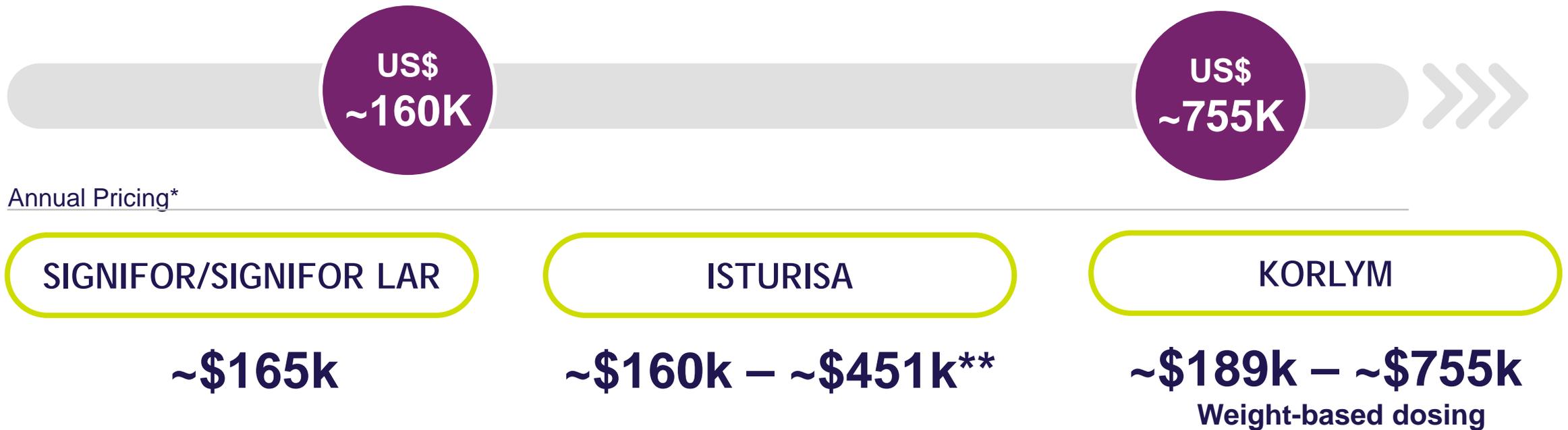
35% of HCPs surveyed use ketoconazole in less than 20% of their CS prescribing

- Acknowledge that safety concerns and FDA warnings exist
- Use Keto based on clinical experience
- See benefit of FDA approved product with supporting data in CS

The 75% of the market that either does not use keto or uses keto in less than 20% of their CS prescribing indicated a high likelihood to prescribe Recorlev



Precedent established for CS branded pricing*



Annual Pricing*

SIGNIFOR/SIGNIFOR LAR

~\$165k

ISTURISA

~\$160k – ~\$451k**

KORLYM

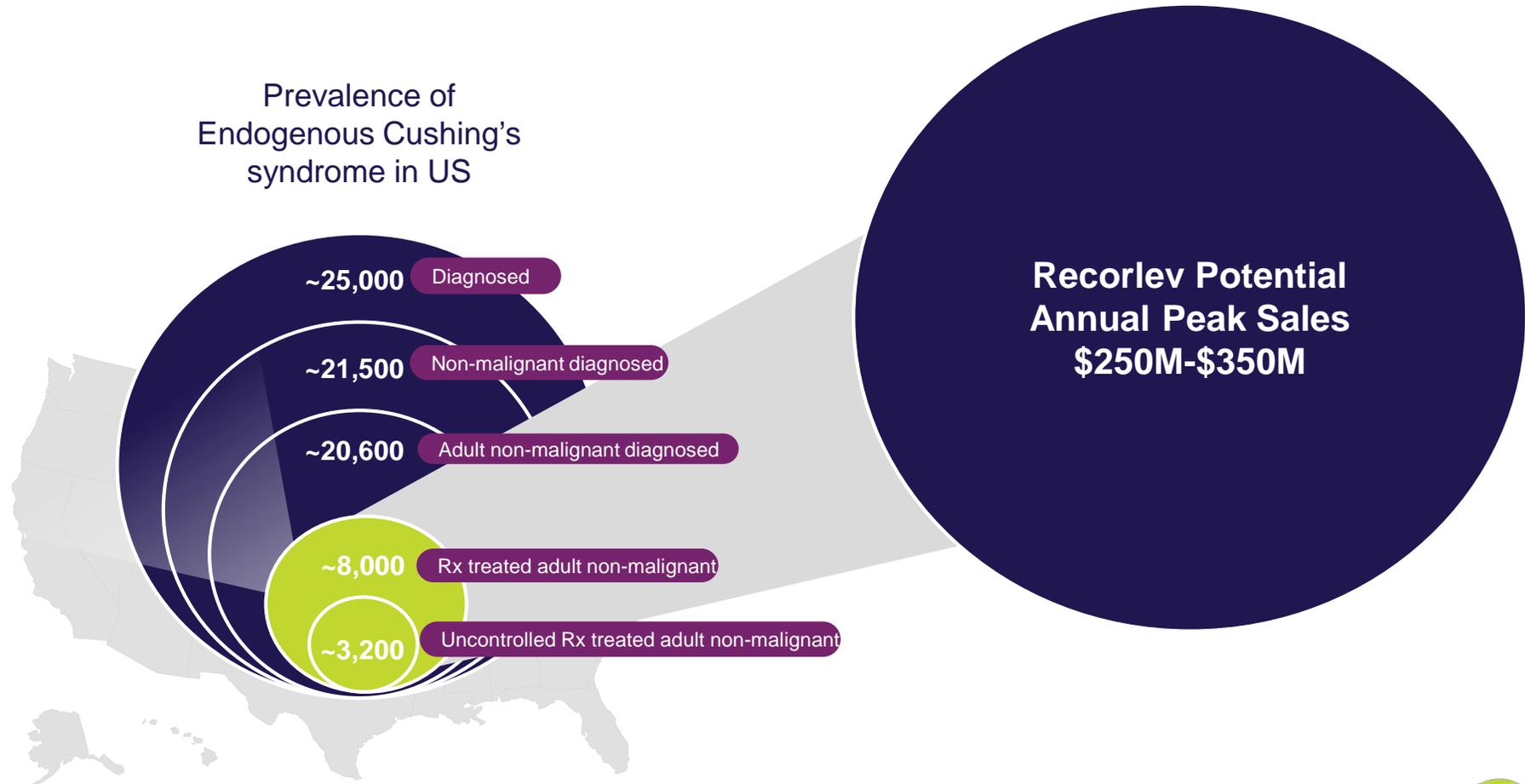
~\$189k – ~\$755k
Weight-based dosing

Source: Red Book, Signifor Prescribing Info, Signifor LAR Prescribing Information, Korlym Prescribing Information, Isturisa Prescribing Information

* Wholesale/ Acquisition Cost

** Isturisa estimated annual cost based on maintenance dose range of 2mg-7mg twice daily.. At the highest recommended maintenance dose the annual cost of Isturisa would be ~\$1M..

Recorlev represents the potential to capitalize on a \$2B+ total addressable annual market



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

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

PPP

Causes recurrent, progressive, and debilitating episodes of muscle weakness and temporary paralysis²⁻⁴

Symptoms/Triggers



Symptoms
clumsiness, extreme fatigue, weakness, palpitations, pain



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

Impact of Attacks

Paralytic attacks are acute episodes that can be debilitating⁴

Attacks may last from one hour to several days¹

As patients age, muscle weakness can become permanent³

Frequency



have **weekly** attacks



have **daily** attacks

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.

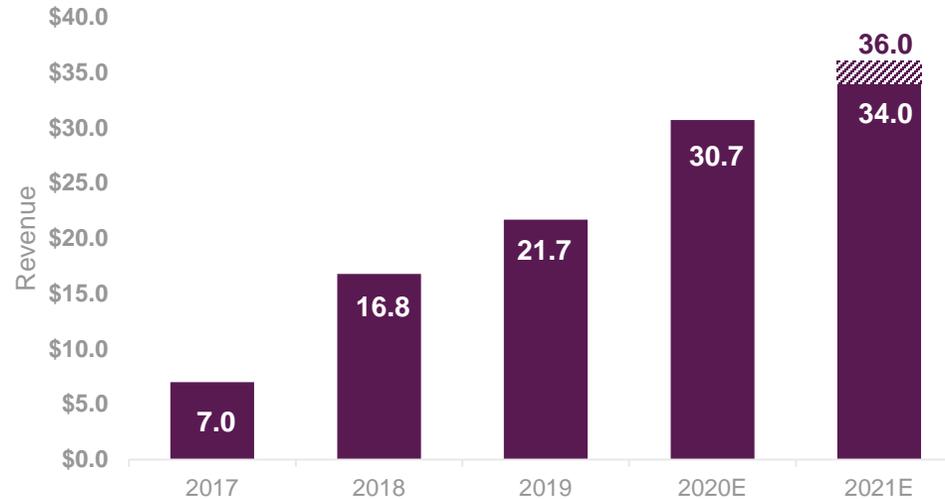
Keveyis provides revenue and commercial experience for Strongbridge



~4,000 - 5,000*

Diagnosed PPP patients
in the United States

Total addressable market
is more than \$500M
annually



With continued market exclusivity, we believe Keveyis has the potential to exceed peak sales of \$50M annually



Established Rare
Disease Commercial
Experience and
Expertise

- Sales
- Marketing/Analytics
- Patient Access Managers
- Patient Services
- Advocacy

We are attempting to extend Keveyis exclusivity by pursuing >12 patent applications

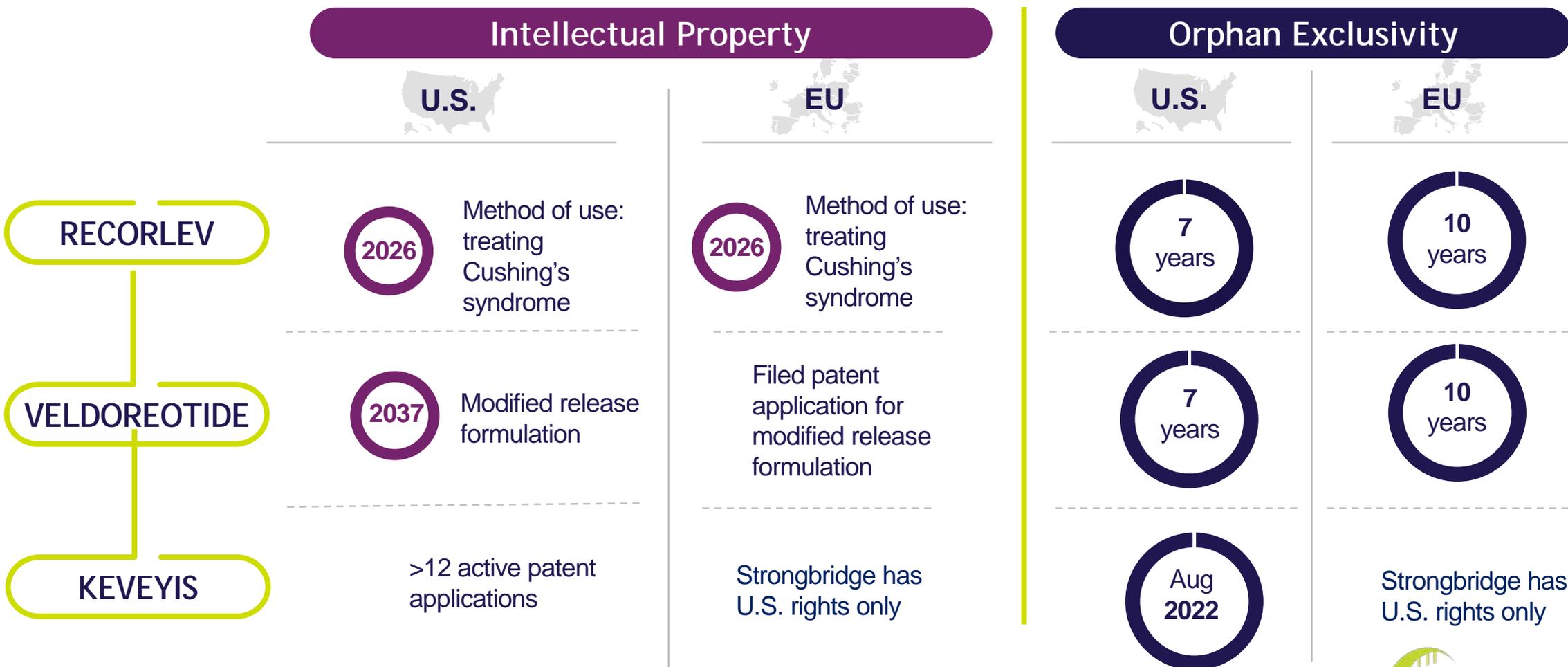
IP & FINANCIALS & CLOSING

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

Intellectual property and orphan exclusivity

Recorlev U.S. Exclusivity: At least 7 years from launch

Keveyis U.S. Exclusivity: Expires August 2022 unless extended via IP efforts



Strongbridge projects it can fund operations into and potentially beyond Q1 2023*



~\$87.5M Cash

Cash and cash equivalents as of 12/31/20

\$30M Debt Facility

- \$10M drawn at close
- \$10M drawn Q4 2020 following positive Recorlev data
- Up to an additional \$10M available upon Recorlev approval and lender consent
- No revenue or cash liquidity covenants



Cash
runway

Into and
potentially beyond

Q1 2023*



2021
Keveyis revenue
guidance
\$34M–\$36M



~67.2M
shares
outstanding

Near-term key priorities

RECORLEV®
(levoketoconazole)

- **Submit an NDA for Recorlev to the U.S. FDA Q1 2021**
- **Launch planning**

 **KEVEYIS®**
dichlorphenamide 50 mg tablets

- **Achieve or surpass our full year 2021 guidance range of \$34-\$36M**
- **Continue vigorous prosecution of KEVEYIS IP**

Corporate

- **Manage expenses to achieve or exceed runway guidance of cash lasting into and potentially beyond Q1 2023**