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Regains Worldwide Rights to Muscarinic Agonist Programs

StaR® / SBDD precision-designed selective muscarinic M_4, M_1 and dual M_1/M_4 agonists

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References to "FY" in this presentation for periods prior to January 1, 2018 are to the 12-month periods commencing in each case on April 1 of the year indicated and ending on March 31 of the following year, and the nine-month period from April 1, 2017 to December 31, 2017. From January 1, 2018 the Company changed its fiscal year to the 12-month period commencing in each case on January 1. References to "FY" in this presentation should be construed accordingly.

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Executive summary

1 Sosei Heptares regains worldwide rights to muscarinic agonist programs

- Decision a result of AbbVie's pipeline strategy, not based on any efficacy, safety or other data
- Sosei Heptares receives all programs under development, together with the associated IP and preclinical and clinical data generated from the partnership with Allergan
  - Includes a pipeline of next-generation selective muscarinic agonists with newly developed chemistry (benefitting from insights from clinical trials and our precision SBDD technologies)

2 Executing our own review and will start activities to re-partner selected programs immediately

- Plan is to focus on rapidly developing these programs towards inflection points in order to re-partner them in the near term in-line with our strategy to execute 2 to 3 high value deals every year
- Strong track record of executing new business development deals from regained assets (A2a from Shire to AstraZeneca, CGRP from Teva to Biohaven)

Executive summary (cont'd)

3 Muscarinic programs highly attractive – selective M_4 agonist and selective M_1 agonist safe and well tolerated at active doses in Phase 1 studies

- Muscarinic M_4 and M_1 receptors are validated targets for the treatment of psychosis and cognition
- M_4 has completed (HTL'878) Phase 1a studies and was found to be safe and well tolerated in younger and older subjects, with the potential to be a first-in-class opportunity to revolutionize treatment options for SZ, AD and other neurological diseases
  - Prior to out-licensing to Allergan in 2016, SZ was Heptares' preferred lead indication and tractable clinical pathway for HTL'878, and we will now once again focus on this strategy
- M_1 has completed (HTL'318) Phase 1b studies in patients, is safe and well tolerated in humans, and demonstrated evidence of target engagement and effects on cognition in AD patients
  - We will now take full control of toxicology studies which will be concluded in early 2021
  - A next-generation selective M_1 agonist with new chemistry is progressing to preclinical studies

1 Sosei Heptares regains worldwide rights to muscarinic agonist programs

Decision is based on AbbVie's pipeline strategy, not as a result of safety or efficacy data

Decision is based on AbbVie's pipeline strategy

Muscarinic programs offer potential symptomatic treatment options, as opposed to disease-modifying approaches

Very common for big pharma to re-organize pipelines following a major acquisition

AbbVie Completes Transformative Acquisition of Allergan

NORTH CHICAGO, Ill., May 8, 2020

- Creates biopharmaceutical company with leadership positions in key therapeutic areas: Immunology, Hematologic Oncology, Neuroscience, and Allergan Aesthetics
- Robust portfolio of on-market and pipeline assets well-positioned for sustainable long-term growth
- Provides immediate scale and profitability to AbbVie's Growth Platform (ex-Humira)
- Elects Thomas C. Freyman to its Board of Directors

Assembly Biosciences Regains Worldwide Rights to Microbiome Gastrointestinal Development Programs

-- Process to explore strategic alternatives underway --

June 18, 2020

AbbVie and Allergan Announce Agreements to Divest Brazikumab and Zenpep

Jan 27, 2020

AstraZeneca (NYSE: AZN) will acquire brazikumab

Nestle (Swiss: NESN) will acquire and take full operational ownership of Zenpep

Muscarinic programs regained by Sosei Heptares as a result of AbbVie's pipeline strategy focus

1

Sosei Heptares regains worldwide rights to muscarinic agonist programs

Now a greatly advanced and enriched portfolio of selective muscarinic agonists

Sosei Heptares receives all programs under development, together with the associated IP and preclinical and clinical data generated from the partnership with Allergan

Includes a pipeline of next-generation selective muscarinic agonists with newly developed chemistry

StaR® and SBDD precision-design platform has delivered a patent estate of chemically diverse M_4, M_1 and M_1/M_4 muscarinic agonist back-ups in preclinical development

Program	Compound	Stage
M_4 agonist	HTL'878	Ph 1
	Undisclosed	**Preclinical**
M_1 agonist	HTL'318	Ph 1
	HTL'936	Ph 1
	Undisclosed	**Candidate Selection**
	Undisclosed	Discovery
	Undisclosed	Discovery
M_1 / M_4 dual agonist	**Undisclosed**	**Candidate Selection**

We regain a **larger and strengthened IP portfolio** following over $55m of investment from Allergan, including a pipeline of next-generation selective muscarinic agonists with novel and diverse chemistry

Note: **Blue** denotes currently in preclinical stage or about to enter preclinical stage

2

Back in control and executing our own review and planning

Aiming to advance development of the muscarinic programs for future re-partnering

Expert consultant appointed to support our rapid review of all regained muscarinic preclinical and clinical data

Following the outcome of this review, we will focus on rapidly advancing selected muscarinic programs towards new value inflection points

Aiming to re-partner selected muscarinic programs in the near term in-line with our strategy to execute 2 to 3 high value deals every year

Strong track record of extracting value from regained programs (A2a, CGRP)

A2a antagonists	CGRP antagonists	Muscarinic agonists
Shire	teva	Allergan
2012	2015	2016
Regains	Regains	Regains
SOSEI HEPTARES	SOSEI HEPTARES	SOSEI HEPTARES
Re-partnered	Re-partnered	Plan to re-partner
AstraZeneca ✓	biohaven pharmaceuticals ✓	???
2015	2020	

Track record of executing new business development deals from regained programs.
We will immediately commence discussions with potential future out-licensing partners.

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3

Potential to deliver transformative new treatments for patients

Muscarinic M_4 and M_1 receptors are validated targets for psychosis and cognition

Muscarinic M_4 and M_1 receptors represent validated targets for the treatment of psychosis and cognition, respectively

Selective orthosteric agonists have been very challenging despite over 25 years of effort by major global pharma

~20M
SCHIZOPHRENIA


GLOBAL SUFFERERS

~50M
DEMENTIA

$818BN
SOCIETAL COST


COST OF DEMENTIA

1.1%
GLOBAL GDP

Xanomeline, the M_4/M_1 preferring agonist, achieved human Proof of Concept in double-blind, placebo-controlled trials in SZ and AD patients

Selective muscarinic receptor agonist xanomeline as a novel treatment approach for schizophrenia

Anantha Shekhar [1], William Z Potter, Jeffrey Lightfoot, John Lienemann, Sanjay Dubé, Craig Mallinckrodt, Frank P Bymaster, David L McKinzie, Christian C Felder

Effects of xanomeline, a selective muscarinic receptor agonist, on cognitive function and behavioral symptoms in Alzheimer disease

N C Bodick [1], W W Offen, A I Levey, N R Cutler, S G Gauthier, A Satlin, H E Shannon, G D Tollefson, K Rasmussen, F P Bymaster, D J Hurley, W Z Potter, S M Paul

Muscarinic M_4 and/or M_1 receptor agonists **with selectivity** over peripheral muscarinic M_2 and M_3 receptor subtypes have the **potential to be transformative treatments**

Source: World Health Organization

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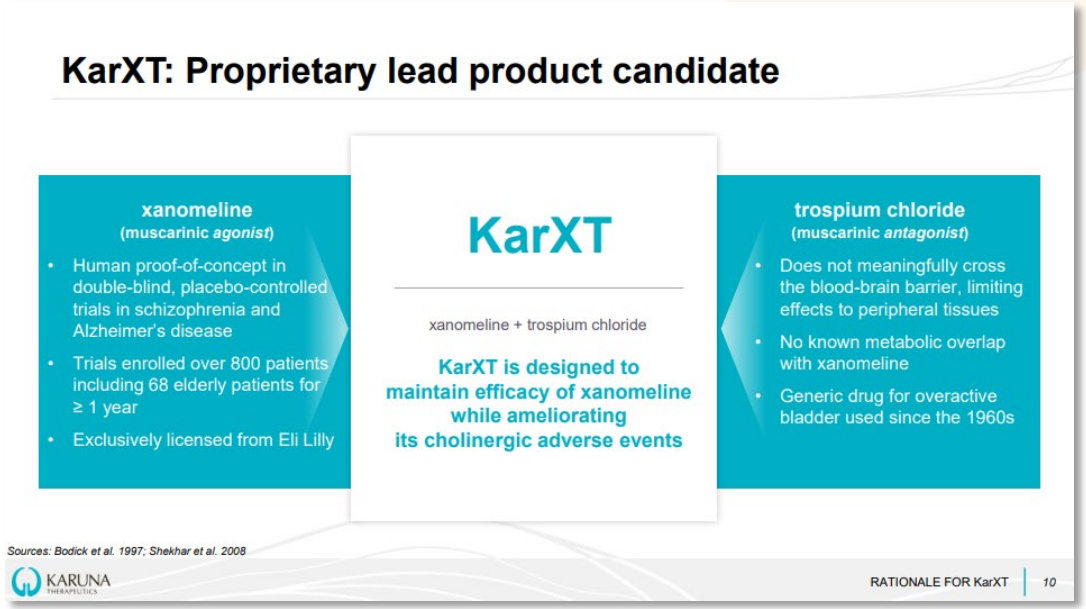
Potential to deliver transformative new treatments for patients

Karuna Therapeutics and Cerevel Therapeutics are advancing supportive muscarinic stories

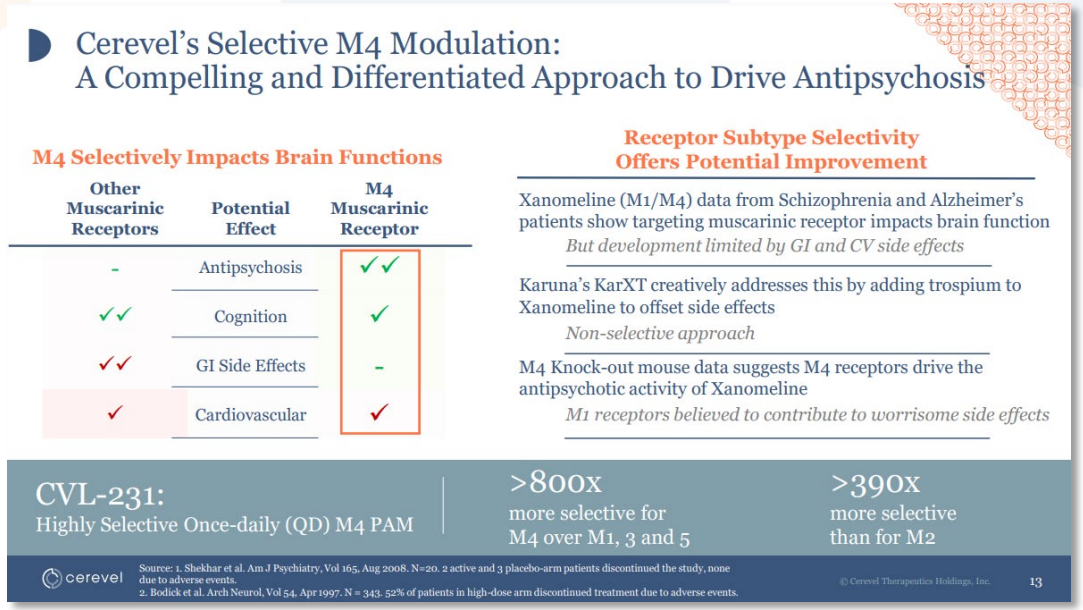
KARUNA THERAPEUTICS

cerevel

KarXT (M_1/M_4 agonist, M_2/M_3 antagonist)



CVL-231 (M_4 PAM)



Karuna Therapeutics' KarXT[1] and Cerevel Therapeutics CVL-231[2] have reawakened investors and the pharma industry to the potential of muscarinic programs for the treatment of psychosis and cognition

1. KarXT is combination of xanomeline (muscarinic M_1/M_4 preferring agonist) and trospium chloride (muscarinic M_2/M_3 antagonist). Source: Karuna Therapeutics Company Presentation (December 2020) LINK
2. CVL-231 is a selective muscarinic M_4 positive allosteric modulator (PAM). Source: Cerevel Therapeutics Company Presentation (November 2020) LINK

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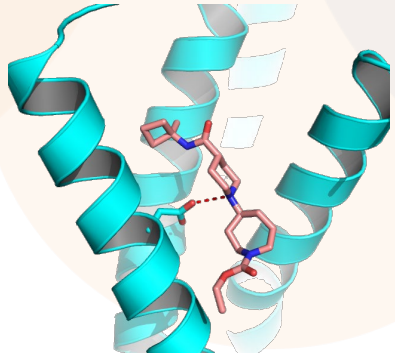
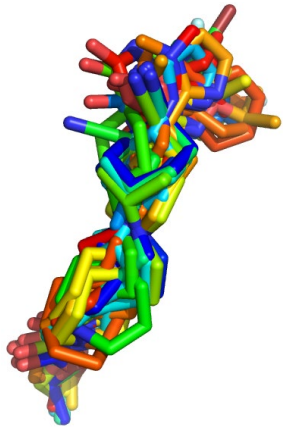
Potential to deliver transformative treatments for patients

M_4 agonist program a potential next-generation, first-in-class treatment for SZ

Using our proprietary StaR® technology, we have developed crystallography systems for Muscarinic receptors stabilized in agonist forms

Details obtained from structures of a compound series enable tuning of interactions and affinities across receptor sub-types





HTL'878

Highly selective M_4 receptor agonist for the treatment of psychosis in schizophrenia and dementias

- Potent orthosteric agonist of the M_4 receptor
- Highly selective vs other muscarinic receptor subtypes
- Highly selective vs other GPCRs and other drug targets
- Excellent CNS penetration and good druglike properties to ensure access to the target (target engagement)

Our StaR® / SBDD precision designed M_4 agonist program is **highly selective for the muscarinic M_4 receptor subtype**, offering a differentiated approach versus the competitors in development

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Potential to deliver transformative treatments for patients

SZ remains a huge unmet medical need

Large market with blockbuster sales profiles…

~20M — SZ patients worldwide

Blockbusters sales profiles despite limited efficacy and severe side effects

$10BN+ (2020) → $13BN+ (2026)

Zyprexa Olanzapine | Seroquel quetiapina | Abilify (aripiprazole) 2, 5, 10, 15, 20, 30 mg Tablets

…Despite no innovation in 70 years

Current treatments use the same MOA from the 1950s

1st Gen	D2 modulating
Atypicals	Dual D2/5HT modulating
2nd Gen Atypicals	Dual D2/5HT modulating

Vraylar (cariprazine) capsules | Rexulti brexpiprazole | Caplyta (lumateperone) capsules

Huge opportunity for HTL'878

- ✓ Selective M_4 agonist
- ✓ Potential First in Class therapy with a novel MOA
- ✓ Improved tolerability
- ✓ Significant need for new treatment options

The severe side effect profile of Atypicals continues to drive high relapse rates, disease progression and discontinuation of treatment – **there is a significant need for new treatment options**

Source: World Health Organization; EvaluatePharma

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Potential to deliver transformative new treatments for patients

Both KarXT and CVL-231 are advancing through clinical patient studies for SZ

KarXT (M_1/M_4 agonist, M_2/M_3 antagonist)

KarXT is a promising drug candidate, however GI side effects have been observed[1]

Summary of safety and tolerability

Well-tolerated with a discontinuation rate equivalent to placebo

Overall completion rate similar between KarXT and placebo (80%)

- The number of discontinuations due to TEAEs was equal in each treatment group (KarXT n=2; placebo n=2)
- All TEAEs were mild or moderate, with the exception of one serious AE: one patient on KarXT discontinued treatment, subsequently sought hospital care for worsening psychosis
- Most common AEs (≥5%) were all mild or moderate in severity and did not lead to any discontinuations
- BP and QTc similar to placebo; 5.5 bpm peak mean placebo-adjusted resting HR increase with downward trend after day 8; no syncope

Dose escalation on KarXT was high and similar to placebo

- Dose escalation based on tolerability
- 91% of KarXT subjects escalated to 125/30 KarXT (vs. 97% on placebo)
- 4% percent de-escalated back to 100/20 KarXT dose (vs. 1% on placebo)

Adverse Events (AEs) and Safety During the Treatment Period

	KarXT (n=89) number (%)	Placebo (n=90) number (%)
Patients with any treatment-emergent adverse events (TEAE)	48 (53.9%)	39 (43.3%)
Patients with a serious TEAE	1 (1.1%)	0 (0%)
Patient with a severe TEAE	1 (1.1%)	1 (1.1%)
Patients with a TEAE leading to withdrawal	2 (2.2%)	2 (2.2%)
AEs ≥ 5%		
Constipation	15 (16.9%)	3 (3.3%)
Nausea	15 (16.9%)	4 (4.4%)
Dry mouth	8 (9.0%)	1 (1.1%)
Dyspepsia	8 (9.0%)	4 (4.4%)
Vomiting	8 (9.0%)	4 (4.4%)
Headache	6 (6.7%)	5 (5.6%)
Somnolence	5 (5.6%)	4 (4.4%)

Safety population received ≥1 dose study medication

KARUNA THERAPEUTICS EMERGENT-1 RESULTS 24

CVL-231 (M_4 PAM)

CVL-231 is a promising drug candidate, however potential CV effects have been observed[2]

Cerevel's product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if obtained.

Undesirable side effects have been observed in Cerevel's product candidates to date. For example, in clinical trials of tavapadon, a dose-dependent increase in the frequency of nausea and headache was observed, with nausea, vomiting, dyskinesia, fall, fatigue, sleep disorder and tremors being the most common adverse events leading to discontinuation of tavapadon. **In clinical trials of CVL-231, some moderate treatment-emergent increases in heart rate and blood pressure were observed following single doses of CVL-231 (>10 mg), which may be due to CVL-231's activity on the M4 receptor subtype and its subsequent reduction of striatal dopamine levels.**

KarXT and CVL-231 have attracted significant funding and investor interest for their respective muscarinic programs despite obvious GI and CV side effect profiles

[1] Source: Karuna Therapeutics Company Presentation (December 2020) LINK

[2] Source: Cerevel Therapeutics Form S-1 Registration Statement (November 2020) LINK

3

Potential to deliver transformative treatments for patients

Highly selective muscarinic M_4 agonist with potential to be best-in-class treatment

M_4 Selectivity Impacts Brain Functions

M_4 Muscarinic Receptor	Potential Effect	Other Muscarinic Receptors
✓✓	Antipsychosis	–
?	Cognition	✓✓
–	GI Side Effects	✓✓
?	CV Side Effects	✓

Receptor Subtype Selectivity Offers Potential Improvement

Xanomeline (M_1/M_4) data from SZ and AD patients show targeting muscarinic receptor impacts brain function

Development limited by GI and CV side effects

Karuna's KarXT addresses this by adding trospium (M_2/M_3 antagonist) to offset the GI and CV side effects

Non-selective approach

Cerevel's CVL-231 is a Positive Allosteric Modulator (PAM) with selectivity for M_4 over M_1, M_3 and M_5 (>800x) and over M_2 (>390x)

However, has demonstrated moderate treatment-emergent increases in heart rate

HTL'878 Highly Selective Muscarinic M_4 agonist

HTL'878 much more selective for M_4 (over M_1, M_2 and M_3) compared with xanomeline and orthosteric agonists have quite different profile to PAMs

Source: Sosei Heptares Internal Data; Cerevel Therapeutics Company Presentation (November 2020) LINK; Shekhar et al. Am J Psychiatry, Vol 165, Aug 2008. N=20. 2 active and 3 placebo-arm patients discontinued the study, none due to adverse events; Bodick et al. Arch Neurol, Vol 54, Apr 1997. N = 343. 52% of patients in high-dose arm discontinued treatment due to adverse events.

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3 Potential to deliver transformative treatments for patients

HTL'878 is safe and well tolerated following evaluation in 120 healthy volunteers

- HTL'878 promising Phase 1 data in healthy volunteers
- Lower dose level of selective M_4 agonist may be sufficient in patients
  - Observed from pharmacodynamic effects including cerebrospinal fluid (CSF) levels of free drug (> pEC50), electrophysiology (EEG) and mismatched negativity (MMN) in ERP, and episodic memory cognitive testing
- Potential for better tolerability and improved therapeutic index versus other muscarinic modulators in development

Phase 1a study (NCT03244228)

Up to 7 days of **oral single** and **twice-daily dosing**.
Safe and well tolerated in the young at dose that is expected to be efficacious

- 89 young subjects (Male)
- 31 elderly subjects (Male and Female)
- No serious adverse events
- No typical muscarinic side effects
- Minor CV effects observed but deemed acceptable when dosed for up to 7 days to a dose level demonstrating SZ-relevant pharmacodynamic effects (as seen with KarXT)

HTL'878 has demonstrated clear validation of a selective M_4 orthosteric agonist on cognitive measures.
More details regarding our development plans for this program will be disclosed later this year

3

Potential to deliver transformative treatments for patients

Progress update regarding HTL'318 and next-generation selective M_1 agonist backups

HTL'318 – safe and well tolerated in humans, evidence of target engagement and effects on cognition

- Safe and well tolerated in humans with very few side effects at likely active doses
- Evidence of target engagement and effects on cognition in AD patients from our Phase 1b study in AD patients (NCT03456349)
  - HTL'318 well tolerated at 28 days using a titration regimen in AD patients on top of donepezil - indications of both pro-cognitive effects and potential effects on neuropsychiatric symptoms (study not powered for statistical significance)
- HTL'318 remains on voluntary clinical hold due to findings of rare tumour in Non-Human Primates (NHPs) in a separate long-term preclinical toxicology study
- No clinical findings of concern have been identified in any human subjects that received HTL'318
  - Extensive testing including imaging has been conducted
- Investigations are ongoing
  - We will conduct our own further toxicology studies before making any decisions regarding HTL'318

Next-generation selective M_1 agonist programs are now also part of our focus

- In parallel we are advancing development of next-generation selective M_1 agonists with new chemistry
- Next-generation compounds are advancing towards preclinical development in 2021

Next-generation M_1 agonists with novel chemistry are advancing.
We will decide by the end of 2021 at the latest which selective M_1 agonist program to prioritize after further analysis.

Summary

1. Sosei Heptares regains worldwide rights to muscarinic agonist programs
2. Executing our own review and will start activities to re-partner selected programs immediately
3. Muscarinic programs highly attractive – selective M_4 agonist and selective M_1 agonist safe and well tolerated at active doses in Phase 1 studies

Locations

SOSEI HEPTARES

PMO Hanzomon 11F

2-1 Kojimachi, Chiyoda-ku

Tokyo 102-0083

Japan

Steinmetz Building

Granta Park, Cambridge

CB21 6DG

United Kingdom

North West House

119 Marylebone Road

London NW1 5PU

United Kingdom