



World leading drug discovery
targeting GPCRs

39th Annual J.P. Morgan Healthcare Conference

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References to "FY" in this presentation for periods prior to 1 January 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 9 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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World leading drug discovery targeting GPCRs

World leader in
GPCR drug discovery
and early development

Proprietary GPCR-targeted
StaR® technology and SBDD
platform capabilities

Japan-anchored biotech, with
state-of-the-art R&D center in
Cambridge, UK

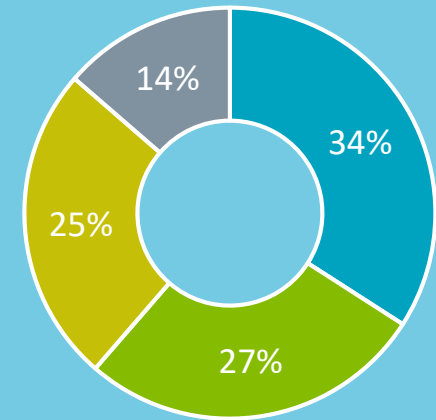
Listed on Tokyo Stock Exchange
(4565-JP)



EVOLVING WITH A SPECIALIST THERAPEUTIC FOCUS

Advancing a broad and deep
pipeline of **over 40** partnered
and in-house programs across
multiple therapeutic areas:

- Neurology
- Immunology
- Gastroenterology
- Other



200+
EMPLOYEES
WORLDWIDE



300+
STRUCTURES
SOLVED



500+
GLOBAL
PATENTS



15+
WORLD-LEADING
PARTNERS

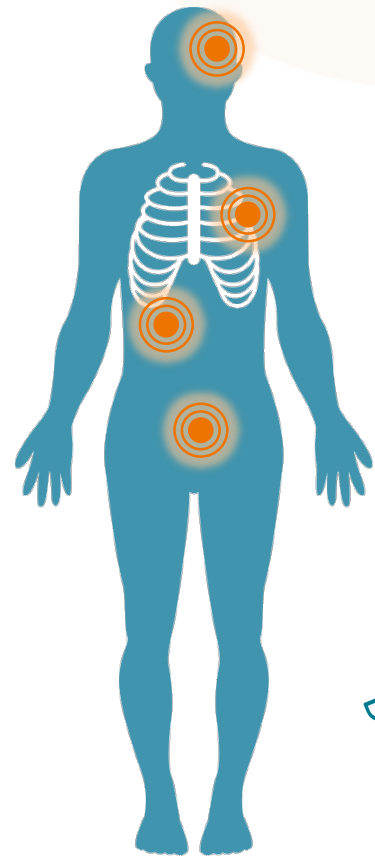


\$700M+
PARTNER REV.
RECEIVED TO DATE¹

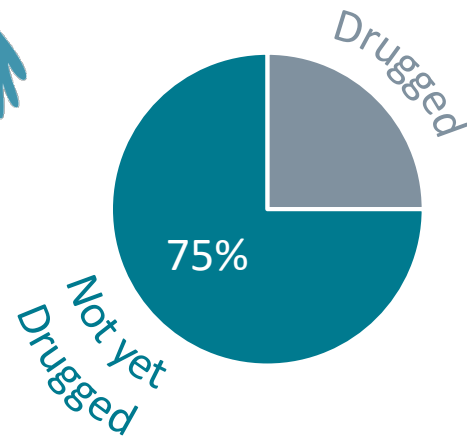
¹ Includes upfront and milestone payments, royalties and R&D funding received from active, inactive and completed partnerships from 2005 to 2020.

We can unlock the potential of GPCRs with our StaR[®] technology

GPCRs are well-known targets with **significant untapped opportunity**



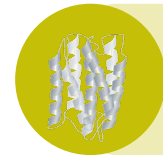
~400
GPCR
PROTEINS



StaR[®] enables us to **unlock the potential of GPCRs** via advanced understanding of their **structure and atomic/molecular interactions**



Unstable
native GPCR



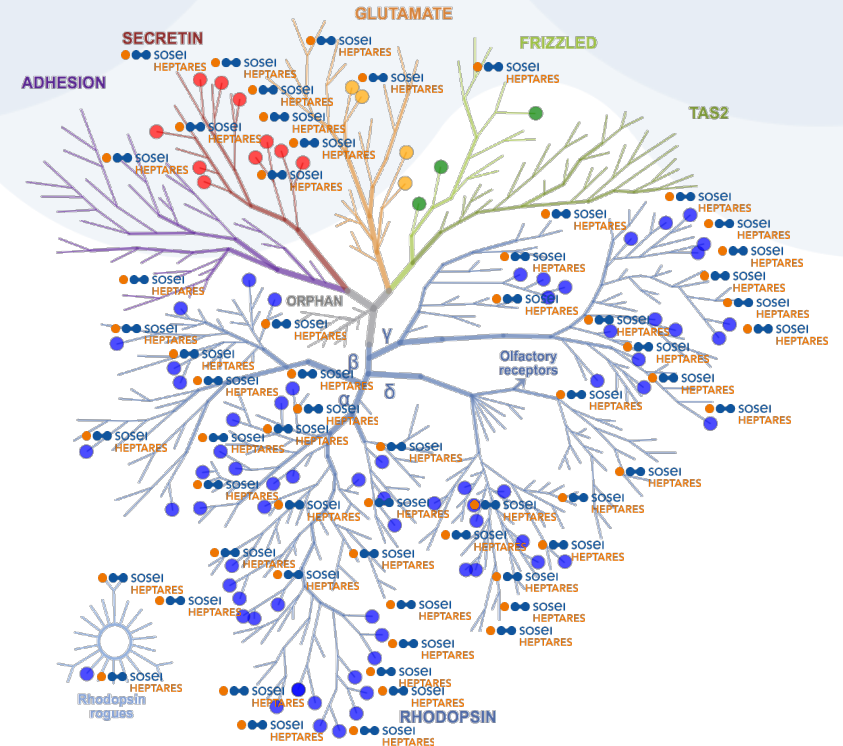
Stabilized
StaR[®] protein

Enables mAb discovery



Novel drug
candidate

SMEs and Peptides



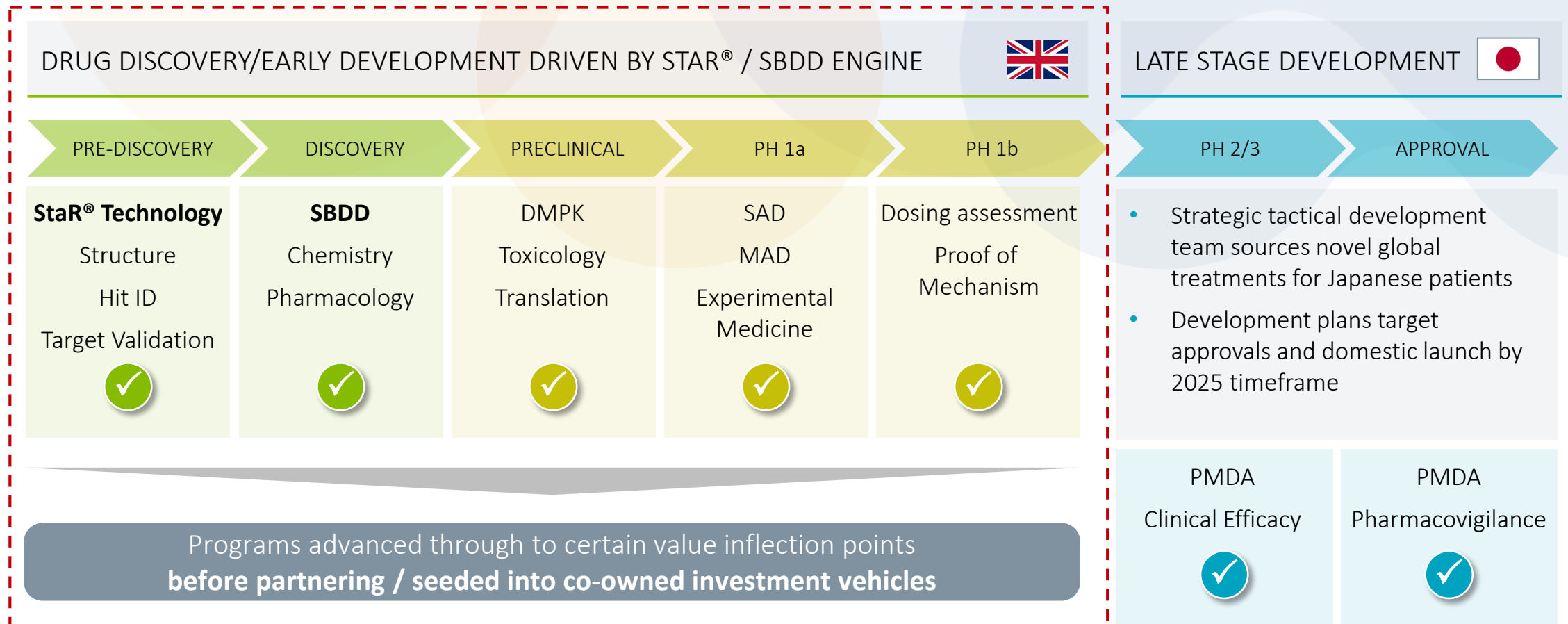
Solved **300+** molecular structures
from **30+** different receptors / **60+** StaRs

Sources: "Unexplored opportunities in the druggable human genome", Nature Reviews, 2016 ;
"Trends in GPCR in Drug Discovery – new agents, targets and indications", Nature Reviews,
4 2017; Management analyses

● Receptors for which a structure has been released in Protein Data Bank (public domain)

●●● Sosei Heptares Receptors for which Sosei Heptares has developed a StaR[®]

Strategy leverages core capabilities in drug discovery and development



Established track record of attracting world-leading partners

Active Partnerships



Active Spin-Out Asset Centric Vehicles



~\$700 million

Upfront and milestone payments, royalties and R&D funding received from partners to date¹

~\$7 billion

Total potential deal value of active partnerships²

¹ Encompasses payments received from active, inactive and completed partnerships from 2005 to 2020. ² Includes potential option fees, upfront, development, regulatory and commercial milestone payments and committed R&D funding. Excludes potential royalty payments.

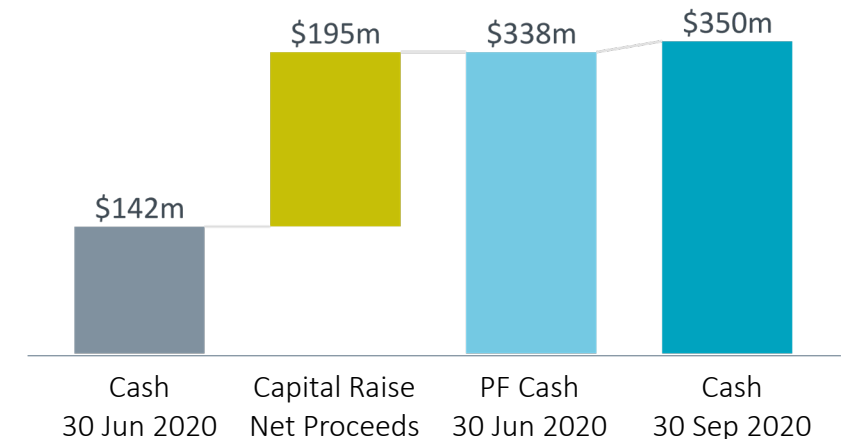
Successful ~\$200m capital raise to fast track our corporate ambition

- ✓ Funds will be deployed, with a focus on **accelerating long-term revenue growth through M&A and future-proofing and expanding our drug discovery platform**
- ✓ **Largest biotech-focused capital raise** out of Japan during COVID-19 pandemic
- ✓ Despite uncertain global economic outlook, **strong levels of investor support** enabled successful transaction
- ✓ Significantly **improved level of financial flexibility** and enhances our strategic options

June 2020



~\$50m Equity Follow-On
~\$150m Euro Yen Convertible Notes



Note: USDJPY FX rate of 107.74 used

Excellent operational progress despite the ongoing pandemic



Energair® Breezhaler® launched in Japan and EU by **Novartis** for treating uncontrolled asthma








Significant scientific progress by **Orexia** and **Inexia** triggered second tranche of funding from Medicxi

Second novel drug candidate (CCR6 antagonist) from **Pfizer** multi-target collaboration entered clinical trials

Created new company **Tempero Bio** to advance clinical development of mGlu5 NAM program in neurological diseases

New collaboration deals with **AbbVie, Biohaven** and **GSK** targeting inflammatory, neurological, gastrointestinal and immunology diseases

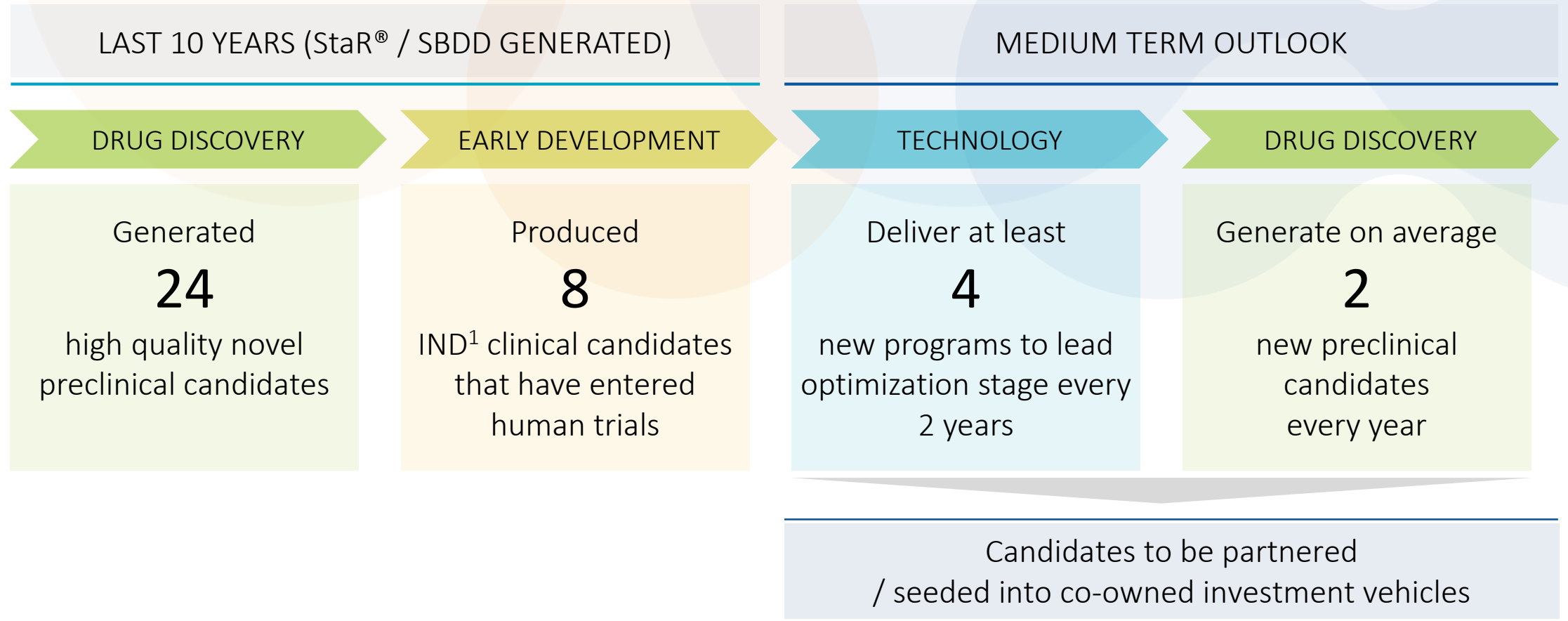
Executing high value collaborations with therapeutic area specialists

Partner	Active Partnered Program	Therapeutic Area	UF / Near Term Payments	Potential deal value ¹
	2020 Collaboration and Licensing Agreement for GPR35 agonist	Gastrointestinal, immunology	\$44m	\$480m+
	2020 Collaboration and Licensing Agreement for CGRP antagonist	Neurology	\$10m	\$380m+
	2020 Discovery Collaboration and Option to License ²	Inflammatory and Autoimmune	\$32m	\$400m+
	2019 Multi-target Collaboration	Multiple; Initial focus on Gastrointestinal	\$26m	\$1.2bn+
 <small>A Member of the Roche Group</small>	2019 Multi-target Collaboration	Multiple	\$26m	\$1.0bn+
	2015 Multi-target Collaboration	Multiple	Nil	\$1.8bn+
	2015 Collaboration and Licensing Agreement for A _{2a} antagonist	Immuno-oncology	\$10m	\$500m+
TOTAL			\$148m	\$5.9bn+

¹ Potential option fees, development, regulatory and commercial milestone payments, plus royalties on global commercial sales;

² AbbVie has the option to expand the collaboration by an additional three targets

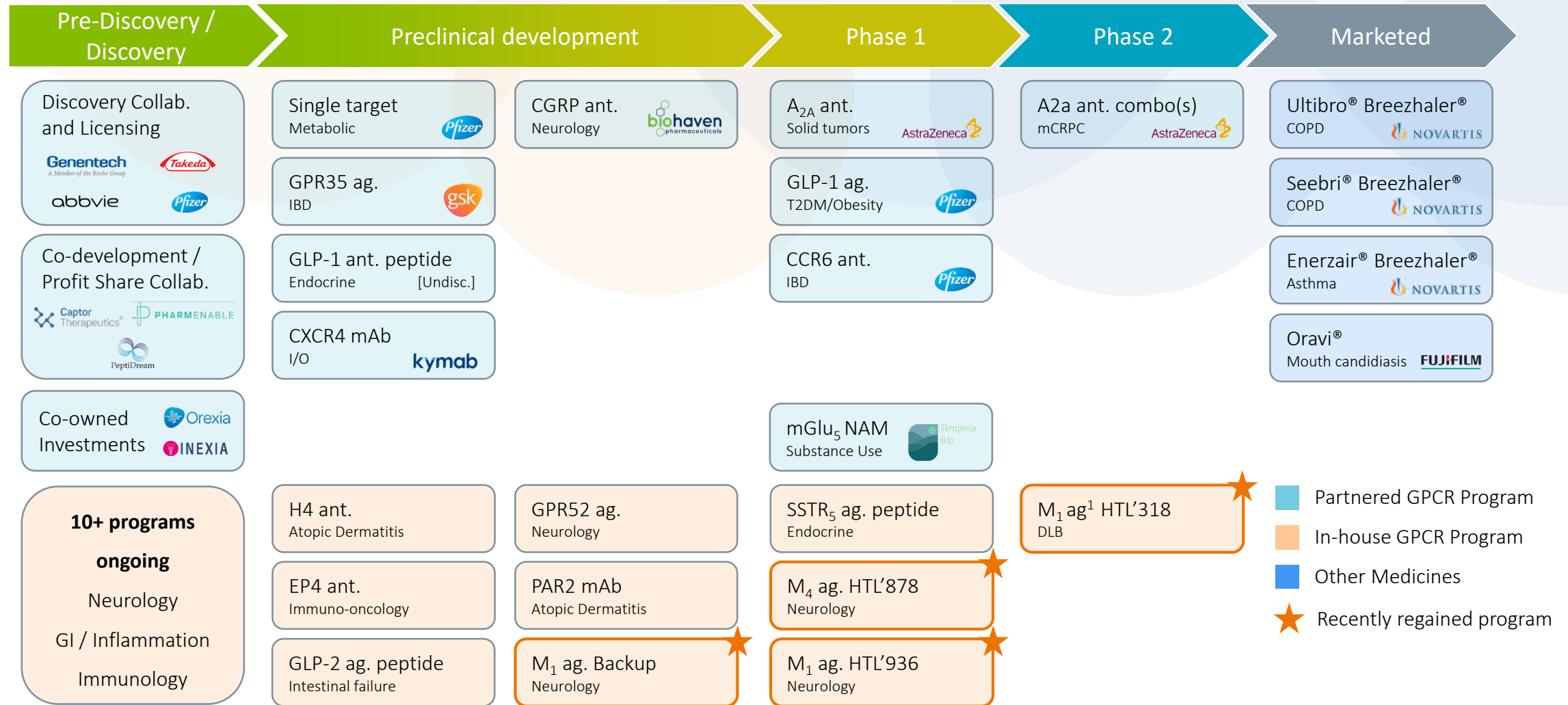
Productive discovery engine generating multiple high quality candidates



Focus on targets across immunology, neurology and gastroenterology, with validated translational biology. Further emphasis on small molecule chemistry with efficient synthesis.

Note: ¹IND = Investigational New Drug

Robust partnered and proprietary pipeline to fuel future value creation



Note: Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG. ¹ Phase 2 trial of HTL0018318 for DLB in Japan has been withdrawn. The Group plans to resubmit a new clinical trial notification for HTL0018318 (or another novel M₁ agonist) to the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in the future.

Regained global rights to muscarinic agonist programs from AbbVie

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 M₄, M₁ and M₁/M₄ 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 regained 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

Potential to deliver transformative new treatments for patients

Muscarinic M₄ and M₁ receptors are validated targets for psychosis and cognition

Muscarinic M₄ and M₁ 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 M₄/M₁ 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 Shekhar¹, 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 Bodick¹, 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 M₄ and/or M₁ receptor agonists **with selectivity** over peripheral muscarinic M₂ and M₃ receptor subtypes have the **potential to be transformative treatments**

Source: World Health Organization

HTL'878 potential to deliver transformative treatments for patients

Schizophrenia remains a huge unmet medical need

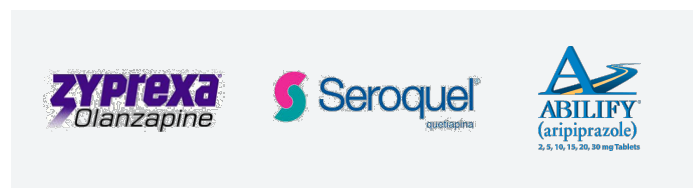


Large market with blockbuster sales profiles...

~20M SZ patients worldwide

Blockbusters sales profiles despite limited efficacy and severe side effects

\$10BN+ (2020) → \$13BN+ (2026)



...Despite no innovation in 70 years

Current treatments use the same MOA from the 1950s

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



Huge opportunity for HTL'878

- ✓ Selective M₄ agonist
- ✓ Potential First in Class therapy with a novel MOA
- ✓ Improved tolerability
- ✓ Significant need for new treatment options in SZ

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

HTL'878 potential to deliver transformative treatments for patients

Highly selective muscarinic M₄ agonist with potential to be best-in-class treatment

M₄ 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 (M₁/M₄) 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 tropium (M₂/M₃ 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 M₄ over M₁, M₃ and M₅ (>800x) and over M₂ (>390x)

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

HTL'878

Highly Selective
Muscarinic M₄ agonist

HTL'878 much more selective for M₄
(over M₁, M₂ and M₃) 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.

Strongly enabled to fast-track our strategic corporate ambitions



Entered a strategic technology collaboration with **Captor Therapeutics**, the European leader in **targeted protein degradation**.

Initial focus to identify small molecules targeting a GPCR with a key role in a strongly validated signalling pathway implicated in **gastrointestinal disorders**.

Dec 2020



Entered a technology collaboration with **PharmEnable** to leverage its proprietary **artificial intelligence-enabled** and medicinal chemistry technologies.

Collaboration to drive novel drug discovery against a challenging **peptidergic GPCR target** associated with **neurological diseases**.

Jan 2021



Priority objectives for FY2021



Commitment to sustainable development goals

- Promote sustainable ESG practices and policies across global business
- Advance coronavirus program and establish collaborations with industry partners to further develop candidates as oral treatments for human coronaviruses



Progress organic growth plan

- Extend technology / platform leadership
- Generate high quality novel candidates
- Advance discovery and development pipeline
- **Execute high value partnerships**



Execute strategic growth plan

- **Transformative revenue-generating acquisition**
- **In-license late-stage assets for Japan market**
- Invest / collaborate in novel technologies
- Expand drug target classes beyond GPCRs

World leading drug discovery targeting GPCRs



G-Protein Coupled Receptors are the largest family of clinically relevant targets in the human genome

Focus on targets across **neurology, immunology, gastroenterology** and **inflammation**, with validated translational biology



Discovery engine generates on average **two preclinical candidates p.a.** to be partnered or seeded into co-owned investment vehicles

Four marketed products and **over 40** partnered and in-house programs in the pipeline, including **eight** assets in Ph I/II¹



Well capitalized to execute on organic and strategic growth plans

Cash balance of \$350m post Jun-20 international offering²

Potential to receive **over \$7bn** in payments from current partnerships³

Our vision is to become one of Japan's global biotechnology and drug discovery champions

Note: ¹ IND clinical candidates produced by StarR®/SBDD platform that have entered human trials; ² Cash balance as of 30 September 2020 based on USDJPY FX rate of 107.74; ³ Includes potential option fees, upfront, development, regulatory and commercial milestone payments and committed R&D funding. Excludes potential royalty payments.

Thank you for your attention

Chris Cargill
Chief Financial Officer

IR@soseiheptares.com

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



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