

# World leading drug discovery targeting GPCRs

UBS Healthcare Virtual 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 centre in Cambridge, UK

Listed on Tokyo Stock Exchange (4565-JP)

200+

EMPLOYEES

WORLDWIDE



WORLD-LEADING

PARTNERS

#### EVOLVING WITH A SPECIALIST THERAPEUTIC FOCUS

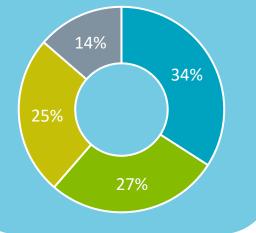
Advancing a broad and deep pipeline of **over 40** partnered and in-house programs across multiple therapeutic areas:

- Neurology
- Immunology
- Gastroenterology
- Other

\$700M+

PARTNER REV.

RECEIVED TO DATE<sup>1</sup>





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

500+

GLOBAL

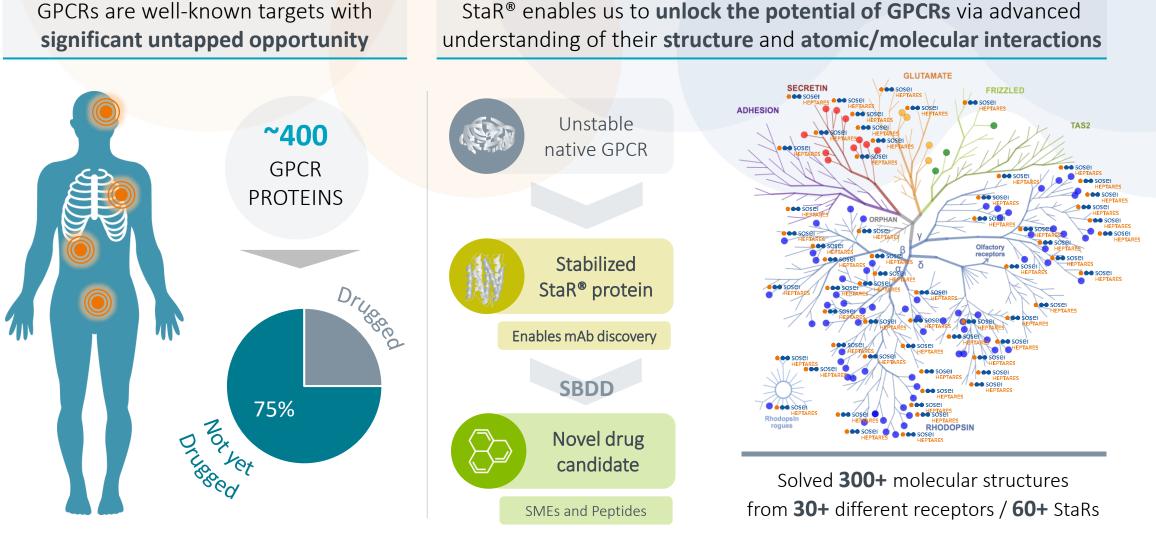
PATENTS

300+

STRUCTURES

SOLVED

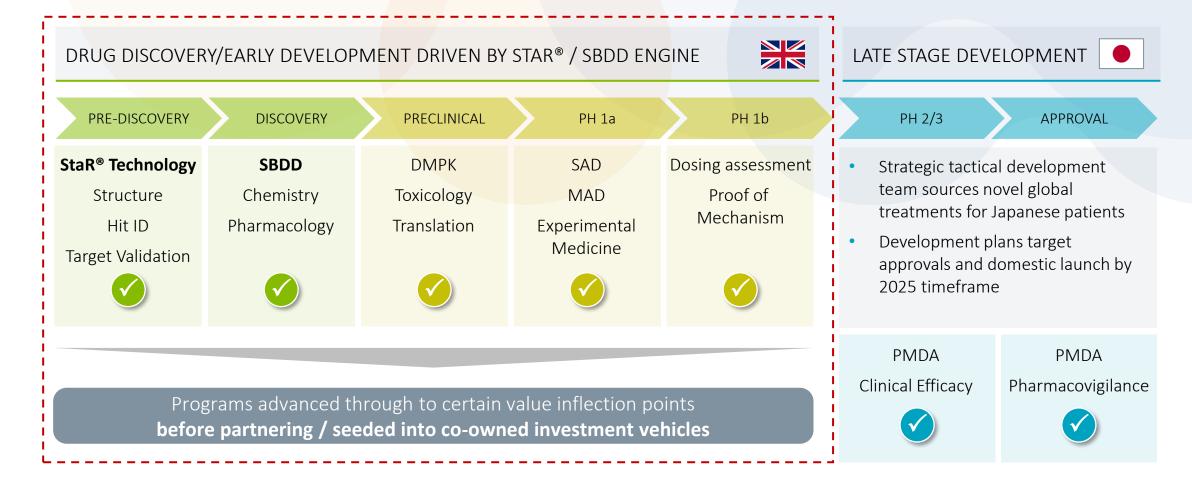
#### We can unlock the potential of GPCRs with our StaR<sup>®</sup> technology



Sources: "Unexplored opportunities in the druggable human genome", Nature Reviews, 2016; "Trends in GPCR in Drug Discovery – new agents, targets and indications", Nature Reviews, 2017; Management analyses Receptors for which a structure has been released in Protein Data Bank (public domain) ••• sosei HEPTARES has developed a StaR®



Core capabilities in drug discovery and early development, with a late-stage development team in Japan focused on in-licensing





#### Established track record of attracting world-leading partners



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



#### Organic growth plan driving our world-leading GPCR drug discovery



Building a broad pipeline to fuel the continued execution of high-value partnerships and co-investments



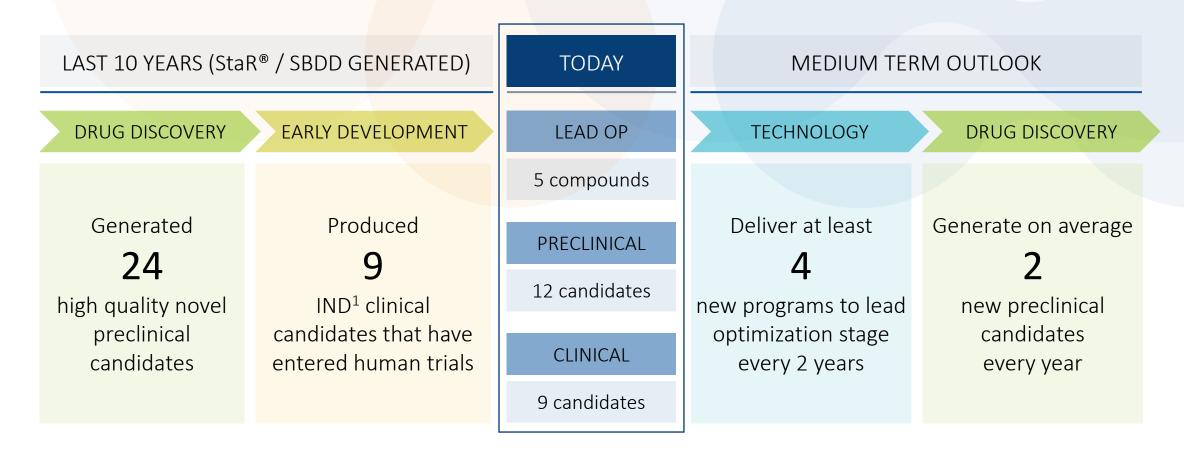
#### Organic growth plan driving our world-leading GPCR drug discovery



All organic growth objectives successfully achieved



Our StaR<sup>®</sup> technology and SBDD platform enables productive drug discovery and generates multiple high quality candidates



One of the most productive GPCR drug discovery teams in the world over the past 10 years

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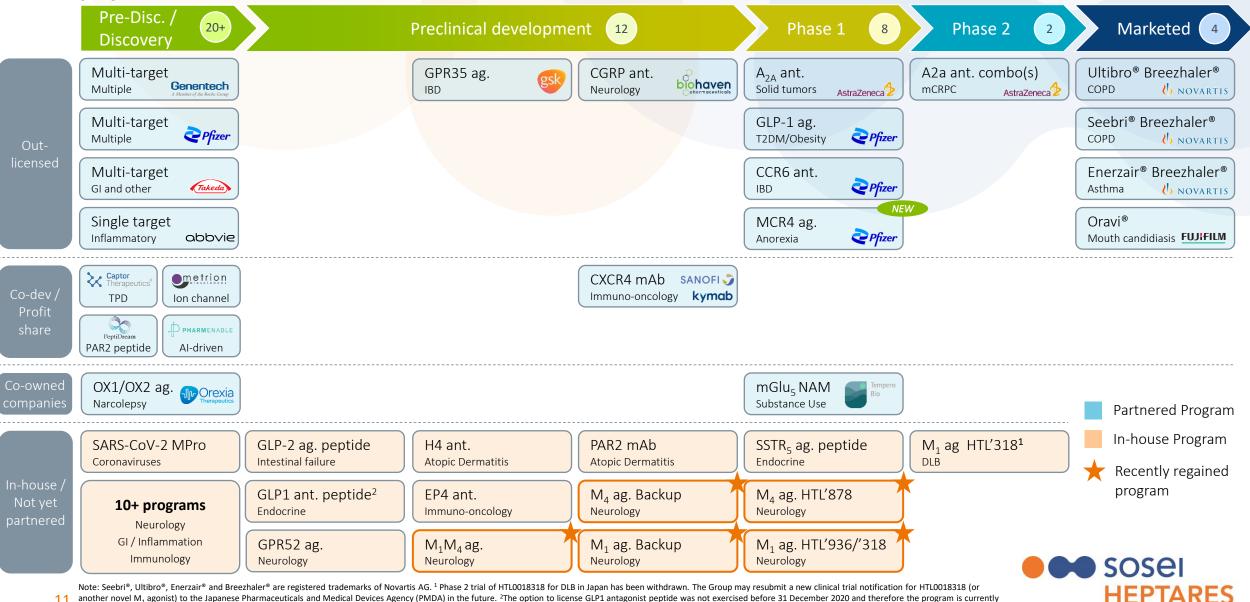
Note: <sup>1</sup> IND = Investigational New Drug

# We continued to make excellent progress in collaborative drug discovery, adding three new pharma partnerships in 2020

Partner	Active Partnered Program	Therapeutic Area	UF / Near Term Payments	Potential deal value <sup>1</sup>
gsk	2020 Collaborat <mark>ion and Licensing</mark> Agreement for GPR35 agonist	Gastrointestinal, immunology	\$44m	\$480m+
biohaven	2020 Collaboration and Licensing Agreement for CGRP antagonist	Neurology	\$10m	\$380m+
abb∨ie	2020 Discovery Collaboration and Option to License <sup>2</sup>	Inflammatory and Autoimmune	\$32m	\$400m+
Takeda	2019 Multi-target Collaboration	Multiple; Initial focus on Gastrointestinal	\$26m	\$1.2bn+
<b>Genentech</b> A Member of the Roche Group	2019 Multi-target Collaboration	Multiple	\$26m	\$1.0bn+
<b>Pfizer</b>	2015 Multi-target Collaboration	Multiple	Nil	\$1.8bn+
AstraZeneca	2015 Collaboration and Licensing Agreement for A <sub>2a</sub> antagonist	Immuno-oncology	\$10m	\$500m+
TOTAL			\$148m	\$5.9bn+
	gulatory and commercial milestone payments, plus royalties on global ollaboration by an additional three targets			

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# We added multiple new partnered and in-house programs to our deep pipeline, which will drive more collaborations and value creation



11 another novel M<sub>1</sub> agonist) to the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in the future. <sup>2</sup>The option to license GLP1 antagonist peptide was not exercised before 31 December 2020 and therefore the program is currently wholly in-house.

# Potential to deliver transformative new treatments for patients

Muscarinic M<sub>4</sub> and M<sub>1</sub> 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



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

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

Anantha Shekhar <sup>1</sup>, 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 <sup>1</sup>, 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

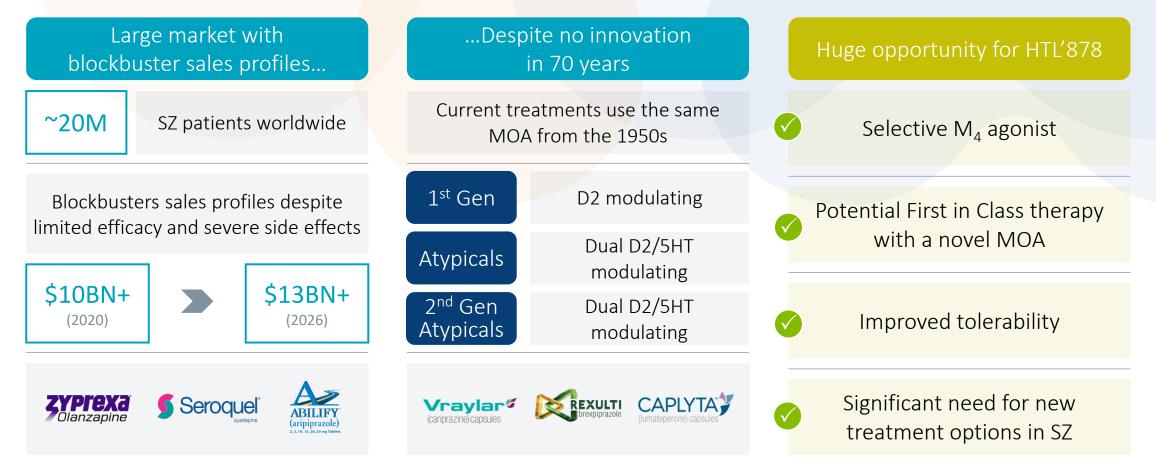
Muscarinic  $M_4$  and/or  $M_1$  receptor agonists with selectivity over peripheral muscarinic  $M_2$  and  $M_3$  receptor subtypes have the **potential to be transformative treatments** 



Source: World Health Organization

## HTL'878 potential to deliver transformative treatments for patients

Schizophrenia remains a huge unmet medical need



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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HTL'878 is now the focus of increased capital allocation from us to enable acceleration, whilst maintaining investment other programs

Program	Compound	Stage	FY2021	FY2022	Muscarinic budget R&D allocation <sup>*</sup>
M <sub>4</sub> agonist	HTL'878	Ph 1	Preparation for Phase 2	Phase 2 start Phase 2 trial activity	50%
M <sub>1</sub> agonist	HTĽ 318	Ph 1	Toxicity test Data analysis / comparison with backup	Prioritization of which selective M <sub>1</sub> agonist	25%
	Undisclosed (M <sub>1</sub> Backup)	Candidate Selection	Preclinical development	program to progress, to be decided by end of 2021	2370
M <sub>1</sub> / M <sub>4</sub> dual agonist	Undisclosed	Candidate Selection	Preclinical development		25% 🔶
Portfolio Partnering Activity			Active negotiations with multiple potential partners	Targeting partnership execution by end of 2021	-

Note: Progress schedule outlined for key muscarinic programs only. \*Budget allocation within the Muscarine program, not overall R&D budget allocation



#### Strategic growth plan driving corporate value expansion



Adding new revenues, and accessing new technologies, to expand our future-proof our capabilities





### Summary Financial Highlights (FY20 and 1Q 21)



Our balanced business model supports a **biotech with a unique investment/risk profile**. **Strong potential upside** from novel drug discovery, with the **stability of sustainable financials** 

Note: USD:JPY FX rates used - 108.91 (FY2021), 106.77 (FY2020) and 109.03 (FY2019)



#### Priority objectives for FY2021

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



# 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



#### Thank you for your attention

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