World-leading drug discovery targeting GPCRs

40th Annual J.P. Morgan Healthcare Conference
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The important factors that could cause our actual results, performance or achievements to differ materially from those in the forward looking statements include, among others, risks associated with product discovery and development, uncertainties related to the outcome of clinical trials, slower than expected rates of patient recruitment, unforeseen safety issues resulting from the administration of our products in patients, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products obsolete, and other factors. These factors include, without limitation, those discussed in our public reports filed with the Tokyo Stock Exchange and the Financial Services Agency of Japan. Although the Company believes that the expectations and assumptions reflected in the forward-looking statements are reasonably based on information currently available to the Company’s management, certain forward looking statements are based upon assumptions of future events which may not prove to be accurate. The forward looking statements in this document speak only as at the date of this presentation and the company does not assume any obligations to update or revise any of these forward looking statements, even if new information becomes available in the future.

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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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We are a world-leading team of GPCR drug hunters

**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


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**200+** EMPLOYEES WORLDWIDE

**340+** STRUCTURES SOLVED

**500+** GLOBAL PATENTS

**15+** WORLD-LEADING PARTNERS

**$500M+** CASH ON BALANCE SHEET

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**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

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34%

27%

25%

14%
We unlock the potential of GPCRs with our StaR® technology

GPCRs are well-known targets with significant untapped opportunity

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

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

Unstable native GPCR

Stabilized StaR® protein Enables mAb discovery

Novel drug candidate SMEs and Peptides

Solved 340+ molecular structures from 40+ different receptors / 70+ StaRs

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

Receptors for which Sosei Heptares has developed a StaR®
Core capabilities in drug discovery and early development

<table>
<thead>
<tr>
<th>DRUG DISCOVERY/EARLY DEVELOPMENT DRIVEN BY STAR® / SBDD ENGINE</th>
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<tbody>
<tr>
<td><strong>PRE-DISCOVERY</strong></td>
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<tr>
<td><strong>StaR® Technology</strong></td>
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<tr>
<td>Structure</td>
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<tr>
<td>Hit ID</td>
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<tr>
<td>Target Validation</td>
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</tbody>
</table>

- Programs advanced through to certain value inflection points before partnering / seeded into co-owned investment vehicles

<table>
<thead>
<tr>
<th>LATE STAGE DEVELOPMENT</th>
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<td><strong>PH 2/3</strong></td>
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<tr>
<td>PMDA Clinical Efficacy</td>
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</table>

- **Strategic tactical development team sources novel global treatments for Japanese patients**
- **Development plans target approvals and domestic launch by 2025 timeframe**
Our approach is validated through 20+ active GPCR programs with world class partners.

Active Partnerships: We have active partnerships with world-class companies such as Abbvie, Neurocrine, Biohaven, Captor Therapeutics, Hisamitsu, Genentech, GSK, Invenio AI, Kymab, Metron, Novartis, PeptiDream, Pharmaenable, Takeda, TWIST Bioscience, and Verily.

Active Spin-Out Asset Centric Vehicles: Our active spin-out asset-centric vehicles include SOSEI HEPTARES, Medicxi, and Aditum Bio.

- **~$800 million**: Upfront and milestone payments, royalties and R&D funding received from partners to date. This figure encompasses payments received from active, inactive and completed partnerships from 2005 to 2020.
- **~$7 billion**: Total potential deal value of active partnerships. This includes potential option fees, upfront, development, regulatory and commercial milestone payments and committed R&D funding. Excludes potential royalty payments.

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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.
Ten drug candidates generated from our SBDD platform have been successfully advanced into clinical trials in the past 7 years.

We are one of the most productive drug discovery teams in the world over the past 10 years. Up to six new preclinical candidates expected in the next 2 years across both internal and collaboration programs.

*T5 programs (1 x Phase 1, 2 x Preclinical, 2 x Discovery) have been prioritised for academic or industrial partnerships. More information here: [https://soseiheptares.com/other-programs-for-partnering](https://soseiheptares.com/other-programs-for-partnering)
Broad and balanced pipeline of partnered and in-house programs, plus new technology collaborations will drive long-term momentum

Out-licensed
- Multi-target
  - Multiple
- Multi-target
  - GI and other
- Single target
  - Inflammatory

Co-dev / Profit share
- Co-owned companies
  - OX1/OX2 ag.
    - Narcolepsy
- In-house / Not yet partnered
  - SARS-CoV-2 MPro
    - Coronaviruses
  - PAR2 mAb
    - Atopic Dermatitis
  - 10+ other programs

Pre-Disc. / Discovery
- Multi-target
  - Multiple
- Multi-target
  - GI and other
- Single target
  - Inflammatory

Preclinical studies
- M2, M4 ag.
  - Neurology
- M1 Ag.
  - B/U
  - Neurology
- GPR35 ag.
  - IBD
- CXCR4 mAb
  - Immuno-oncology

Phase 1
- M2 ag.
  - HTL’878
  - Neurology
- M1 ag.
  - HTL’936/318
  - Neurology
- CGRP ant.
  - Neurology
- MC4 ant.
  - Anorexia
- GLP-1 ag.
  - T2DM/Obesity
- CCR6 ant.
  - IBD
- A2a ant.
  - mCRPC

Phase 2
- GLP-1 ant.
  - T2DM/Obesity
- CCR6 ant.
  - IBD
- A2a ant.
  - mCRPC
- MC4 ant.
  - Anorexia

Marketed
- Ultibro® Breezhaler®
  - COPD
- Seebri® Breezhaler®
  - COPD
- Enerzair® Breezhaler®
  - Asthma
- Oravi®
  - Mouth candidiasis

Partnered Program
In-house Program
To be discussed further on following slides

Note: Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG. * The in-house pipeline displayed above includes fully funded programs only and excludes back-up programs and similar indication programs for one target. For example – A2a ant, SSTR5 ag, GLP-1 ant, GLP-2 ant, M1 and M4 backup programs (list not exhaustive). ** AstraZeneca have removed the A2a program from their clinical pipeline as at Q3 2021.
New strategic collaboration with Neurocrine to progress a portfolio of selective Muscarinic agonists

$100m upfront received and up to $2.6bn in future economics

1. Neurocrine gained **rights to a portfolio of potential best-in-class selective muscarinic receptor agonists** in development for the treatment of major CNS disorders

2. Sosei Heptares received **US$100 million upfront**

3. Sosei Heptares to receive **ongoing R&D funding** and **up to US$1.5 billion** in potential development and regulatory milestones, **up to US$1.1 billion** in commercial milestones, **plus tiered up to mid-teen percentage royalties** on net sales

4. Sosei Heptares also **retained the rights to develop all muscarinic M1 agonists in Japan in all indications**, with Neurocrine receiving co-development and profit share options

Developing novel muscarinic receptor agonists for schizophrenia and other neuropsychiatric disorders
# Neurocrine M4 agonist (HTL’878) program – 4th-gen candidate aiming to be a highly effective and safer treatment for Sz

Of the fourth-generation treatments in development, HTL’878 stands out as a potentially superior approach

<table>
<thead>
<tr>
<th></th>
<th>Efficacy</th>
<th>Safety</th>
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<tbody>
<tr>
<td></td>
<td>Positive symptoms</td>
<td>Negative symptom</td>
</tr>
<tr>
<td>Number of patients</td>
<td>20M*</td>
<td>11.5M*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MoA</th>
<th>Typical medicine</th>
<th>Peak sales example</th>
<th>Generation</th>
<th>Number of patients</th>
<th>Number of patients</th>
<th>Number of patients</th>
<th>Weight gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical antipsychotic</td>
<td></td>
<td></td>
<td>1st</td>
<td></td>
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<td></td>
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<tr>
<td>D2 Ant</td>
<td>Haldol</td>
<td>(Historic data unavailable)</td>
<td></td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>Atypical antipsychotics</td>
<td></td>
<td></td>
<td>2nd</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2 Ant + 5-HT Regulator</td>
<td>Zyprexa Risperdal</td>
<td>Zyprexa $5,000M+</td>
<td>2nd</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td></td>
<td>Latuda</td>
<td>(2010)</td>
<td></td>
<td></td>
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<tr>
<td>D2 partial Ag + 5-HT Regulator</td>
<td>Abilify REXULTI</td>
<td>Abilify $6,100M+</td>
<td>3rd</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>Latuda</td>
<td>(2013)</td>
<td></td>
<td></td>
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<tr>
<td>M4 Agonist***</td>
<td>KarXT CVL-231</td>
<td>-</td>
<td>4th</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>HTL’878</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*As 1 patient can have several symptoms, number of patients in 3 symptoms is overlapping
**Drug-induced movement disorders including involuntary or uncontrollable movements. tremors, muscle contractions. It is said to be related with D2 receptor occupancy balance.
***Expected efficacy and expected safety derived from ongoing clinical trials of KarXT and CVL-231.

Four upcoming wholly-owned programs prioritised for development over the next 12 to 24 months

- **Schizophrenia and Psychosis**
  - GPR52 agonist
  - Once daily oral small molecule
  - 24hr target engagement

- **Atopic Dermatitis**
  - H4 antagonist
  - Once daily oral small molecule
  - To be used as a monotherapy or in combination

- **Immunosuppression in solid tumors**
  - EP4 antagonist
  - Once daily oral small molecule
  - To be used in combination with checkpoint inhibitors

- **Inflammatory Bowel Disease**
  - EP4 agonist
  - Oral GI restricted
  - Good potency and selectivity
  - Minimal GI systemic exposure
New initiatives and future innovations
Strategic growth plan driving corporate value expansion

Seeking to add new revenues, access new technologies, and expand and future-proof our capabilities

OBJECTIVE

Capital raise completed to pursue revenue focused deals in 2022

OBJECTIVE

Seek out revenue-generating opportunities

Invest / collaborate in novel technologies

OBJECTIVE

Expand drug target classes beyond GPCRs

In-license late-stage programs for Japan

OBJECTIVE

Add new technology capabilities to our SBDD platform

Bring international medicines to Japanese patients in areas of unmet need
Three big challenges in drug discovery and development

**KEY OPPORTUNITY**

**Choosing**
the right target

- Will modulating the target affect disease?
- Can a good modulator of the target be found?

**Discovering**
a therapeutic agent

- Identifying a modulator with the appropriate profile
- Differentiating from competitors (if any)

**Conducting**
the right patient studies

- Demonstrating the value of the agent in treating disease
- Utilizing biomarkers to support patient stratification

Our greatest opportunity is to leverage technology to choose the right drug targets that will become the transformational therapies of the future.
In January 2021 we established our **New target ID and validation (TIV) framework** to accelerate our hunt for novel GPCR targets...

**Aim**
To support the identification and validation of **new drug GPCR targets** across our core therapeutic areas (GI, immunology, immuno-oncology and neuroscience)

**How**
By leveraging top-end external company **omics platforms/databases** and validation capabilities

**Why**
To add exciting novel GPCR targets to our pipeline which have evidence of a **direct involvement in a disease / mechanism process** to fuel partnering activity and higher value creation

Continuously expanding our know-how and SBDD platform to maintain our leadership position in GPCR drug discovery
...with **three new key partnerships executed** in the past 12 months

<table>
<thead>
<tr>
<th><strong>verily</strong></th>
<th><strong>InveniAI</strong></th>
<th><strong>Twist Bioscience</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Research collaboration combining Verily’s immune profiling capabilities and SH’s StaR® platform and SBDD capabilities</td>
<td>- Discovery collaboration combining InveniAI’s AI-powered platform for target discovery with SH’s GPCR SBDD and early development capabilities</td>
<td>- Discovery collaboration combining Twist’s synthetic antibody libraries and bioinformatics expertise with SH’s StaR® platform</td>
</tr>
<tr>
<td>- Collaboration aims to identify GPCRs expressed in immune cells, enhance our understanding of their functional relevance and prosecute as potential drug targets in <strong>immune-mediated diseases</strong></td>
<td>- Collaboration aims to identify new therapeutic product concepts for <strong>immune diseases</strong> and generate novel compounds that could improve responses to existing immunotherapies</td>
<td>- Collaboration aims to discover <strong>therapeutic antibodies</strong> against GPCRs identified by SH</td>
</tr>
<tr>
<td>- SH will have exclusive, full global rights to develop and commercialize any antibody leads identified and directed to the targets of interest</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Leveraging the best technologies to drive synergies with our platform and accelerate novel drug discovery
New multi-target collaboration with Verily aims to accelerate the development of novel therapies for immune-mediated diseases.

300+ Potential GPCRs

High priority candidate targets

Structure-based drug development

verily Immune Profiler

Data
8 million readouts per sample + Reference data

Analysis
Integrative analysis + Quality Control

Cell sorting & frequencies
Gene expression
Disease score, treatment / response
Chromatin accessibility & contacts
Prioritized pathways & signatures
Multi-faceted evidence
Public datasets
Wet lab validation

= Better Tx & Better Dx

StaR® Platform

GPCRs are proteins that represent the target and site of action for more drugs marketed today or in development than any other class of proteins.
We are building a **Future Innovations Portfolio** to explore ways to leverage our platform expertise in new directions.

<table>
<thead>
<tr>
<th>Targeted GPCR Degradation</th>
<th>Ion Channels</th>
<th>COVID-19 Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Captor Therapeutics" /></td>
<td><img src="image2.png" alt="Metrion Biosciences" /></td>
<td><img src="image3.png" alt="Wellcome" /></td>
</tr>
<tr>
<td>• Technology collaboration to initially identify novel small molecules that target a GPCR for degradation as potential therapeutic agents for <strong>gastrointestinal disorders</strong></td>
<td>• Technology collaboration to demonstrate the potential of SBDD to address disease-associated ion channels</td>
<td>• In-house program funded by Wellcome through the Covid-19 Therapeutics Accelerator</td>
</tr>
<tr>
<td>• Further aim to generate high resolution structural information around the GPCR-E3 ligase complex to enhance drug discovery efforts</td>
<td>• Initial focus to identify novel, highly specific drug leads for further development against a single ion channel associated with <strong>neurological diseases</strong></td>
<td>• Currently advancing the pre-clinical development of novel oral anti-viral small molecules targeting the main protease of SARS-CoV-2 (M(^{pro})) as potential treatments for <strong>COVID-19</strong></td>
</tr>
</tbody>
</table>

**Our SBDD platform is also now being applied to areas outside our traditional GPCR space.**
Priority objectives for FY2022

**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**
- Invest / collaborate in novel technologies
- Diligence potential strategic M&A opportunities
- Diligence potential opportunities for Japan
- Expand drug target classes beyond GPCRs

**Commitment to sustainable development goals**
- Promote sustainable ESG practices and policies across global business
- Advance Mpro inhibitor program and seek collaboration to further develop candidates as oral treatments for human coronaviruses
Appendix
**Our new partner Neurocrine** is committed to a transformative treatment for Schizophrenia with the M4 agonist HTL-0016878

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### Large addressable market with blockbuster sales profiles...

<table>
<thead>
<tr>
<th>Schizophrenia patients worldwide</th>
<th>~20M</th>
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Blockbusters sales profiles despite limited efficacy and severe side effects

<table>
<thead>
<tr>
<th>Current treatments use the same mechanism of action from the 1950s</th>
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<tbody>
<tr>
<td><strong>1st Gen</strong></td>
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<tr>
<td><strong>Atypical</strong></td>
</tr>
<tr>
<td><strong>2nd Gen Atypical</strong></td>
</tr>
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### Limited innovation in 70 years

- **Highly selective M4 agonists**
- **Potential Best-in-Class therapy** with a novel mechanism
- **Improved tolerability**
- **Significant need for new treatment options**

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The current standard of care can be improved. Selective M4 agonism represents a unique opportunity

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Source: World Health Organization; EvaluatePharma

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The current standard of care can be improved. Selective M4 agonism represents a unique opportunity
## Partnered Pipeline

<table>
<thead>
<tr>
<th>Compound</th>
<th>Target / Mechanism of Action</th>
<th>Modality</th>
<th>Indication</th>
<th>Partner</th>
<th>Disc.</th>
<th>PCC</th>
<th>Ph1</th>
<th>Ph2</th>
<th>Ph3</th>
<th>App</th>
<th>Mkt</th>
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<tbody>
<tr>
<td><strong>Traditional Out-licensing Collaborations</strong></td>
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<td>Seebrï Breezhaler®</td>
<td>LAMA</td>
<td>SME</td>
<td>COPD</td>
<td>Novartis</td>
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<tr>
<td>Ultibro® Breezhaler®</td>
<td>LAMA+LABA</td>
<td>SME</td>
<td>COPD</td>
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<tr>
<td>Enerzair® Breezhaler®</td>
<td>LAMA+LABA+ICS</td>
<td>SME</td>
<td>Asthma</td>
<td>Novartis</td>
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<tr>
<td>ORAVI®</td>
<td>Antifungal agent miconazole</td>
<td>SME</td>
<td>Oropharyngeal candidiasis</td>
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<tr>
<td>Imaradenant**</td>
<td>Adenosine A2a ant. combo</td>
<td>SME</td>
<td>mCRPC</td>
<td>AstraZeneca</td>
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<tr>
<td>HTL’878</td>
<td>Muscarinic M4 agonist</td>
<td>SME</td>
<td>Neurology diseases</td>
<td>neurocrine</td>
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<tr>
<td>HTL’318 ¹</td>
<td>Muscarinic M1 agonist</td>
<td>SME</td>
<td>Neurology diseases</td>
<td>neurocrine</td>
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<td>Neurology diseases</td>
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<td>Neurology diseases</td>
<td>neurocrine</td>
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Note: SME = small molecule, LME = large molecule. Seebrï®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG. ** AstraZeneca have removed the A2a program from their clinical pipeline as at Q3 2021
### Partnered Pipeline (cont’d)

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# In-house Pipeline

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