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References to “FY” in this presentation are to the Company's fiscal years, namely the 12-month periods commencing in each case on April 1 of the year indicated and ending on March 31 of the following year, unless specifically otherwise indicated.
A Japan-listed biotech with a difference

- **World-leader in GPCR-focused drug design** based on unique IP protected StaR® GPCR technology & enabled SBDD platform

- **Partnered clinical-stage pipeline** in neurology, immuno-oncology, CNS & other diseases, with $5bn plus in potential economics

- **Proprietary pipeline** led by dementia with Lewy bodies (DLB) Phase 2 program in Japan, plus multiple novel candidates in development

- **Robust royalties from legacy respiratory products** provide source non-dilutive cash flows

- **Strong cash position of ~$260m** to drive global growth strategy

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Global operations and aspirations - aiming to build Japan’s first global biotech champion

---

1 Stabilized receptor technology
2 Structure-based drug design

Listed 2004 in Tokyo (TSE Mothers: 4565)
Market capitalization: c.$1.3bn
Global management team
Main scientific campus in the U.K.
Unique management team for a Japan-listed company

Significant pharma and biotech expertise

Peter BAINS
Chief Executive Officer
- Former Senior VP of International Commercial Development at GSK
- Former CEO of Syngene

Andrew OAKLEY
Chief Financial Officer
- Former CFO of Actelion Pharmaceuticals Ltd
- Former CFO of Vectura plc

Dr. Malcolm WEIR
Chief R&D Officer
- CEO and Co-Founder Heptares
- Former Head of Molecular Science Division at Glaxo Wellcome

Dr. Tim TASKER
Chief Medical Officer
- GSK and Former Executive VP of Clinical Development at Evotec
Why do we target G-Protein-Coupled Receptors (GPCRs)?

**GPCRs are active in a wide range of disease areas**

- ~400 GPCR targets active in diseases
- ~34% of FDA approvals target GPCRs
- 27% of global sales are GPCR drugs

**Targeting a new FIC and/or improved BIC GPCR medicines**

<table>
<thead>
<tr>
<th>BEST-IN-CLASS</th>
<th>FIRST OR BEST-IN-CLASS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugged 27%</td>
<td>In trials 17%</td>
</tr>
<tr>
<td>As yet undrugged 56%</td>
<td></td>
</tr>
</tbody>
</table>

**FIRST-IN-CLASS**

- Neurological disorders
- Oncology
- Gastrointestinal diseases
- Cardiovascular
- Metabolic disorders
- Respiratory

Huge opportunity to create new drugs or improve existing drugs

---

StaR® is Revolutionary for GPCR Structure-Based Drug Design

StaR® technology stabilizes and “unlocks” GPCRs

Native GPCRs are unstable, don’t maintain shape, and are difficult to drug

Patent-protected
StaR® technology stabilizes GPCRs on a commercial level

With a StaR® GPCR, the high-tech tools of science can develop structures...

X-ray Crystallography
Biophysical Mapping
Cryo-EM

... and stable GPCR structures enable a variety of SBDD technologies for drug design

Structural information creates better, differentiated drug candidates

- Improved physiochemical properties
- Better safety and efficacy
- Reduced clinical attrition
- Small molecule, peptide or antibody discovery

Unique, scalable and sustainable platform, delivering differentiated pipeline candidates
Leveraging unique GPCR technology to deliver differentiated drug candidates

**StaR® technology + SBDD platform**

**Partner**
(Traditional out-licensing / major indications)
- Allergan
- AstraZeneca
- Pfizer

**Partner**
(Co-development/ profit share)
- PeptiDream
- kymab

**Proprietary**
(Self-commercialize / rare / orphan / specialty)
- M₁
- mGlu₅
- SSTR
- CGRP
- GLP-1
- GLP-2

Risk-balanced business model creates and captures optimal value

---

1. Stabilized receptor technology
2. Structure-based drug design
## Advancing a Partnered GPCR pipeline in multiple therapeutic areas

Balanced and diversified

### Partnered GPCR Pipeline (Traditional out-licensing/collaboration projects)

<table>
<thead>
<tr>
<th>Product/Program</th>
<th>Modality</th>
<th>Indication</th>
<th>Partner</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Marketed</th>
</tr>
</thead>
<tbody>
<tr>
<td>M₁ agonist</td>
<td>SME</td>
<td>Alzheimer’s disease</td>
<td>Allergan</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>M₄ agonist</td>
<td>SME</td>
<td>Alzheimer’s disease</td>
<td>Allergan</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>M₁/M₄ dual agonist</td>
<td>SME</td>
<td>Alzheimer’s disease</td>
<td>Allergan</td>
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<td></td>
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</tr>
<tr>
<td>A2a antagonist</td>
<td>SME</td>
<td>Cancer I/O</td>
<td>AstraZeneca</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>A2a antagonist</td>
<td>SME</td>
<td>Cancer I/O</td>
<td>AstraZeneca</td>
<td></td>
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</tr>
<tr>
<td>Multiple targets</td>
<td>SME</td>
<td>Pain</td>
<td>Daiichi-Sankyo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple targets</td>
<td>SME/mAb</td>
<td>Multiple indications</td>
<td>Morphosys</td>
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<tr>
<td>Multiple targets</td>
<td>SME</td>
<td>Not disclosed</td>
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</tr>
</tbody>
</table>

### Partnered GPCR Pipeline (Co-development/profit share)

<table>
<thead>
<tr>
<th>Product/Program</th>
<th>Modality</th>
<th>Indication</th>
<th>Partner</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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</thead>
<tbody>
<tr>
<td>Multiple targets</td>
<td>Peptide</td>
<td>Inflammation</td>
<td>Gilead</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Multiple targets</td>
<td>mAb</td>
<td>Cancer I/O</td>
<td>Kymab</td>
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</tbody>
</table>

### Partnered Pipeline - Legacy Respiratory Products (Traditional out-licensing)

<table>
<thead>
<tr>
<th>Product/Program</th>
<th>Modality</th>
<th>Indication</th>
<th>Partner</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seebri®/Ultibro®</td>
<td>SME</td>
<td>COPD</td>
<td>Novartis</td>
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<td></td>
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</tr>
<tr>
<td>QVM149</td>
<td>SME</td>
<td>Asthma</td>
<td>Novartis</td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

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1 Note: SME = small molecule; PEP = Peptide; mAb = monoclonal antibody

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See slide 9
See slide 11
**Muscarinic M₁ Agonist Program for Alzheimer’s disease**

A novel approach for symptomatic treatment of AD

HTL0018318 represents a novel approach to stimulating M₁

- **Direct stimulation of M₁ receptor**, mediating cognition - different approach to donepezil
- **HTL0018318** bypasses presynaptic activity, and **does not rely on ACh levels in the brain**
- **Acts directly** to stimulate the M₁ receptor as an analogue of ACh post the synapse
- **Circumvents the underlying neurochemical deficit** in Alzheimer’s disease patients
- **HTL0018318 offers a potential first-in-class therapy**

**Selective muscarinic M₁ receptor agonism offers a potential first-in-class therapy for AD patients**
HTL0018318 is a potential first-in-class therapy for Alzheimer’s disease
Highly selective M₁ receptor agonist derived from StaR® and SBDD

Overview of the HTL0018318 muscarinic M₁ agonist

- **Cognitive benefits of M₁ agonism supported** by Lilly’s clinical studies of xanomeline¹
- Xanomeline’s development stopped due to unacceptable CV and GI side effects linked to stimulation of M₂ & M₃
- **HTL0018318 is a potent muscarinic M₁ agonist with negligible M₂/M₃ agonism**
- StaR® & SBDD “designed out” unwanted selectivity over the M₂ & M₃ receptors

Source: Internal analysis

1 Bodick et. al. “Effects of Xanomeline, a Selective Muscarinic Receptor Agonist, on Cognitive Function and Behavioural Symptoms in Alzheimer’s Disease” Arch Neurol. 1997;54:465-473
AZD4635 has emerged as a potential next-generation I/O therapy
First A2a R antagonist structurally derived from StaR® and SBDD

Checkpoint inhibitors are a key cancer treatment

PD-L1
- durvalumab (2017)
- avelumab (2017)
- atezolizumab (2016)

PD-1
- nivolumab (2014)
- pembrolizumab (2014)

CTLA-4
- ipilimumab (2011)

Checkpointer inhibitors are highly effective against certain types of tumors (e.g. lung, skin, and renal)

Next-gen I/O therapies to enhance treatment

AZD4635
A2a R antagonist
MONOTHERAPY

AZD4635
A2a R antagonist
+ durvalumab
Anti-PD-L1
COMBO THERAPY

AZD4635
A2a R antagonist
+ MEDI9447
Anti-CD73
COMBO THERAPY

Next-gen I/O may enhance efficacy of approved checkpoint inhibitors across more tumor types
AZD4635 has emerged as a potential next-generation I/O therapy
First A2a R antagonist structurally derived from StaR® and SBDD

**Excellent clinical progress to date**
- Phase 1a maximum tolerated dose (MTD) achieved
- Phase 1b dose expansion and signal seeking in patients ongoing across multiple tumor types
- Monotherapy and combination with durvalumab (anti-PD-L1)
- NEW Phase 1b/2 study with MEDI9447 (anti-C'D73 antibody, open and has started to enrol subjects)

**New supportive preclinical data presented at AACR 2018**
- AZD4635 alone and in combination with an anti-PD-L1 led to a reduction in tumor growth in both adenosine high and adenosine low syngeneic tumor models
- Inhibition of A2a R signaling by AZD4635 in combination with anti-PD-L1 can act to increase host immune surveillance and response
- AZD4635 exhibits dose dependent tumor growth inhibition, and requires a working host immune system for effects

1 MC38 syngeneic colorectal cancer
2 MCA205 syngeneic fibrosarcoma cancer
# Proprietary pipeline now led by M₁ DLB opportunity in Japan
Focus on selected rare/orphan and specialty indications or markets

## Proprietary pipeline

<table>
<thead>
<tr>
<th>Product</th>
<th>Modality</th>
<th>Indication</th>
<th>Originator</th>
<th>Phase</th>
<th>Q2 CY18</th>
<th>Q3 CY18</th>
<th>Q4 CY18</th>
<th>H1 CY19</th>
<th>H2 CY19</th>
</tr>
</thead>
<tbody>
<tr>
<td>M₁</td>
<td>SME</td>
<td>DLB (Japan)</td>
<td>☀️☀️SOS©️</td>
<td>Phase 1</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>mGlu₅</td>
<td>SME</td>
<td>Neurological disorders</td>
<td>☀️☀️SOS©️</td>
<td>Preclinical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSTR</td>
<td>SME</td>
<td>Endocrine/Neuroendocrine disorders</td>
<td>☀️☀️SOS©️</td>
<td>Preclinical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGRP</td>
<td>SME</td>
<td>Migraine and other severe headaches</td>
<td>☀️☀️SOS©️</td>
<td>Preclinical</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>GLP-1</td>
<td>SME</td>
<td>Metabolic diseases</td>
<td>☀️☀️SOS©️</td>
<td>Preclinical</td>
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</tr>
<tr>
<td>GLP-2</td>
<td>SME</td>
<td>Intestinal failure</td>
<td>☀️☀️SOS©️</td>
<td>Preclinical</td>
<td></td>
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</tr>
</tbody>
</table>

**Proprietary GPCR Pipeline (Go-to-market/commercialize)**

- **M₁ SME DLB (Japan) Phase 1**
  - **Phase 2a PoC clinical trial start**

**Note:** SME = small molecule

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**Investment in StaR® technology driving Proprietary GPCR pipeline progress**
- average of 3 novel drug candidates into clinical development every year commencing CY2018

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1. See slide 14
HTL0018318 for DLB in Japan
Great potential for $M_1$ agonist treatment for DLB in Japan

- DLB is the second most common form of dementia and highly relevant in Japan
- Real patient need in Japan - ageing population
- Recognition and diagnosis of DLB symptoms significantly more advanced in Japan
- $M_1$ agonist will show activity more rapidly and easily in DLB than in Alzheimer's due greater cholinergic defect
- Potential to have a superior profile to donepezil as HTL0018318 acts independently of presynaptic system
- Potentially favourable environment - regulators in US/EU adapting dementia guidelines to meet increased disease understanding
- HTL0018318 represents a new treatment approach with potential to show meaningful patient benefits
HTL0018318 for DLB in Japan
Summary of clinical program to date

Summary of clinical progress

- HTL0018318 derived from Heptares’ StaR® technology and SBDD
- HTL0018318 - same compound being investigated in AD trials with our partner Allergan
  - Allergan paid $125 million upfront for a portfolio of muscarinic compounds, including HTL0018318
- In Phase 1a studies, HTL0018318 demonstrated to be safe and well tolerated, including in elderly people
- Ethnic bridging studies were completed by Heptares - safe and well tolerated in Japanese subjects
- HTL0018318 currently in a Phase 1b trial in patients with AD in Europe
- Agreed with Allergan that Sosei has rights for approval and commercialization of HTL0018318 for DLB in Japan

Clinical progress to date encouraging.
Advancing preparation to commence Phase 2 PoC study in DLB in Japan in Q3 CY18

1 EU study of HTL0018318 in AD https://www.clinicaltrials.gov/ct2/show/NCT03456349
Strategic investment in saRNA technology
Exclusive option to move from 25.6% to 100% ownership at pre-determined economics

Pioneering RNA activation

- saRNAs are a new therapeutic class and reversibly activate gene expression
- Novel platform leveraging advances of siRNA therapeutics, including clinically validated delivery platform
- Unique opportunity to address undruggable targets
- Recent deal with Boehringer Ingelheim further supports MiNA/saRNA’s potential

Lead candidate CEBPA in Ph 1/2a for liver cancer

- CEBPA regulates multiple pathways in the liver and saRNA is a unique modality for targeting CEBPA
- MTL-CEBPA has preclinical efficacy across progression of liver disease
- MTL-CEBPA is the first saRNA to reach the clinic – currently in clinical trials in patients for liver cancer, an orphan indication

A Novel RNA Oligonucleotide Improves Liver Function and Inhibits Liver Carcinogenesis in Vivo

1. Loading of saRNA into Ago protein
2. saRNA-Ago targets gene promoter
3. saRNA-Ago activates gene transcription
4. Long lasting protein up-regulation

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1. CEBPA (CCAAT/Enhancer Binding Protein Alpha)
Balance sheet strengthened to scale and progress the business
Allergan upfront milestone in FY2016 drives P&L variance

Summary financials (reported)

<table>
<thead>
<tr>
<th>(JPY m)¹</th>
<th>FY2016</th>
<th>FY2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>18,901²</td>
<td>6,955</td>
</tr>
<tr>
<td>Cash Opex</td>
<td>5,496</td>
<td>7,790</td>
</tr>
<tr>
<td>Cash &amp; cash equivalents</td>
<td>13,899</td>
<td>28,281</td>
</tr>
<tr>
<td>Interest-bearing debt</td>
<td>6,900</td>
<td>9,173</td>
</tr>
</tbody>
</table>

Revenue (ex Allergan upfront)

<table>
<thead>
<tr>
<th>JPY (m)</th>
<th>FY2016</th>
<th>FY2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>5,357</td>
<td>6,955</td>
</tr>
<tr>
<td>Cash Opex</td>
<td>2,918</td>
<td>2,561</td>
</tr>
<tr>
<td>Cash &amp; cash equivalents</td>
<td>1,880</td>
<td>3,840</td>
</tr>
</tbody>
</table>

Successful ~$200m raise in November 2017 via a Global Offering of shares to international investors. Current cash balance of ~$260m provides runway of ~2 years based on organic business plan

¹ Reporting currency in JPY
² Includes USD 125m upfront payment from Allergan
Substantial economic returns secured from lead compounds
Provides potential source of non-dilutive finance for proprietary pipeline

Summary of potential economic returns from out-licensing / collaboration projects

<table>
<thead>
<tr>
<th>Partner</th>
<th>Program / Indication</th>
<th>Upfront received (US$m)</th>
<th>Total Development Milestones (US$m)</th>
<th>Total Sales Milestones (US$m)</th>
<th>Total UF + Milestones (US$m)</th>
<th>Royalty (US$m)</th>
<th>Additional Details</th>
</tr>
</thead>
</table>
| Allergan  | Muscarinic Receptor program | 125                     | 665                                 | 2,575                        | 3,365                       | 15             | Exclusive global rights  
  Allergan committed $50m to a joint R&D program through Ph 2a |
| AstraZeneca | A2a Receptor program  | 10                      | 500                                 | 510                          | 22                          | Tiered, double-digit | Exclusive global rights to A2a4635  
  Collaboration to discover further A2a receptor blocking compounds for development |
| Pfizer    | Up to 10 targets     | Nil                     | ~189 per target                     | N.D.                         | 1,890                       | Tiered (single digit) | Discovery of potential novel GPCR agents selected by Pfizer (up to 10 targets)  
  Pfizer will be responsible for developing and commercializing any agents discovered |

**TOTAL**  
135 5,765 37

$5bn plus in potential development, regulatory and commercial milestones to come, in addition to royalties on sales
Global operations and aspirations - aiming to build Japan’s first global biotech champion

- **World-leader in GPCR-focused drug design** based on unique IP protected StaR®\(^1\) GPCR technology & enabled SBDD\(^2\) platform

- **Partnered clinical-stage pipeline** in neurology, immuno-oncology, CNS & other diseases, with $5bn plus in potential economics

- **Proprietary pipeline** led by dementia with Lewy bodies (DLB) Phase 2 program in Japan, plus multiple novel candidates in development

- **Strategic investment in saRNA therapeutics** with lead candidate in Phase 1/2a for liver cancer, an orphan indication

- **Robust royalties from legacy respiratory products** provide source non-dilutive cash flows

- **Strong cash position of ~$260m** to drive global growth strategy

---

\(^1\) Stabilized receptor technology

\(^2\) Structure-based drug design

Thank you!
Locations

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