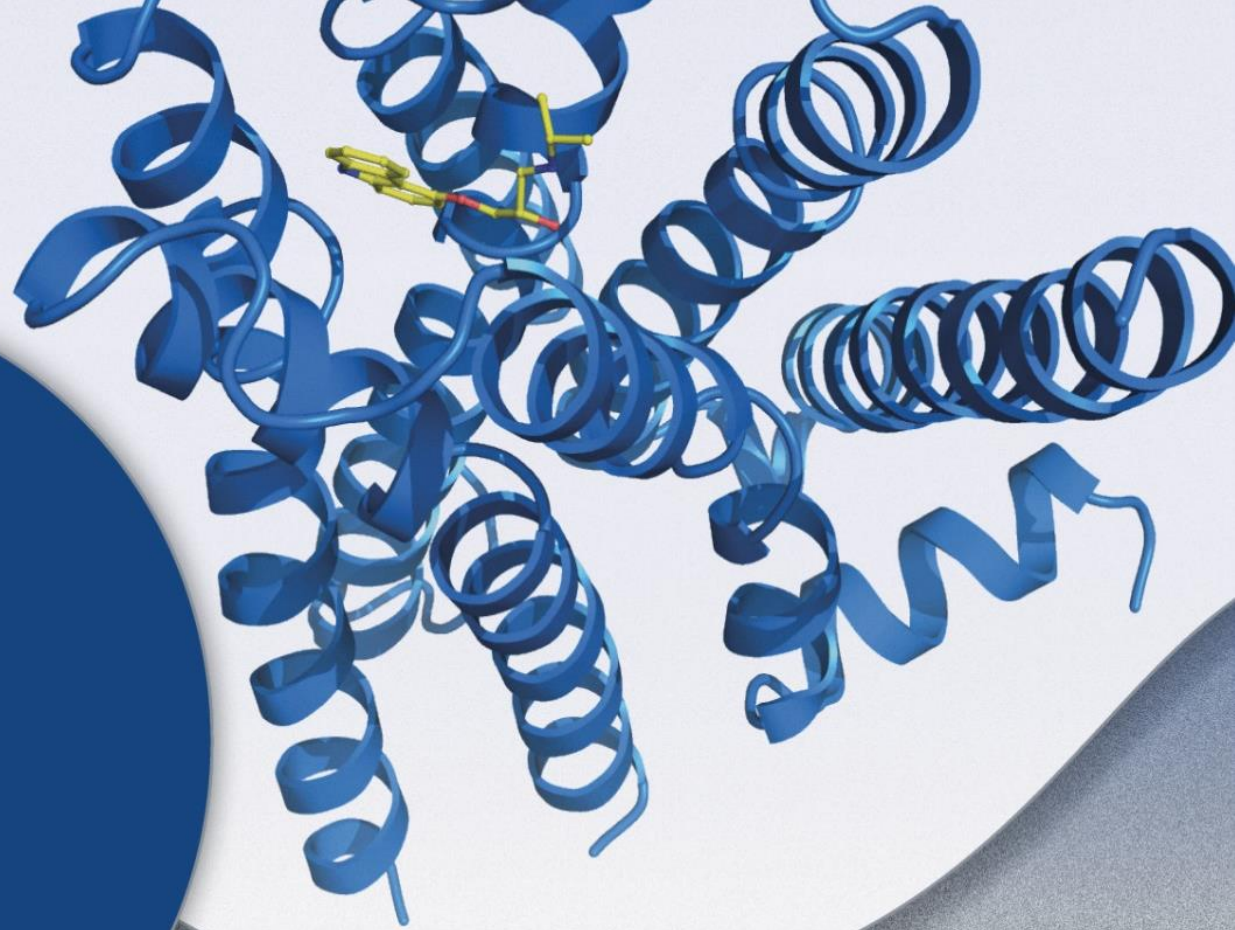


**Sosei Group Corporation**

# **36<sup>th</sup> Annual J.P. Morgan Healthcare Conference**

8 January 2018



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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.

Listed 2004 in Tokyo (TSE Mothers: 4565)

Global management team

Main scientific campus in the U.K.

Market capitalization: c.\$2.0bn

## A Japan-listed biotech with a difference

- **World-leader in GPCR-focused drug design** based on unique IP protected StaR®<sup>1</sup> GPCR technology & enabled SBDD<sup>2</sup> platform
- **Partnered clinical-stage pipeline** in neurology, immuno-oncology, CNS & other diseases, with up to c.\$6bn 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
- **Growing royalties from legacy respiratory products** provide source non-dilutive cash flows
- **Strong cash position of c.\$300m** to drive global growth strategy

Tokyo listed, global operations. We are building Japan's first biotech champion



## 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



**Dr. Malcolm WEIR**

*Chief R&D Officer*

- CEO and Co-Founder Heptares
- Former Head of Molecular Science Division at Glaxo Wellcome



**Dr. Fiona MARSHALL**

*Chief Scientific Officer*

- CSO and Co-Founder at Heptares
- Former Head of Molecular Pharmacology Department at Glaxo Wellcome



**Andrew OAKLEY**

*Chief Financial Officer*

- Former CFO of Actelion Pharmaceuticals Ltd
- Former CFO of Vectura plc



**Dr. Tim TASKER**

*Chief Medical Officer*

- GSK and Former Executive VP of Clinical Development at Evotec

### Scientific Advisory Board experience



## Three corporate events have shaped Sosei

**2005**

**Acquired  
Arakis  
(UK)**

- **Glycopyrrolate**, later licensed to NVS for respiratory products (Seebri/Ultibro)
- Ongoing royalties provide long term source of non-dilutive funds

**2015**

**Acquired  
Heptares Tx  
(UK)**

- **Platform: StaR® technology** for stabilising GPCRs
- Partnered GPCR pipeline
- Proprietary GPCR pipeline

**2017**

**Investment in  
MiNA Tx  
(UK)**

- **Platform: small activating RNA (saRNA) technology**
- Proprietary candidate in Phase 1/2a for liver cancer

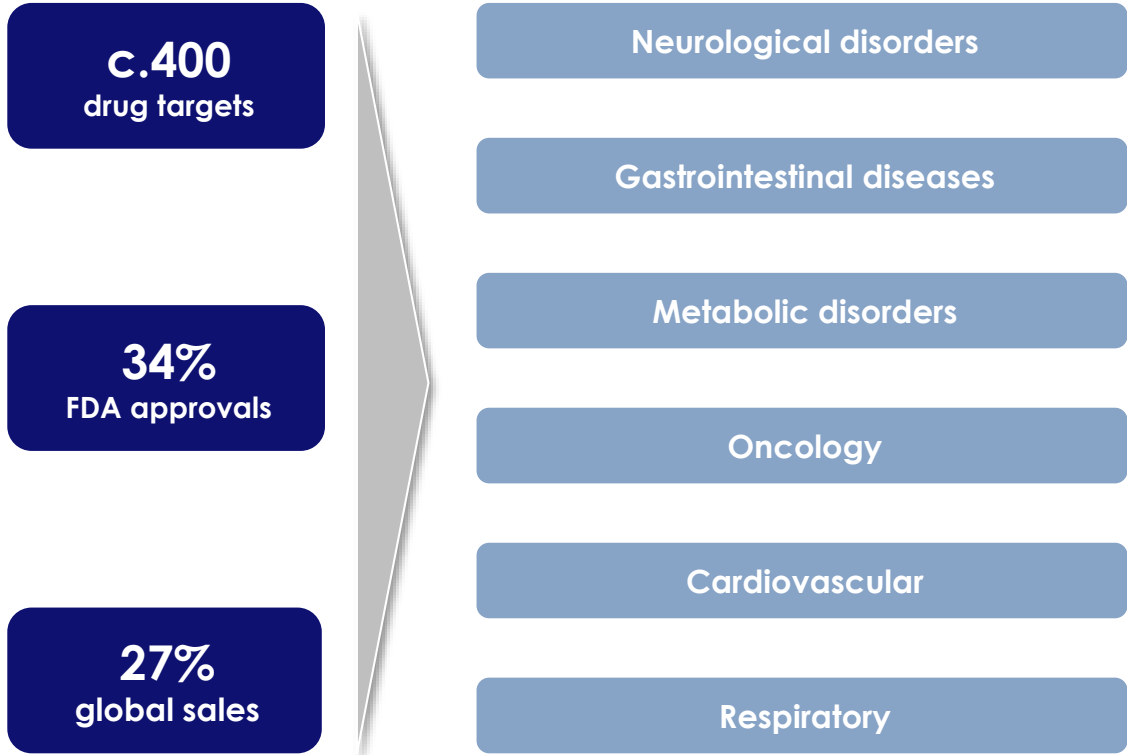
### Our world-leading Partners



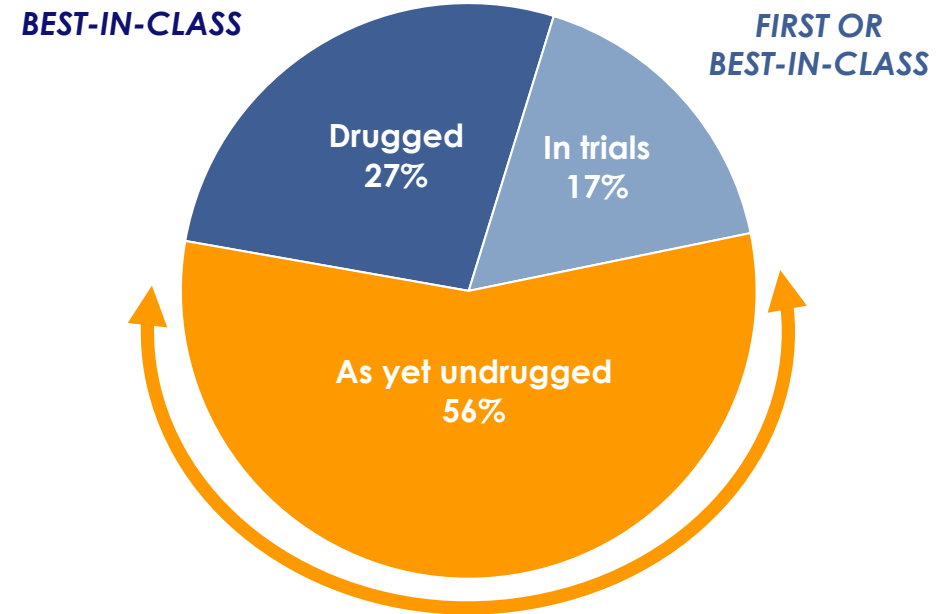
Our patent-protected StaR® technology enables Structure-Based Drug Design, consolidating our position as the world leader in GPCR medicine discovery and design

# Vast opportunity targeting GPCRs, however many high-value targets remain untapped

*GPCRs are the backbone of the pharma industry*



**c.400 non-olfactory GPCR targets in the human genome**



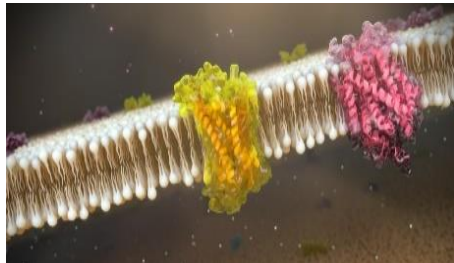
**Targeting first-in-class or best-in-class GPCR medicines**

**GPCRs are active in a wide range of disease areas, and offer broad therapeutic potential**

# StaR® technology enables us to stabilize and “unlock” GPCRs

## Revolution for GPCR structure-based discovery

### Difficulty drugging native/“wild-type” GPCRs



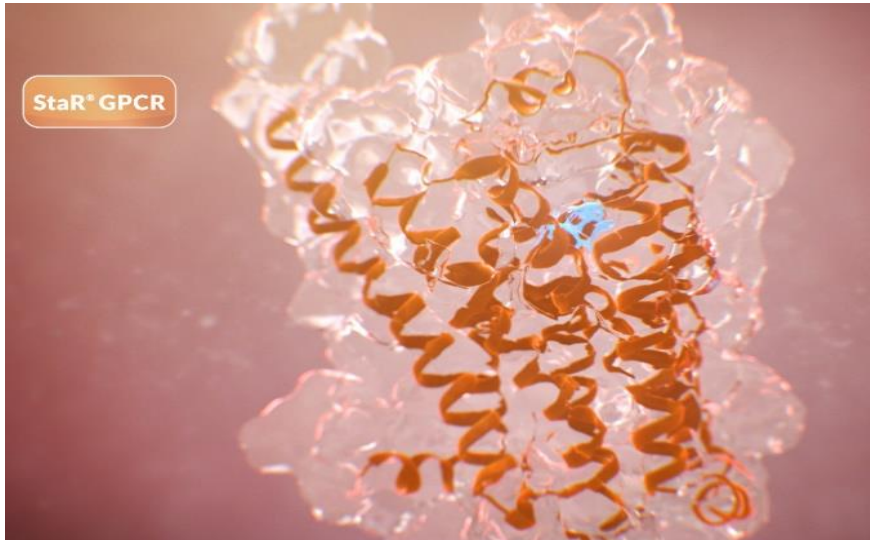
GPCRs are receptors with seven-transmembrane structures, that span the cell membrane



Highly unstable when removed – aggregate and lose function when purified, preventing structural determination

- Structural tools of science cannot be applied to native GPCRs
- Results in many sub-optimally drugged targets
- Unstable nature also prevents ability to generate stable antigen to raise antibodies

### Our solution: proprietary StaR® technology



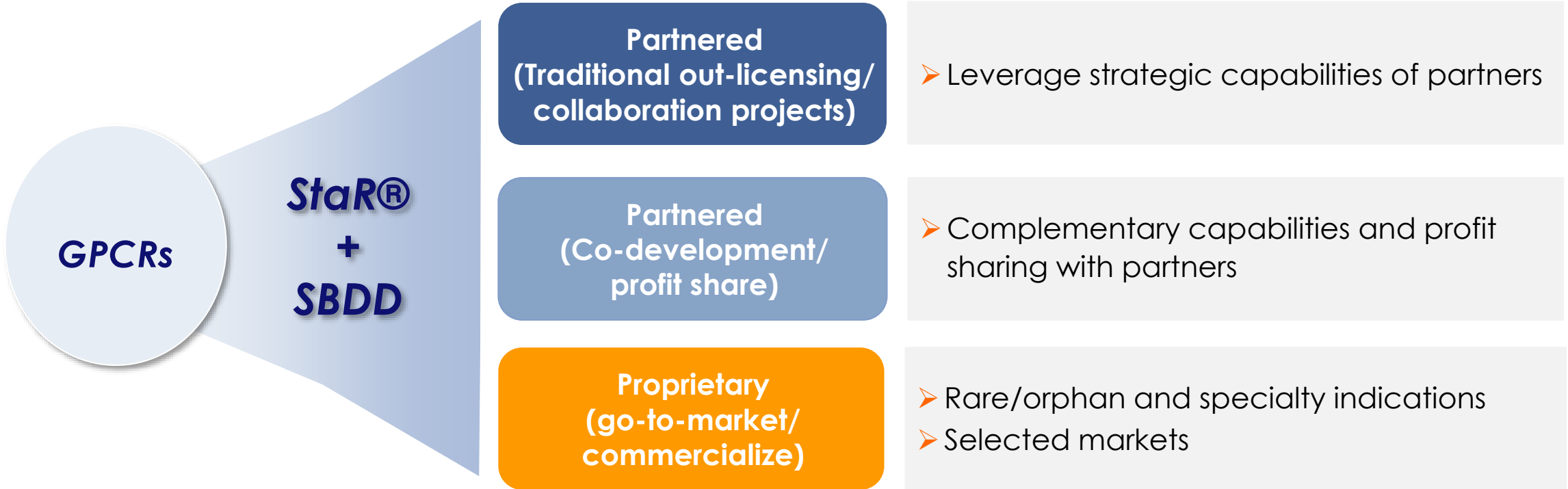
- Single point mutations stabilize GPCRs to create a StaR® that can be purified and retains function
- StaR® technology is the basis for our integrated structure/ chemistry/ pharmacology platform (SBDD)

**StaR® proteins enable crystallisation for structural determination, and the technology is protected by a robust IP estate and high levels of know-how.**

**StaR® proteins enable SME, peptide or antibody discovery**

# Risk-balanced strategy to leverage leadership and capitalize on GPCR opportunity

*Creates and captures value*

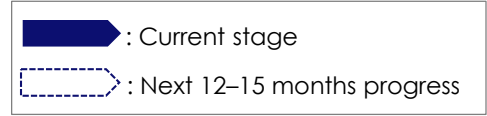


**Reserving the right to choose which strategy is most appropriate for each drug candidate, with a goal to commercialize ourselves in selected indications and markets**



# Advancing a Partnered GPCR pipeline in multiple therapeutic areas

Balanced and diversified



Product/Program	Modality	Indication	Partner	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Market
<b>M<sub>1</sub> AD agonist</b>	SME	Alzheimer's disease	Allergan	▬	▬	▬	▬		
<b>M<sub>4</sub> AD/Sz agonist</b>	SME	NeuroB Sx in AD	Allergan	▬	▬	▬			
<b>M<sub>1</sub>/M<sub>4</sub> agonist</b>	SME	AD/NeuroB Sx in AD	Allergan	▬					
<b>A<sub>2A</sub> antagonist</b>	SME	Cancer I/O	AstraZeneca	▬	▬	▬	▬		
<b>CGRP antagonist</b>	SME	Migraine	TEVA	▬	▬				
	SME/ mAb	Multiple indications	Pfizer	▬	▬				
	SME	Pain	Daiichi-Sankyo	▬	▬				
	SME	Not disclosed	morphosys	▬	▬				
<b>Partnered GPCR Pipeline (Co-development/profit share)</b>									
	PEP	Inflammation	PeptiDream	▬					
	mAb	Immuno-oncology	kymab	▬					

Multiple big pharma partners, across multiple modalities, validate our StaR® and SBDD approach

## Up to \$6bn in potential economics secured from lead Partnered compounds

*Provides potential source of non-dilutive financing*

Partner	Program / Indication	Upfront received (US\$m)	Total Development Milestones (US\$m)	Total Sales Milestones (US\$m)	Total UF + Milestones (US\$m)	Milestones Received (US\$m)	Royalty (US\$m)	Additional Details
	<b>M<sub>R</sub> PRGM</b> Cognition/Psych.	125	665	2,575	3,365	15	Tiered, double-digit	<ul style="list-style-type: none"> <li>➢ Exclusive global rights</li> <li>➢ Allergan committed \$50m to a joint R&amp;D program through Ph 2a</li> </ul>
	<b>A<sub>2A</sub></b> Immuno-oncology	10	500		510	22	Tiered, double-digit	<ul style="list-style-type: none"> <li>➢ Exclusive global rights to AZD4635</li> <li>➢ Collaboration to discover further A<sub>2A</sub> receptor blocking compounds for development</li> </ul>
	<b>CGRP</b> Migraine	10	400		410	5	Tiered, double-digit	<ul style="list-style-type: none"> <li>➢ Exclusive global rights to novel CGPR antagonists</li> <li>➢ Received research funding</li> </ul>
		Nil	~189 per target	N.D.	1,890		Tiered (single digit)	<ul style="list-style-type: none"> <li>➢ Discovery of potential novel GPCR agents selected by Pfizer (up to 10 targets)</li> <li>➢ Pfizer will be responsible for developing and commercializing any agents discovered</li> </ul>
<b>TOTAL</b>		<b>145+</b>			<b>6,175</b>	<b>42</b>		

**c.\$6bn in potential development, regulatory and commercial milestones to come, in addition to royalties on sales**

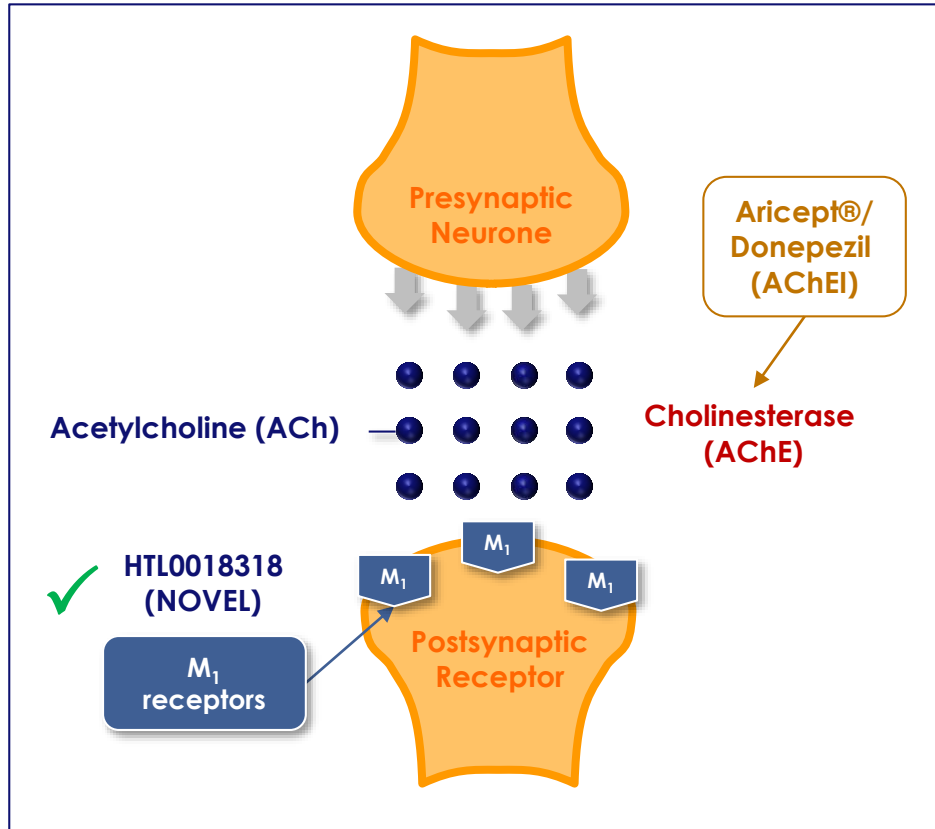
# Muscarinic M<sub>1</sub> receptor agonist program for AD

*A novel approach for symptomatic treatment of AD*

Partnered with:



**M<sub>1</sub> AD**  
Phase 1b



**Aricept®/ Donepezil**  
(standard of care)

- Donepezil inhibits cholinesterase, preventing the breakdown of ACh
- Enhancement of ACh by AChEIs such as Donepezil provides clinical benefits
- Benefits limited due to low/declining levels of ACh as disease progresses, plus adverse side-effects
- Blockbuster drug (c.\$4bn sales pre U.S. patent expiry)

**HTL0018318**  
Novel muscarinic M<sub>1</sub> receptor agonist

- Acts directly on M<sub>1</sub> receptor post synapse, independent of endogenous levels of ACh
- Circumvents the underlying neurochemical deficit in AD
- Offers potential first-in-class therapy

Selective muscarinic M<sub>1</sub> receptor agonism offers a potential first-in-class therapy for AD patients

# HTL0018318 is a potential first-in-class therapy for AD

Highly selective M<sub>1</sub> receptor agonist derived from StarR® and SBDD

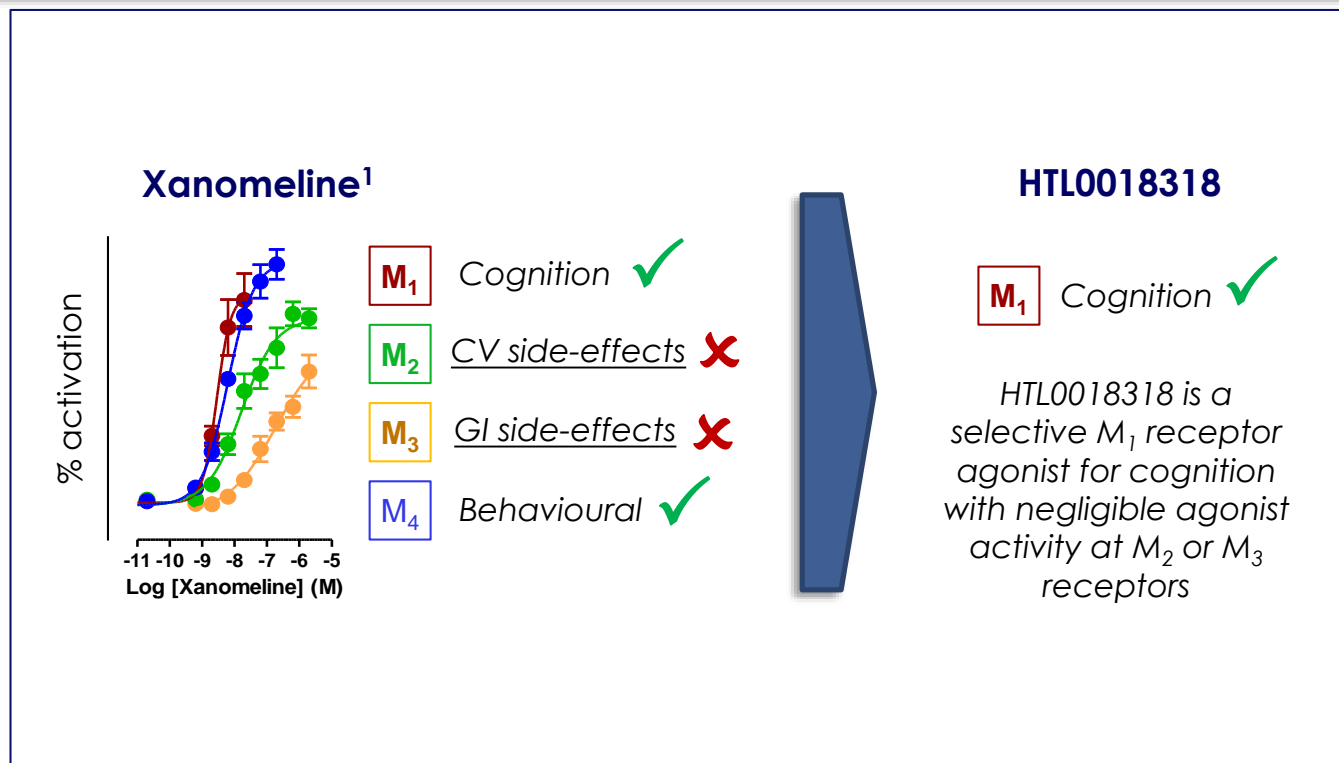
Partnered with:



Phase 1b

## Overview of the HTL0018318 muscarinic M<sub>1</sub> agonist

- **Cognitive benefits of M<sub>1</sub> agonism supported** by Lilly's clinical studies of xanomeline<sup>1</sup>
- Xanomeline's development stopped due to unacceptable CV and GI side effects linked to stimulation of M<sub>2</sub> & M<sub>3</sub>
- **HTL0018318 is a potent muscarinic M<sub>1</sub> agonist with negligible M<sub>2</sub>/M<sub>3</sub> agonism**
- **StarR® & SBDD "designed out" unwanted selectivity** over the M<sub>2</sub> & M<sub>3</sub> receptors
- M<sub>4</sub> agonist also in clinical development for NeuroB Sx in AD – designed using same principle as HTL0018318



Selectivity is crucial. HTL0018318 has a differentiated mechanism of action with the potential to optimise symptomatic benefits in AD patients



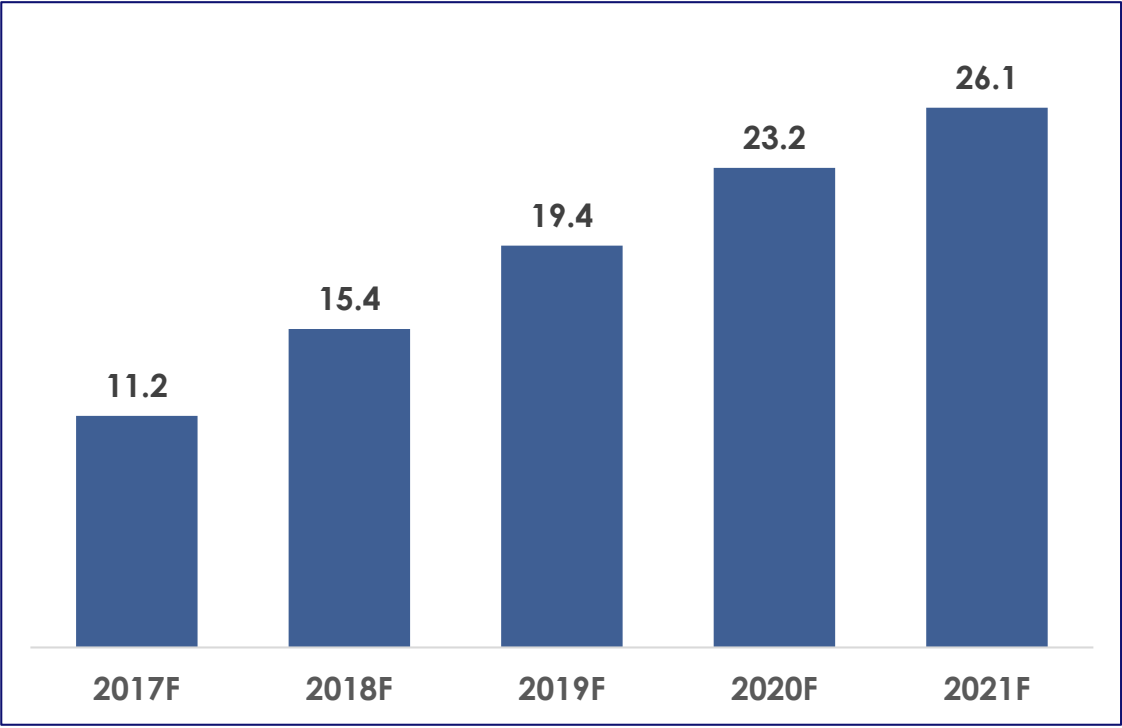
# Adenosine A<sub>2A</sub> antagonist program for cancer treatment

Exciting I/O treatment approach

Partnered with:



## I/O drugs – forecast sales for marketed products (\$bn)<sup>1</sup>



## Potential role of Adenosine A<sub>2A</sub> antagonists in cancer

- Blocks tumor cells' ability to use Adenosine to evade the immune system
- Opportunity in a wide range of tumor types – in particular, link to tumors with hypoxia
- Ability to select patients based on biomarkers of elevated adenosine, e.g. CD73
- **Potential role both as I/O monotherapy, and in combination with other immunotherapy approaches**

**Immunotherapies are at the forefront of cancer treatment with strong forecast growth for I/O drugs. A<sub>2A</sub> antagonists represent an exciting I/O treatment approach**

Source: Management estimates  
<sup>1</sup> Includes sales forecasts for Keytruda (pembrolizumab), Opdivo (nivolumab), Yervoy (ipilimumab), Tecentriaq (atezolizumab), Imfinzi (durvalumab), and Bavencio (avelumab) only

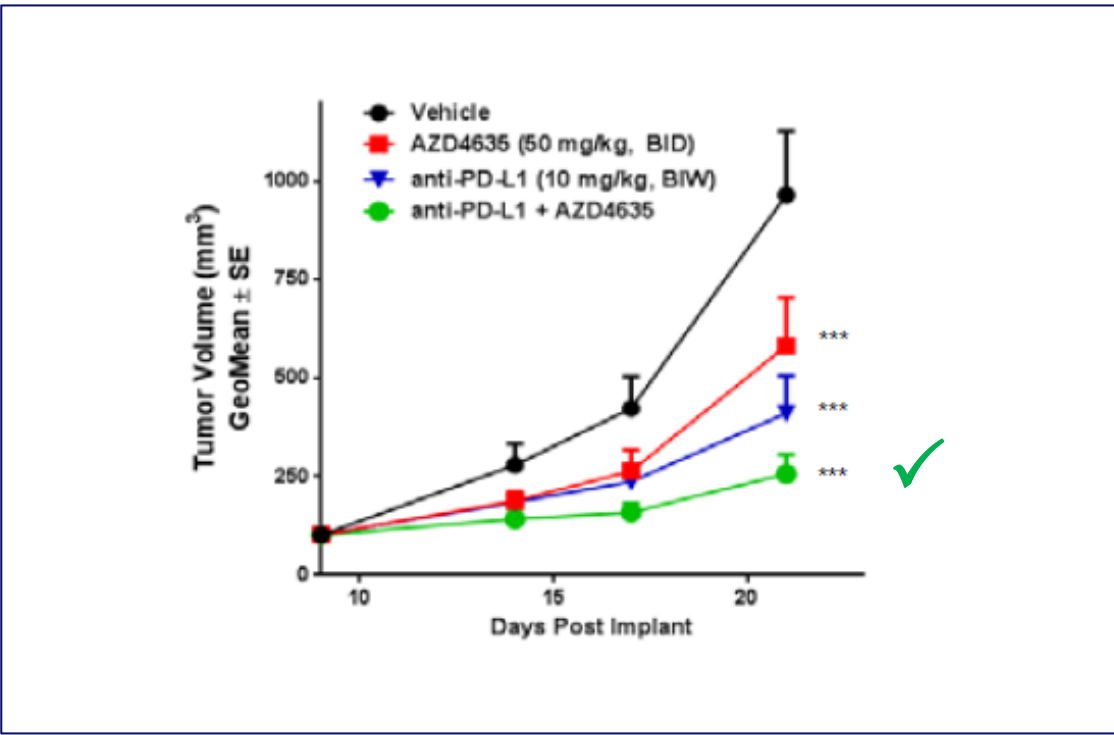
# AZD4635 is a highly potent and selective A<sub>2A</sub> antagonist

The first A<sub>2A</sub> antagonist structurally derived from StaR® and SBDD

Partnered with:



## Preclinical summary of AZD4635



## Phase 1b trials ongoing

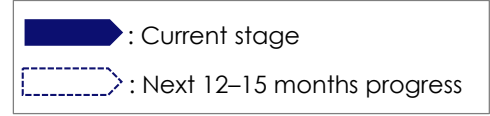
- **Ph. 1b trials in patients with solid malignancies** (mono/combination therapy) progressing well
- MTD for monotherapy complete, dose escalation to establish the MTD in combination with IMFINZI™ near completion
- **Progressing with signal seeking Ph. 1b expansion cohorts in a number of tumor types** with monotherapy and/or in combination with IMFINZI™

**AZD4635 enhances the anti-tumor activity of anti-PD-L1 checkpoint inhibitors in established MC38 syngenic tumors<sup>1</sup>**

<sup>1</sup> As demonstrated preclinically. Preclinical pharmacodynamics and antitumor activity of AZD4635, a novel adenosine 2A receptor inhibitor that reverses adenosine mediated T cell suppression

## Proprietary pipeline now led by M<sub>1</sub> DLB opportunity in Japan

*Focus on selected rare/orphan and specialty indications or markets*



Product/Program	Modality	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Market
<b>Proprietary GPCR Pipeline (Go-to-market/commercialize) - formerly known as "Wave 2"</b>								
<b>M<sub>1</sub> DLB agonist</b>	SME	Dementia with Lewy Bodies (Japan)						
<b>mGlu<sub>5</sub> NAM</b>	SME	CNS						
<b>MOL 1</b>	SME	Undisclosed						
<b>MOL 2</b>	SME	Undisclosed						
<b>MOL 3</b>	SME	Undisclosed						
<b>MOL 4</b>	SME	Undisclosed						
<b>MOL 5</b>	SME	Undisclosed						

**Investment in StaR® technology driving Proprietary GPCR pipeline progress – up to 3 novel drug candidates to enter Phase 1 every year commencing CY2018**

## Sosei is advancing HTL0018318 for DLB in Japan

*Highly selective M<sub>1</sub> receptor agonist designed by StaR® and SBDD*

**M<sub>1</sub> DLB**

**Phase 2 ready**

### Dementia with Lewy Bodies (DLB)

- Progressive neurodegenerative dementia, **second most prevalent behind AD** (c.1m patients in Japan)
- **Advances in diagnosis** have **increased DLB awareness**
- **Social and 'political' priority** in Japan to evaluate new treatments

**Potential Muscarinic M<sub>1</sub> agonist for DLB**

- **Greater cholinergic deficit in DLB than in AD**
- Loss of presynaptic cholinergic system reduces effect of donepezil whilst **intact post synaptic receptors allows response to M1 agonists**

### Overview of our M<sub>1</sub> program for DLB in Japan

- **HTL0018318 – same compound being advanced by Allergan** for AD in our Partnered pipeline
- **Phase 2 POC monotherapy study**, expected to begin in Japan in 2018
- **Strong go-to-market opportunity** for Sosei in Japan
  - **Leverages our clinical capabilities**, and broader track record of successful product development in Japan
  - **Satisfies key element of growth strategy** – manageable indication treated in specialist centres, sizeable market opportunity to build and retain value

**Strong go-to-market opportunity for our lead M<sub>1</sub> program in Japan. Significant unmet medical and social need for a new therapeutic approach to tackle DLB in Japan**



## Strategic investment in saRNA technology

*CEBPA<sup>1</sup> is an attractive, previously ‘undruggable’ target in liver disease*

In May 2017, we acquired a strategic 25.6% stake in MiNA, with an exclusive option to move to 100% ownership at pre-determined economics

### CEBPA regulates multiple pathways in the liver

- **Master regulator of liver function**
- Increases energy generation, energy utilisation, amino-acid metabolism, glucose uptake
- Inhibitor of oncogenic signaling pathways: mTOR, MAPK and YAP1
- Knock-out mice have impaired liver function
- Knock-in mice have reduced susceptibility to HCC and cirrhosis without observable toxicity

### saRNA is a unique modality for targeting CEBPA

- Extremely low drugability score of 0.01 (c.f. PPARg 3.52) for small molecule therapeutics
- Reversible mode of action eliminates long term risks of gene therapy / CRISPR
- Liposomal formulation minimises non-liver toxicity
- **Lead candidate CEBPA currently in a Phase 1/2a clinical trial in patients for liver cancer, an orphan indication**

We are excited about the potential of saRNA therapeutics.  
MiNA’s recent deal with Boehringer Ingelheim further supports MiNA/saRNA’s potential

## Continuing to invest and scale the business

*Allergan upfront milestone in FY2016 drives P&L variance*

(JPY m) <sup>1</sup>	FY2015	FY2016	% change (FY15 vs FY16)	H1 FY 2016	H1 FY 2017	% change (H116 vs H117)
Revenue	8,151	18,901 <sup>3</sup>	132%	15,839 <sup>3</sup>	5,314	(66%)
Opex	7,209	6,790	(6%)	3,726	4,299	15%
Cash & cash equivalents	10,068	13,899	na	15,680	12,413	na
Interest-bearing debt	8,837	6,900	na	7,870	10,635	na



(USD m) <sup>2</sup>	FY2016	H1 FY 2017
Revenue	168.5 <sup>3</sup>	47.4
Opex	60.5	38.3
Cash & cash equivalents	123.9	110.6
Interest-bearing debt	61.5	94.8

**PLUS c.\$200m raised in November 2017 via a Global Offering of shares to international investors.  
Pro forma cash balance of c.\$300m provides runway of approx. 2-3 years based on organic business plan**

<sup>1</sup> reporting currency in JPY

<sup>2</sup> Converted at USD:JPY FX rate 112.9 (JPY:USD FX rate 0.0089) as at 31 March 2017

<sup>3</sup> Includes USD 125m upfront payment from Allergan to Heptares

## Thank you!

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Global management team

Main scientific campus in the U.K.

Market capitalization: c.\$2.0bn

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- **Strong cash position of c.\$300m** to drive global growth strategy

Sosei is a Japan-listed biotech with a difference



# Locations

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## **SOSEI GROUP**

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