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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

Listed 2004 in Tokyo (TSE Mothers: 4565)

Market capitalization: c.\$1.3bn

Global management team

Main scientific campus in the U.K.

- World-leader in GPCR-focused drug design based on unique IP protected StaR®¹ GPCR technology & enabled SBDD² platform
- <u>Partnered</u> 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

Global operations and aspirations - aiming to build Japan's first global 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





Andrew OAKLEYChief Financial Officer

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





Dr. Malcolm WEIRChief R&D Officer

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







Dr. Tim TASKERChief Medical Officer

■ GSK and Former Executive VP of Clinical Development at Evotec

Scientific Advisory Board experience





Why do we target G-Protein-Coupled Receptors (GPCRs)?

GPCRs are active in a wide range of disease areas

~400
GPCR targets
active in diseases²

~34%
of FDA approvals
target GPCRs1

27%
of global sales
are GPCR drugs¹

Neurological disorders

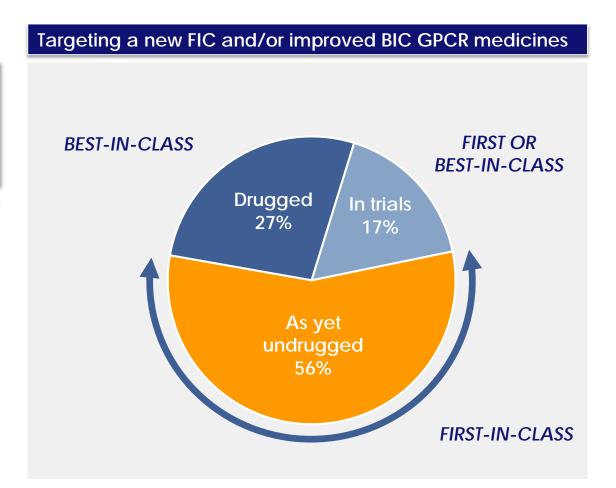
Oncology

Gastrointestinal diseases

Cardiovascular

Metabolic disorders

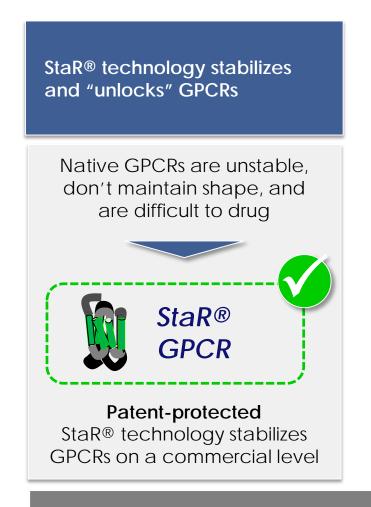
Respiratory

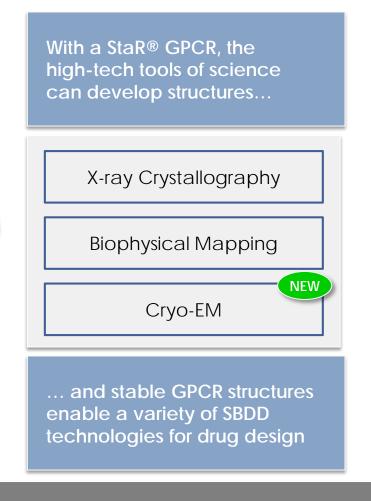


Huge opportunity to create new drugs or improve existing drugs



StaR® is Revolutionary for GPCR Structure-Based Drug Design



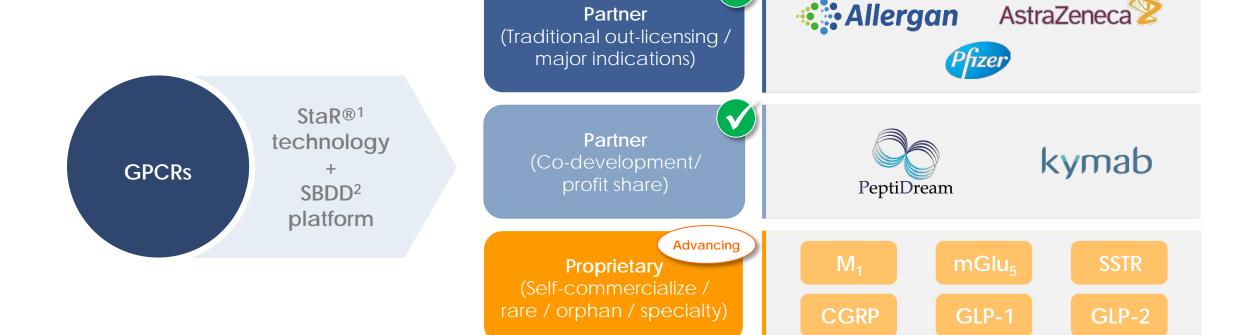


Structural information creates better, differentiated drug candidates Improved physiochemical properties Better safety and efficacy Reduced clinical attrition Small molecule, peptide or antibody discovery

Unique, scalable and sustainable platform, delivering differentiated pipeline candidates



Leveraging unique GPCR technology to deliver differentiated drug candidates



Risk-balanced business model creates and captures optimal value



¹ Stabilized receptor technology

² Structure-based drug design

Partnered GPCR Pipeline Proprietary GPCR Pipeline Strategic Investment

Financials

Advancing a <u>Partnered GPCR pipeline</u> in multiple therapeutic areas Balanced and diversified



Product/Program	Modality ¹	Indication	Partner	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Marketed
Partnered GPCR Pipeline (Traditional out-licensing/collaboration projects)									
M₁ agonist	SME	Alzheimer's disease	:: Allergan						See slide 9
M ₄ agonist	SME	Alzheimer's disease	:: Allergan						
M ₁ /M ₄ dual agonist	SME	Alzheimer's disease	Allergan						
A2a antagonist	SME	Cancer I/O	AstraZeneca 🕏						See slide 11
A2a antagonist	SME	Cancer I/O	AstraZeneca 🕏						see slide 11
Multiple targets	SME	Pain	Daiichi-Sankyo						
Multiple targets	SME/mAb	Multiple indications	Pfizer						
Multiple targets	SME	Not disclosed	morphosys						
Partnered GPCR Pipe	line (Co-deve	elopment/profit share)							
Multiple targets	Peptide	Inflammation	PeptiDream						
Multiple targets	mAb	Cancer I/O	kymab						
Partnered Pipeline - Legacy Respiratory Products (Traditional out-licensing)									
Seebri®/Ultibro®	SME	COPD	U NOVARTIS						
QVM149	SME	Asthma	b novartis						

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



Partnered GPCR Pipelir Proprietary GPCR Pipeline Strategic Investment

Financials

Muscarinic M₁ Agonist Program for Alzheimer's disease A novel approach for symptomatic treatment of AD

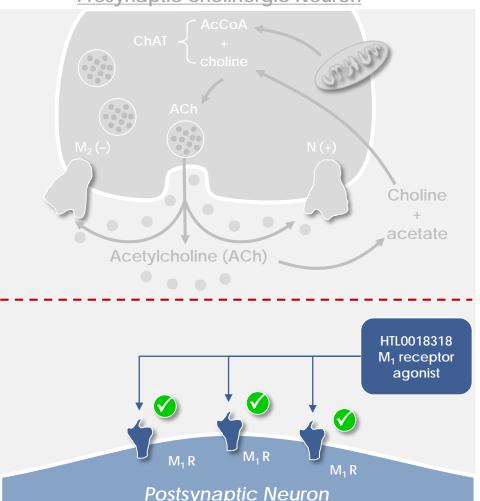
HTL0018318 represents a novel approach to stimulating M₁

- 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



Presynaptic cholinergic Neuron





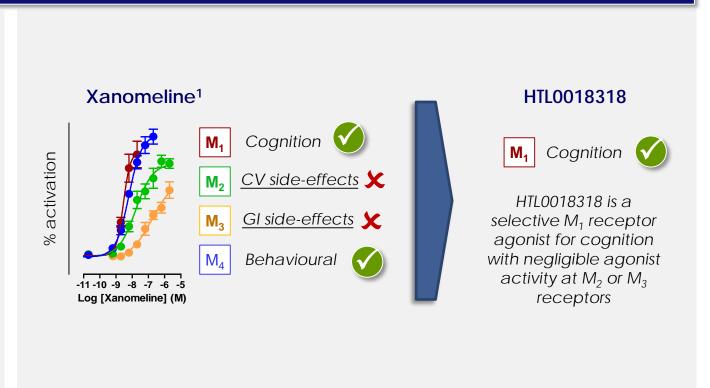
HTL0018318 is a potential first-in-class therapy for Alzheimer's disease Highly selective M₁ receptor agonist derived from StaR® and SBDD





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



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



Partnered GPCR Pipelir Proprietary GPCR Pipeline Strategic Investment

Financials

AZD4635 has emerged as a potential next-generation I/O therapyFirst 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)

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

Next-gen I/O therapies to enhance treatment

A2a R antagonist

AZD4635

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



Partnered GPCR Pipeline Proprietary GPCR Pipeline Strategic Investment

Financials

AZD4635 has emerged as a potential next-generation I/O therapyFirst A2a R antagonist structurally derived from StaR® and SBDD



Excellent clinical progress to date

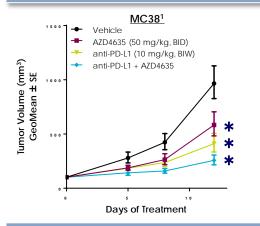
- Phase 1a maximum tolerated dose (MTD) achieved
- Phase 1b dose expansion and signal seeking in patients ongoing across multiple tumor types
- Monotherapy and combination with durvalumab (anti-PD-L1)
- NEW Phase 1b/2 study with MEDI9447 (anti-CD73 antibody, open and has started to enrol subjects)

New supportive preclinical data presented at AACR 2018

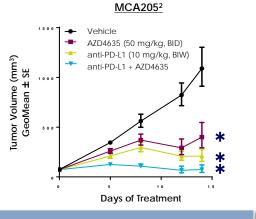
- AZD4635 alone and in combination with an anti-PD-L1 led to a reduction in tumor growth in both adenosine high and adenosine low syngeneic tumor models
- Inhibition of A2a R signaling by AZD4635 in combination with anti-PD-L1 can act to increase host immune surveillance and response
- AZD4635 **exhibits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

New supportive preclinical data presented at AACR 2018

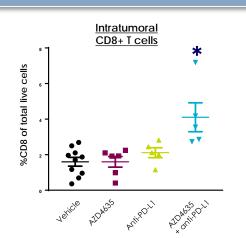
HIGH ADENOSINE TUMOR



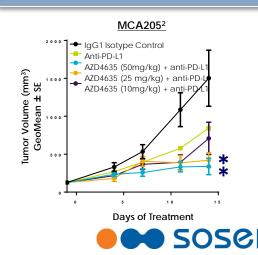
LOW ADENOSINE TUMOR



INCREASED IMMUNE RESPONSE



DOSE DEPENDENT



¹ MC38 syngeneic colorectal cancer

² MCA205 syngeneic fibrosarcoma cancer

<u>Proprietary pipeline</u> now led by M₁ DLB opportunity in Japan

Focus on selected rare/orphan and specialty indications or markets

Propriet	ary pipel	ine							
Product	Modality ¹	Indication	Originator	Phase	Q2 CY18	Q3 CY18	Q4 CY18	H1 CY19	H2 CY19
Proprieta	ry GPCR Pip	eline (Go-to-market/commer	cialize)						
M_1	SME	DLB (Japan)	SOS@I	Phase 1	Phase 2a PoC	clinical trial start			See slide 14
mGlu₅	SME	Neurological disorders	●●● SOS@I	Preclinical	Phase 1 clinic	cal trial start (healt	hy volunteers)		
SSTR	SME	Endocrine / Neuroendocrine disorders	●●● SOS@I	Preclinical	Phase 1 clinic	cal trial start (healt	hy volunteers)		
CGRP	SME	Migraine and other severe headaches	●●● SOS@I	Preclinical		Phase 1 clinic	al trial start (heal	thy volunteers)	
GLP-1	SME	Metabolic diseases	●●● SOS@I	Preclinical			Phase 1 clinic	al trial start (healt	hy volunteers) ^s
GLP-2	SME	Intestinal failure	●●● SOS@I	Preclinical			Phase 1 clinic	al trial start (healt	hy volunteers)

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



Model

GPCR Pipeline GPCR Pipeline

Strategic Investment

Financials

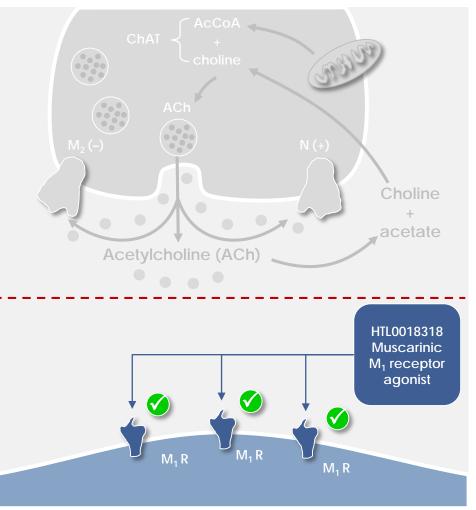
HTL0018318 for DLB in Japan

Great potential for M₁ 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
- M₁ 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

Presynaptic cholinergic Neuron





M₁ DLB

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 Europe¹
- 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



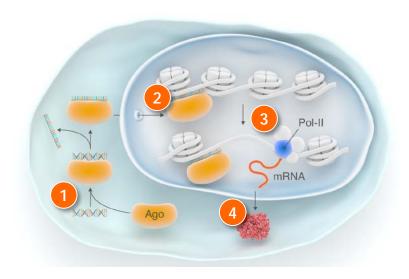
Strategic investment in saRNA technology

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



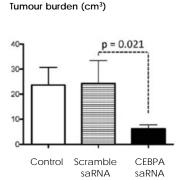
- Loading of saRNA into Ago protein
- saRNA-Ago targets gene promoter
- saRNA-Ago activates gene transcription
- Long lasting protein upregulation

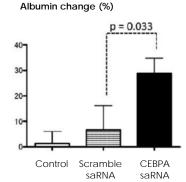
Lead candidate CEBPA¹ in Ph 1/2a for liver cancer

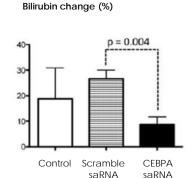
- CEBPA regulates multiple pathways in the liver and saRNA is a unique modality for targeting CEBPA
- MTL-CEBPA has preclinical efficacy across progression of liver disease
- MTL-CEBPA is the first saRNA to reach the clinic currently in clinical trials in patients for liver cancer, an orphan indication



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









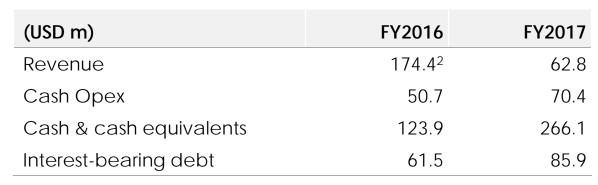
Balance sheet strengthened to scale and progress the business

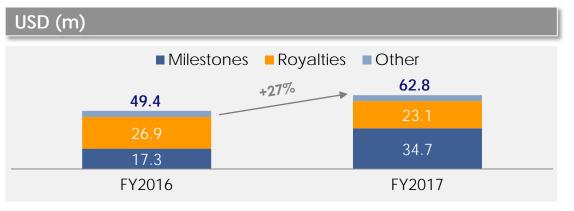
Allergan upfront milestone in FY2016 drives P&L variance

Summary financials (reported)						
(JPY m) ¹	FY2016	FY2017				
Revenue	18,901 ²	6,955				
Cash Opex	5,496	7,790				
Cash & cash equivalents	13,899	28,281				
Interest-bearing debt	6,900	9,173				

(JPY m) ¹	FY2016	FY2017
Revenue	18,901 ²	6,955
Cash Opex	5,496	7,790
Cash & cash equivalents	13,899	28,281
Interest-bearing debt	6,900	9,173

Revenue (ex Allergan upfront)							
JPY (m)							
■ Milest	tones Royalties	Other					
5,357	+30%	6,955					
		2,561					
2,918		3,840					
1,880							
FY2016 FY2017							





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

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
Allergan	Muscarinic Receptor program	125	665	2,575	3,365	15	Tiered, double- digit	 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 AZD4635 Collaboration to discover further A_{2A} 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 SBDD² platform
- <u>Partnered</u> 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

Thank you!



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