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sosei HEPTARES

World-leading drug discovery targeting GPCRs

40th Annual J.P. Morgan Healthcare 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.

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

Listed on Tokyo Stock Exchange (4565-JP). US$1.2bn Mkt. Cap.

200+ EMPLOYEES WORLDWIDE

340+ STRUCTURES SOLVED

500+ GLOBAL PATENTS

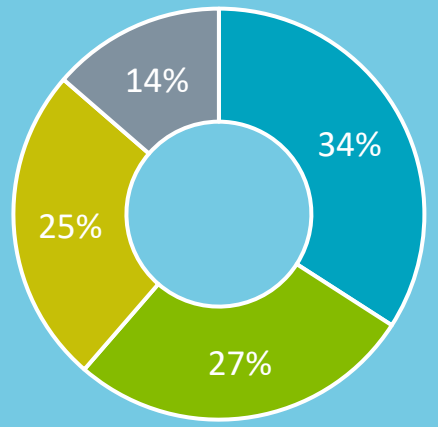
15+ WORLD-LEADING PARTNERS

$500M+ CASH ON BALANCE SHEET

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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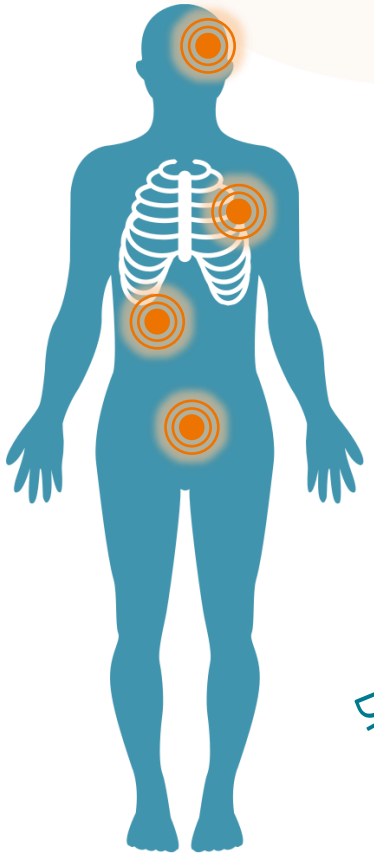
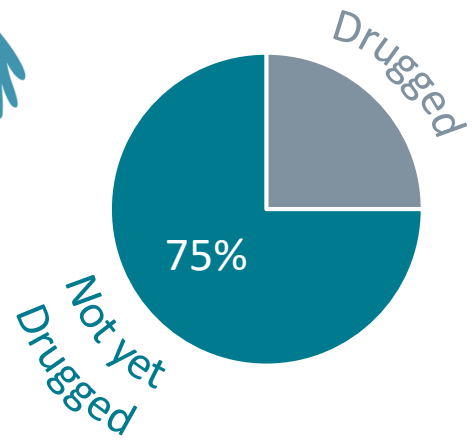
We **unlock the potential of GPCRs** with our **StaR® technology**

GPCRs are well-known targets with **significant untapped opportunity**

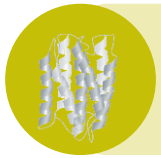


~400 GPCR PROTEINS



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

Unstable native GPCR



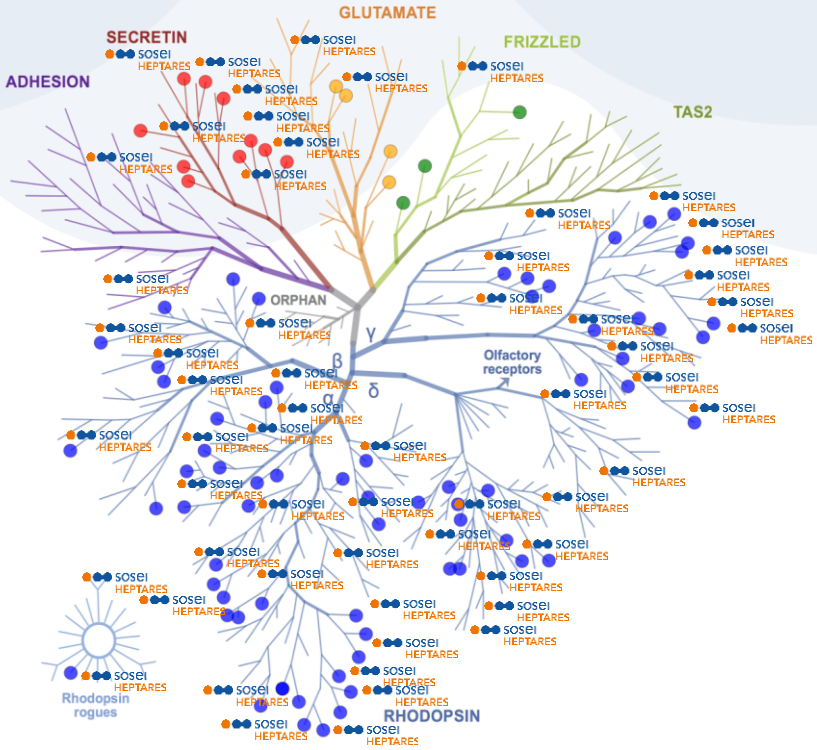
Stabilized StaR® protein

Enables mAb discovery

SBDD

Novel drug candidate

SMEs and Peptides



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

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)

Receptors for which Sosei Heptares has developed a StaR®

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Core capabilities in **drug discovery** and **early development**

DRUG DISCOVERY/EARLY DEVELOPMENT DRIVEN BY STAR® / SBDD ENGINE

LATE STAGE DEVELOPMENT

PRE-DISCOVERY	DISCOVERY	PRECLINICAL	PH 1a	PH 1b
StaR® Technology Structure Hit ID Target Validation ✓	**SBDD** Chemistry Pharmacology ✓	DMPK Toxicology Translation ✓	SAD MAD Experimental Medicine ✓	Dosing assessment Proof of Mechanism ✓

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

PH 2/3	APPROVAL
• Strategic tactical development team sources novel global treatments for Japanese patients • Development plans target approvals and domestic launch by 2025 timeframe	
PMDA Clinical Efficacy ✓	PMDA Pharmacovigilance ✓

Our **approach is validated** through **20+ active GPCR programs** with world class partners

Active Partnerships

abbvie · Neurocrine Biosciences · biohaven pharmaceuticals · Captor Therapeutics · Hisamitsu · Genentech A Member of the Roche Group · gsk · Inveni AI · kymab · metrion biosciences · NOVARTIS · PeptiDream · Pfizer · PHARMENABLE · Takeda · TWIST BIOSCIENCE · verily

Active Spin-Out Asset Centric Vehicles

SOSEI HEPTARES · medicxi · Orexia · INEXIA · CENTESSA PHARMACEUTICALS

SOSEI HEPTARES · Aditum Bio · Tempero Bio

~$800 million Upfront and milestone payments, royalties and R&D funding received from partners to date[1]

~$7 billion Total potential deal value of active partnerships[2]

[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.

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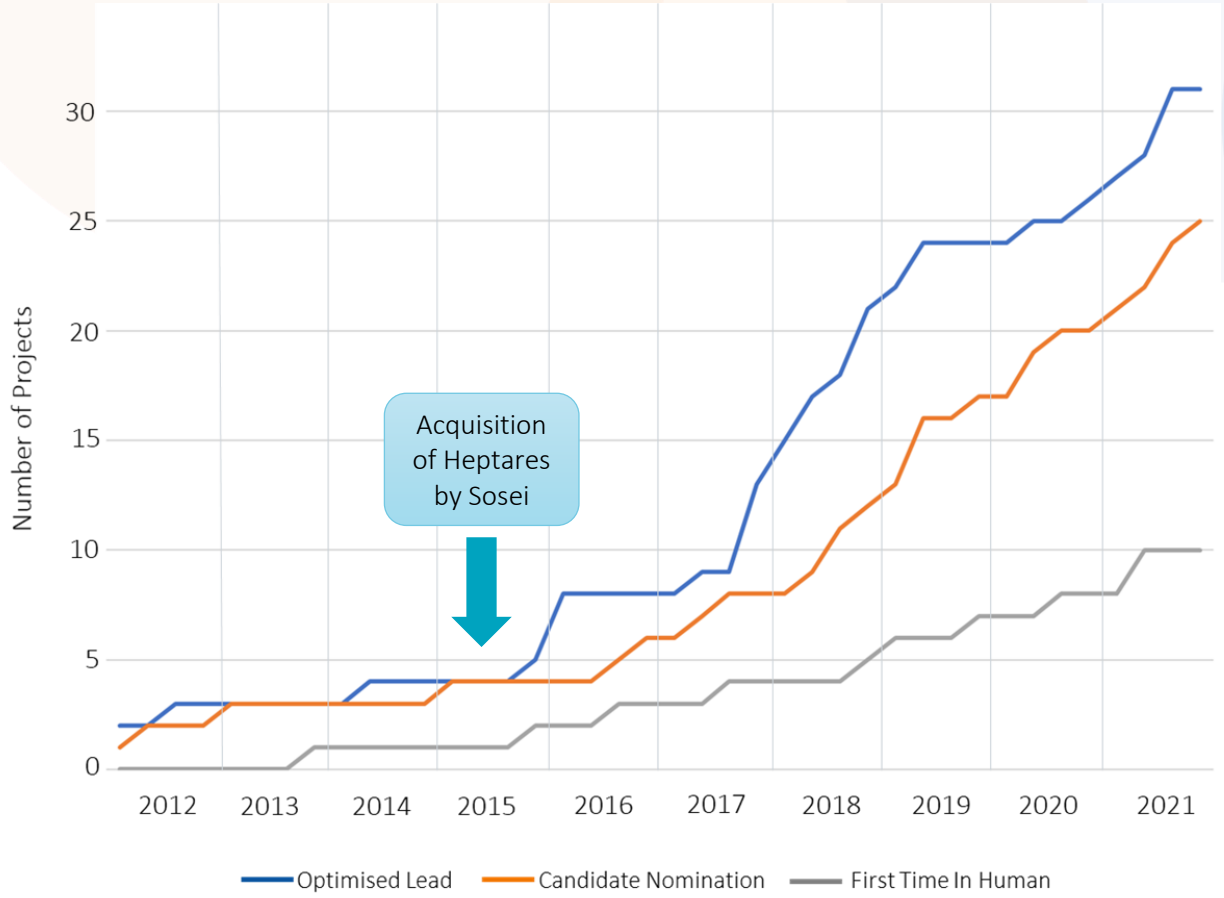
Ten drug candidates generated from our SBDD platform have been successfully advanced into clinical trials in the past 7 years



Generated

25

preclinical candidates

Produced

10

clinical candidates

TODAY*
LEAD OP
6 programs
PRECLINICAL
9 candidates
CLINICAL
9 candidates

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

*5 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

Broad and balanced pipeline of partnered and in-house programs, plus new technology collaborations will drive long-term momentum

	Pre-Disc. / Discovery	Preclinical studies	Phase 1	Phase 2	Marketed
Out-licensed	Multi-target Multiple Genentech	M_1M_4 ag. Neurology Neurocrine	M_4 ag. HTL'878 Neurology Neurocrine	GLP-1 ag. T2DM/Obesity Pfizer	A2a ant. combo(s)** mCRPC AstraZeneca	Ultibro® Breezhaler® COPD NOVARTIS
	Multi-target Multiple Pfizer	$M_{1\ Ag.}$ B/U Neurology Neurocrine	M_1 ag. HTL'936/'318 Neurology Neurocrine	CCR6 ant. IBD Pfizer		Seebri® Breezhaler® COPD NOVARTIS
	Multi-target GI and other Takeda	GPR35 ag. IBD gsk	CGRP ant. Neurology biohaven	MC4 ant. Anorexia Pfizer		Enerzair® Breezhaler® Asthma NOVARTIS
	Single target Inflammatory abbvie					Oravi® Mouth candidiasis Hisamitsu
Co-dev / Profit share	Captor Therapeutics® TPD		CXCR4 mAb Immuno-oncology SANOFI kymab			
	metrion Ion channel					
	PeptiDream PAR2 peptide					
	PHARMENABLE Inveni AI verily AI-driven					
Co-owned companies	OX1/OX2 ag. Narcolepsy CENTESSA Orexia Therapeutics			mGlu$_5$ NAM Substance Use Tempero Bio		
In-house / Not yet partnered*	SARS-CoV-2 MPro Coronaviruses	GPR52 ag. Neurology	H4 ant. Atopic Dermatitis			
	PAR2 mAb Atopic Dermatitis	EP4 ant. Immuno-oncology	EP4 ag. IBD			
	10+ other programs					

Partnered Program

In-house Program

★ To be discussed further on following slides

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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). ** AstraZenenca 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

Licensed Portfolio

M4 agonists
(Global)

Dual M4/M1 agonists
(Global)

M1 agonists
(ex-Japan)

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

					Efficacy			Safety	
					Positive symptoms	Negative symptom	Cognitive impairment	Extrapyramidal symptoms**	Weight gain
	MoA	Typical medicine	Peak sales example	Generation	Number of patients 20M*	Number of patients 11.5M*	Number of patients 16M*	-	-
Typical antipsychotic	D2 Ant	Haldol	(Historic data unavailable)	1st	+++	-	-	++++	+
Atypical antipsychotics	D2 Ant + 5-HT Regulator	Zyprexa Risperdal Latuda	Zyprexa $5,000M+ (2010)	2nd	+++	+	+	++	++++
	D2 partial Ag + 5-HT Regulator	Abilify REXULTI Vraylar	Abilify $6,100M+ (2013)	3rd	+++	+	+	+	+
	M4 Agonist***	KarXT CVL-231 **HTL'878**	-	4th	+++	++	++	-	-

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

*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.
Source : P T. 2014 Sep; 39(9): 638–645, J Clin Psychiatry. 2010;71(3):280–286, Schizophr Bull. 2010 Jan; 36(1): 36–42 and EvaluatePharma

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

Schizophrenia and Psychosis	Atopic Dermatitis	Immunosuppression in solid tumors	Inflammatory Bowel Disease
GPR52 agonist	H4 antagonist	EP4 antagonist	EP4 agonist
TARGET PRODUCT PROFILE			
• Once daily oral small molecule • 24hr target engagement	• Once daily oral small molecule • To be used as a monotherapy or in combination	• Once daily oral small molecule • To be used in combination with checkpoint inhibitors	• Oral GI restricted • Good potency and selectivity • Minimal GI systemic exposure

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New initiatives and future innovations

Strategic growth plan driving corporate value expansion

OBJECTIVE

Capital raise completed to pursue revenue focused deals in 2022

OBJECTIVE

Take steps to expand beyond core GPCR specialty

✓ ometrion biosciences

STRATEGIC GROWTH PLAN

Seek out revenue-generating opportunities

Invest / collaborate in novel technologies

Expand drug target classes beyond GPCRs

In-license late-stage programs for Japan

OBJECTIVE

Add new technology capabilities to our SBDD platform

✓ PHARMENABLE ✓ Inveni AI

✓ TWIST BIOSCIENCE ✓ verily

OBJECTIVE

Bring international medicines to Japanese patients in areas of unmet need

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

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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)

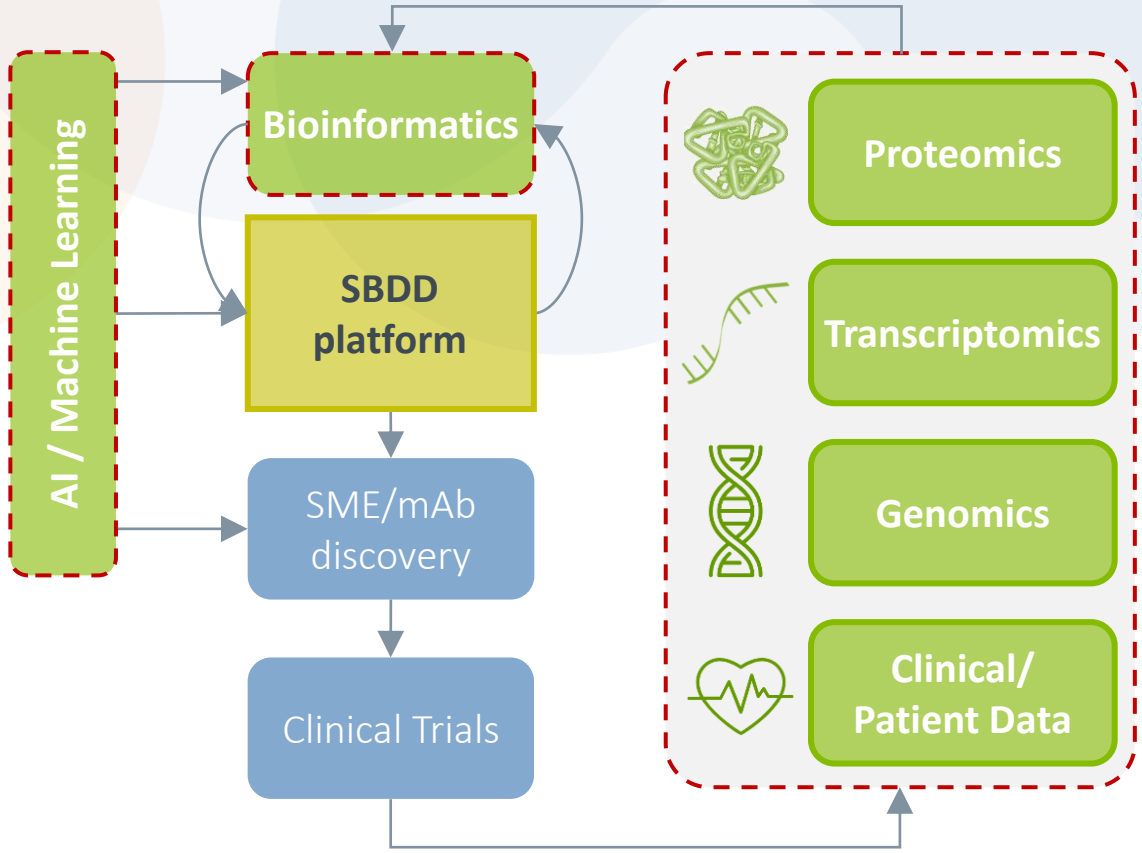
Conducting
the right patient studies

- 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

verily

- Research collaboration combining Verily's immune profiling capabilities and SH's StaR® platform and SBDD capabilities
- Collaboration aims to identify GPCRs expressed in immune cells, enhance our understanding of their functional relevance and prosecute as potential drug targets in **immune-mediated diseases**

InveniAI

Innovate with Intelligence

- Discovery collaboration combining InveniAI's AI-powered platform for target discovery with SH's GPCR SBDD and early development capabilities
- Collaboration aims to identify new therapeutic product concepts for **immune diseases** and generate novel compounds that could improve responses to existing immunotherapies

TWIST BIOSCIENCE

- Discovery collaboration combining Twist's synthetic antibody libraries and bioinformatics expertise with SH's StaR® platform
- Collaboration aims to discover **therapeutic antibodies** against GPCRs identified by SH
- SH will have exclusive, full global rights to develop and commercialize any antibody leads identified and directed to the targets of interest

Leveraging the best technologies to drive synergies with our platform and accelerate novel drug discovery

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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

- Cell sorting & frequencies
- Gene expression
- Disease score, treatment / response
- Chromatin accessibility & contacts

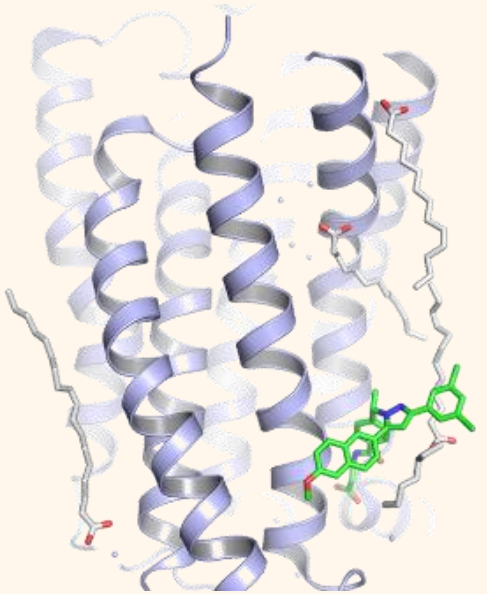
Analysis
Integrative analysis
+ Quality Control

- Prioritized pathways & signatures
- Multi-faceted evidence
- Public datasets
- Wet lab validation

= Better Tx & Better Dx

sosei HEPTARES 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

Targeted GPCR Degradation

Captor Therapeutics®

- Technology collaboration to initially identify novel small molecules that target a GPCR for degradation as potential therapeutic agents for **gastrointestinal disorders**
- Further aim to generate high resolution structural information around the GPCR-E3 ligase complex to enhance drug discovery efforts

Ion Channels

metrion biosciences

- Technology collaboration to demonstrate the potential of SBDD to address disease-associated ion channels
- Initial focus to identify novel, highly specific drug leads for further development against a single ion channel associated with **neurological diseases**

COVID-19 Treatment

Wellcome

- In-house program funded by Wellcome through the Covid-19 Therapeutics Accelerator
- 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 **COVID-19**

Our SBDD platform is also now being applied to areas outside our traditional GPCR space

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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

Large addressable market with blockbuster sales profiles…

~20M Schizophrenia patients worldwide

Blockbusters sales profiles despite limited efficacy and severe side effects

$10BN+ (2020) → **$13BN+** (2026)

Zyprexa Olanzapine · Seroquel quetiapina · Abilify (aripiprazole)

…Limited innovation in 70 years

Current treatments use the same mechanism of action from the 1950s

1st Gen	D2 modulating
Atypicals	Dual D2/5HT modulating
2nd Gen Atypicals	Dual D2/5HT modulating

Vraylar (cariprazine) capsules · Rexulti brexpiprazole · Caplyta (lumateperone) capsules

Huge opportunity for M4 agonists including HTL-0016878

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

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

Source: World Health Organization; EvaluatePharma

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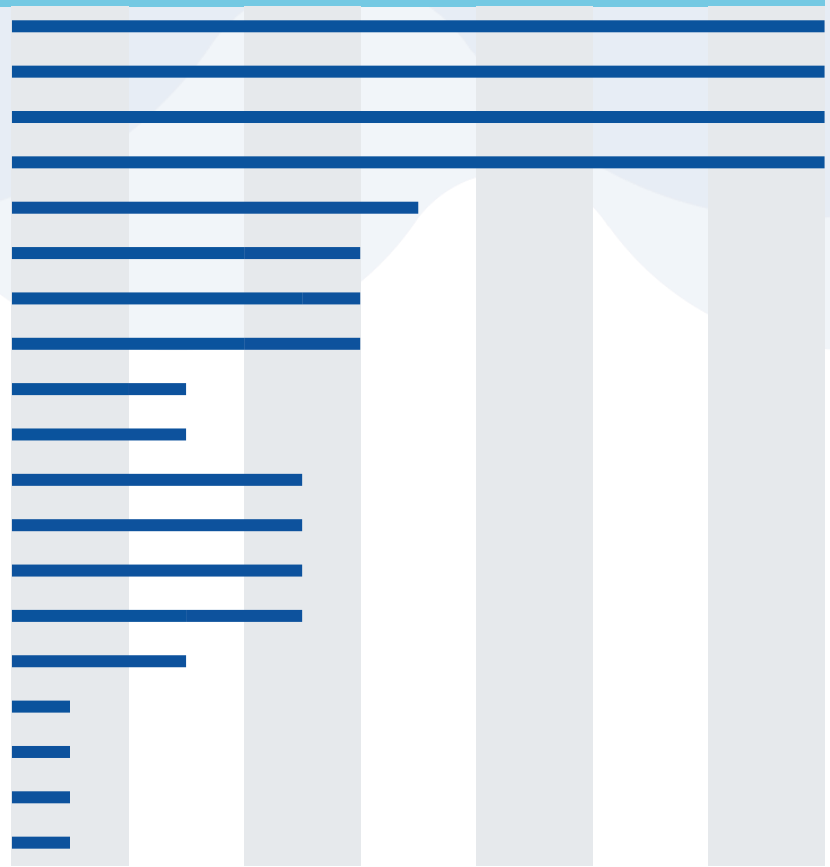
Partnered Pipeline

Compound	Target / Mechanism of Action	Modality	Indication	Partner
Traditional Out-licensing Collaborations				
Seebri® Breezhaler®	LAMA	SME	COPD	Novartis
Ultibro® Breezhaler®	LAMA+LABA	SME	COPD	Novartis
Enerzair® Breezhaler®	LAMA+LABA+ICS	SME	Asthma	Novartis
ORAVI®	Antifungal agent miconazole	SME	Oropharyngeal candidiasis	Hisamitsu
Imaradenant**	Adenosine A2a ant. combo	SME	mCRPC	AstraZeneca
HTL'878	Muscarinic M4 agonist	SME	Neurology diseases	Neurocrine
HTL'318 [1]	Muscarinic M1 agonist	SME	Neurology diseases	Neurocrine
HTL'936	Muscarinic M1 agonist	SME	Neurology diseases	Neurocrine
Not disclosed	Muscarinic M1 agonist (B/U)	SME	Neurology diseases	Neurocrine
Not disclosed	Muscarinic M1/M4 agonist	SME	Neurology diseases	Neurocrine
PF-07081532	GLP-1 agonist	SME	T2DM / Obesity	Pfizer
PF-07054894	CCR6 antagonist	SME	Inflammatory bowel disease	Pfizer
PF-07258669	MC4 antagonist	SME	Anorexia	Pfizer
BHV3100	CGRP antagonist	SME	Neurology diseases	Biohaven
Not disclosed	GPR35 agonist	SME	Inflammatory bowel disease	GSK
Not disclosed	Multi target	SME	Multiple indications	Pfizer
Not disclosed	Multi target	SME/LME	Multiple indications	Genentech
Not disclosed	Multi target	SME/LME	Gastrointestinal and other	Takeda
Not disclosed	Single target	SME	Inflammatory diseases	AbbVie



Note: SME = small molecule. LME = large molecule. Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG. ** AstraZenenca have removed the A2a program from their clinical pipeline as at Q3 2021

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Partnered Pipeline (cont'd)

Compound	Target / Mechanism of Action	Modality	Indication	Partner	Disc.	PCC	Ph1	Ph2	Ph3	App	Mkt
Co-development / Profit-share Collaborations											
KY1051	CXCR4 mAb	mAb	Immuno-oncology	SANOFI kymab							
Not disclosed	PAR-2	Peptide	Inflammatory diseases	PeptiDream							
Not disclosed	Targeted Protein Degradation	SME	Gastrointestinal disorders	Captor Therapeutics							
Not disclosed	AI-Augmented Drug Discovery	SME	Neurology diseases	PHARMENABLE							
Not disclosed	Ion Channel Drug Discovery	SME	Neurology diseases	metrion biosciences							
Not disclosed	Multi target AI-powered	SME/LME	Immune diseases	InveniAI							
Not disclosed	Antibody Discovery	mAb	Disease-relevant GPCR targets	TWIST							
Not disclosed	Multi target AI-powered	SME/LME	Immune diseases	verily							
Co-owned Investments											
TMP301	mGlu5 NAM	SME	Substance use disorders	Tempero Bio							
Not disclosed	OX1/OX2 agonist (oral and intranasal)	SME	Narcolepsy	CENTESSA, Orexia Therapeutics							

Note: SME = small molecule. LME = large molecule. Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG.

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In-house Pipeline

Compound	Target / Mechanism of Action	Modality	Indication	Originator	Dis	PCC	Ph1	Ph2	Ph3	App	Mkt.
In-house Programs (Not yet partnered)											
Not disclosed	H4 antagonist	SME	Atopic Dermatitis	SOSEI HEPTARES							
Not disclosed	EP4 antagonist	SME	Immuno-oncology	SOSEI HEPTARES							
Not disclosed	GPR52 agonist	SME	Neurology diseases	SOSEI HEPTARES							
Not disclosed	EP4 agonist	SME	Inflammatory bowel disease	SOSEI HEPTARES							
Not disclosed	PAR-2 mAb	mAb	Atopic Dermatitis	SOSEI HEPTARES							
SH-879	SARS CoV-2 Mpro	SME	Coronaviruses	SOSEI HEPTARES							
Multiple programs	Not disclosed	SME/LME	Neurology diseases	SOSEI HEPTARES							
Multiple programs	Not disclosed	SME/LME	GI and Inflammatory diseases	SOSEI HEPTARES							
Multiple programs	Not disclosed	SME/LME	Immunology diseases	SOSEI HEPTARES							
In-house Programs (No longer internally funded. Targeting academic / industrial partnership)											
HTL'310	SSTR5 agonist	Peptide	Hypoglycaemic disorders	SOSEI HEPTARES							
HTL'097	GLP-1 antagonist	Peptide	Hypoglycaemic disorders	SOSEI HEPTARES							
HTL'023	Dual GLP-2/GLP-1 agonist	Peptide	Intestinal failure / NASH	SOSEI HEPTARES							
Not disclosed	Apelin agonist	Peptide	Pulmonary Arterial Hypertension	SOSEI HEPTARES							
HTL'641	Dual orexin antagonist	SME	Insomnia and sleep disorders	SOSEI HEPTARES							

Note: SME = small molecule. LME = large molecule. [1] Voluntarily suspended

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