NON-CONFIDENTIAL

FY2020 Financial Results

12-month period ended December 31, 2020

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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.

Agenda

1. FY2020 Financial Results
2. FY2020 Operational Highlights
3. Key Themes for the Future
4. FY2021 Strategic Outlook
5. Appendix

Note: This material was created to explain the details of our company and is not intended to be used for investment decisions. In addition, the contents reflect the views of our company at the time of the creation of the material, and the accuracy of the information is not guaranteed. Investments should be made based on the independent views of investors

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FY2020 Financial Results

Chris Cargill, CFO

Another year of successful execution

Summary Financial Highlights for the 12 months ended 31 December 2020

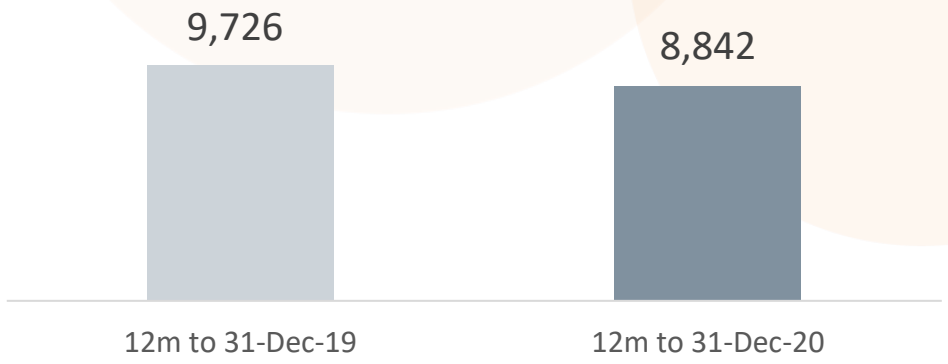
1. **Revenue of ¥8,842m** ($83m) vs. ¥9,726m ($89m) in prior corresponding period, driven by progress with existing collaborations, and effective execution of new partnerships and co-investments
2. **Cash Earnings Profit of ¥2,904m** ($27m) vs. ¥2,846m ($26m) in prior corresponding period, due to rigorous focus on collaborative partnerships, strategic execution and cost control
3. **Operating Profit of ¥928m** ($9m) vs. ¥384m ($4m) in prior corresponding period, successfully achieving our corporate goal to **target sustainable and/or profitable results** for the Full Year
4. **~$200m new growth capital raised**, Japan's largest biotech financing during COVID-19, to support aggressive strategic growth plan
5. **Net cash inflow of ¥24.6bn** ($246m), resulting in a **robust cash balance of ¥40bn** ($387m) at year end

Our unique and balanced business model is driving a **sustainable financial profile**

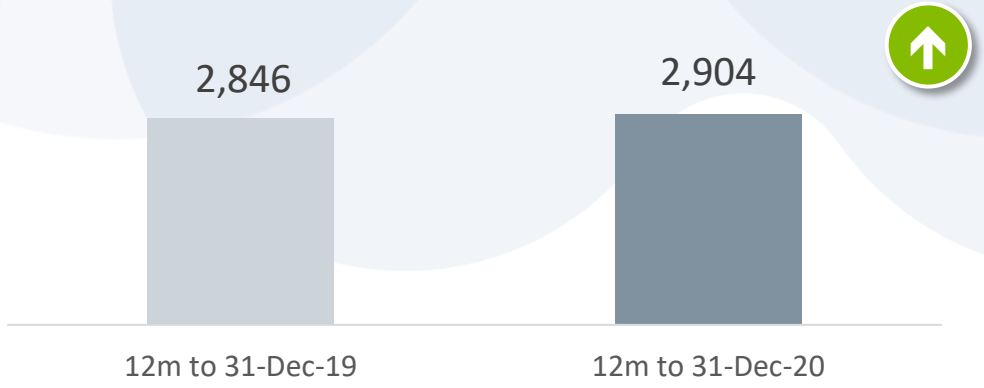
Note: USD:JPY FX rates used – 106.77 (FY2020) and 109.03 (FY2019)

Our focus on cost control and sustainable levels of R&D investment delivered a second consecutive year of profitable results

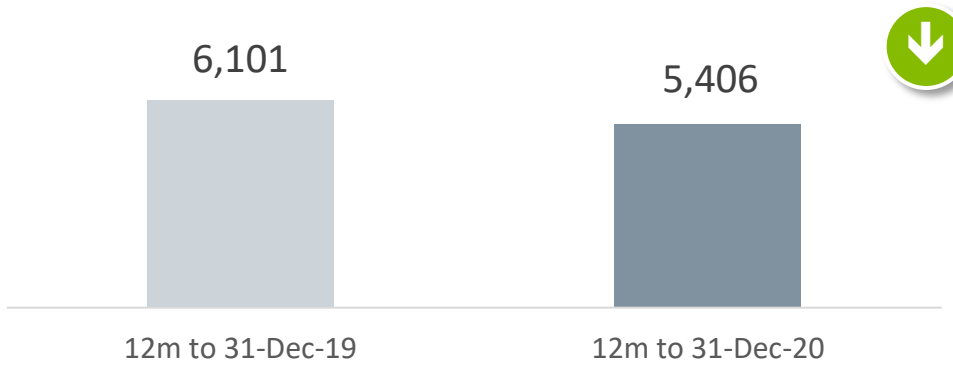
Revenue (JPY million)



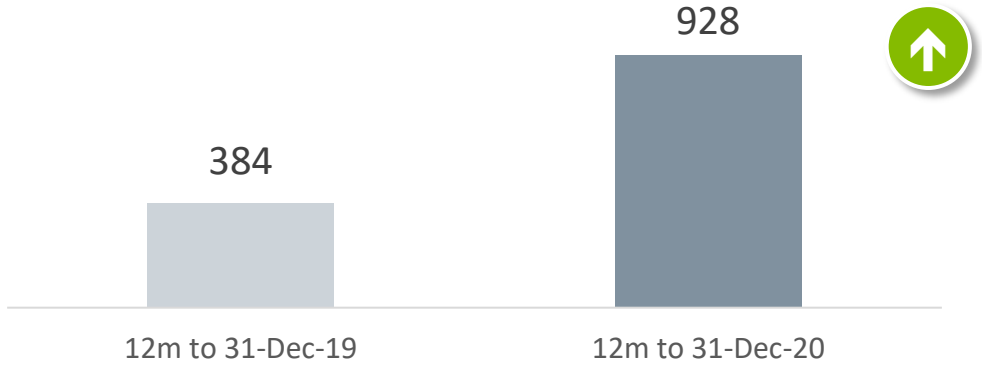
Cash Earnings Profit[1] (JPY million)



Cash Operating Expenses[1,2] (JPY million)



Operating Profit (JPY million)



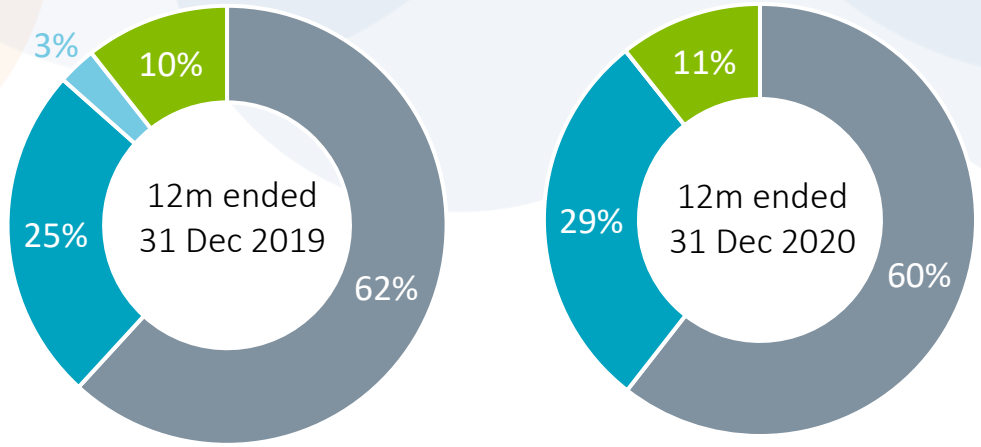
Note: [1] Non-IFRS measure; [2] Cash Operating Expenses = Cash R&D + Cash G&A

Our emphasis on collaborative drug discovery partnerships and co-investments drove a balanced split of revenues

	JPY million		USD million	
	12m ended 31 Dec 2019	12m ended 31 Dec 2020	12m ended 31 Dec 2019	12m ended 31 Dec 2020
Revenue	9,726	8,842	89.2	82.8
Cash Cost of Sales	(807)	(607)	(7.4)	(5.7)
Cash R&D	(3,937)	(3,411)	(36.1)	(31.9)
Cash G&A	(2,164)	(1,995)	(19.8)	(18.7)
Other Cash Income	28	75	0.3	0.7
Cash Earnings Profit	**2,846**	**2,904**	**26.1**	**27.2**
Non-Cash Costs	(2,462)	(1,976)	(22.6)	(18.5)
Operating Profit	**384**	**928**	**3.5**	**8.7**
Net Finance Costs	331	1,050	3.0	9.8
Equity Accounted Investments	(181)	(356)	(1.7)	(3.3)
Net Profit before income tax	**534**	**1,622**	**4.9**	**15.2**
Net Profit	**1,432**	**1,479**	**13.1**	**13.8**

Note: USD:JPY FX rates used – 106.77 (FY2020) and 109.03 (FY2019)

Revenue by Type



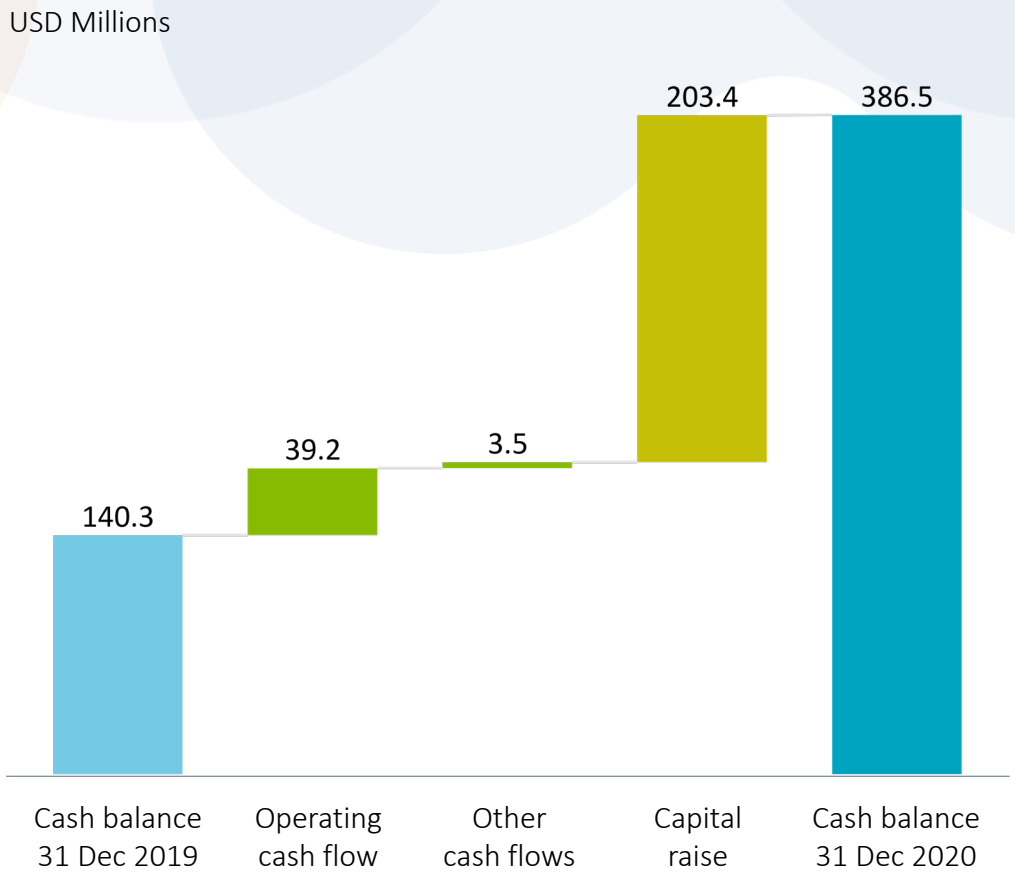
	12m ended 31 Dec 2019		12m ended 31 Dec 2020	
Milestone	¥6,013m	$55.1m	¥5,353m	$50.1m
Royalty	¥2,406m	$22.1m	¥2,544m	$23.8m
Product Sales	¥276m	$2.5m	–	–
Other	¥1,031m	$9.5m	¥945m	$8.9m

Positive operating cash flows and a highly successful capital raising have us well positioned to invest in enhancing corporate value

	JPY million		USD million	
	As of 31 Dec 2019	As of 31 Dec 2020	As of 31 Dec 2019	As of 31 Dec 2020
Goodwill & intangibles	27,364	25,936	249.8	250.5
Property, plant & equip.	4,120	3,824	37.6	36.9
Cash at hand	15,375	40,008	140.3	386.5
Equity Acc. investments	3,539	3,087	32.3	29.8
Other financial assets	2,053	1,593	18.7	15.4
Other assets	4,229	2,017	38.6	19.5
Total Assets	**56,680**	**76,465**	**517.4**	**738.6**
Corporate Bonds	–	14,789	–	142.9
Other liabilities	11,602	9,295	105.9	89.7
Total Liabilities	**11,602**	**24,084**	**105.9**	**232.6**
Net Assets	**45,078**	**52,381**	**411.5**	**506.0**

Note: USD:JPY FX rates used – 106.77 (FY2020) and 109.03 (FY2019)

Cash Flow Bridge (12m ended 31 Dec 2020)



Our commitment to sustainable and balanced risk and reward investing enabled us to keep costs under control

	Cash R&D expenses	Cash G&A expenses
Q3 2020 Guidance	**¥4,200 to 4,700m**	**¥1,800 to 2,300m**
Actual results (Dec-20)	**¥3,411m**	**¥1,995m**

- ✓ Successful negotiations with suppliers to claw back prior year overcharges
- ✓ Increase in new collaborations shifted large development costs to partners
- ✓ Managed slow down in program expenditure from coronavirus delays

- ✓ Prudent cost management
- ✓ Reduction mainly due to UK National Insurance related credit driven by movement in share price

)

Modest increases in investment to fuel programs, add new major partners, and drive a step-up in our corporate valuation

Guidance (Dec-21)

Cash R&D expenses	Cash G&A expenses
¥4,000 to 5,000m	**¥1,800 to 2,300m**
✓ Increased investment in HTL'878 selective M4 agonist program – an extremely valuable opportunity to secure a new major partnership ✓ Accelerate new first-in-class target discovery and advance programs	✓ Continued build-out of Compliance and Governance capabilities ✓ Implementation of Oracle Netsuite ERP system

Investing today to drive growth tomorrow

2

FY2020 Operational Highlights

Chris Cargill, CFO

Organic growth plan driving our world-leading GPCR drug discovery

Building a broad pipeline to fuel the continued execution of high-value partnerships and co-investments

Organic growth plan driving our world-leading GPCR drug discovery

ORGANIC GROWTH PLAN

OBJECTIVES MET

- ✓ **Jan-20** – Orexin agonist scientific breakthrough, triggering next tranche of Medicxi funding (**Orexia, Inexia**)
- ✓ **Dec-20** – Strategic technology collaboration with **Captor Therapeutics** for Targeted Protein Degradation

OBJECTIVES MET

- ✓ **H1 FY20** – Nomination of **H4 ant.** candidate for Atopic Dermatitis
- ✓ **H1 FY20** – Nomination of **EP4 ant.** candidate for I/O
- ✓ **H1 FY20** – Nomination of **GPR35 ag.** candidate for IBD (which was then out-licensed to GSK)

Extend technology / platform leadership

Generate high quality novel candidates

- ✓ **H1 FY20** – **CGRP ant.** advanced to Phase 1 ready
- ✓ **H2 FY20** – **mGlu5 NAM** advanced through Phase 1
- ✓ **Jun/Jul-20** – **Enerzair®** approved in Japan and EU
- ✓ **Sep-20** – **CCR6 ant.** starts Ph 1

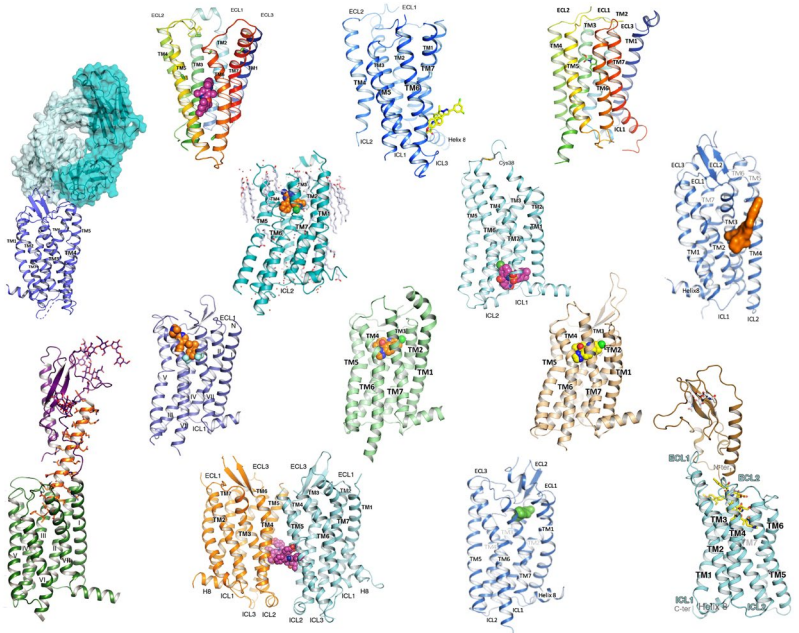
Advance discovery and development pipeline

Execute high value partnerships

- ✓ **Jun-20** – **AbbVie** collaboration targeting inflammatory diseases
- ✓ **Nov-20** – **Tempero Bio** collaboration for mGlu5 NAM
- ✓ **Dec-20** – **Biohaven** collaboration for CGRP antagonist
- ✓ **Dec-20** – **GSK** collaboration for GPR35 agonist

All organic growth objectives successfully achieved

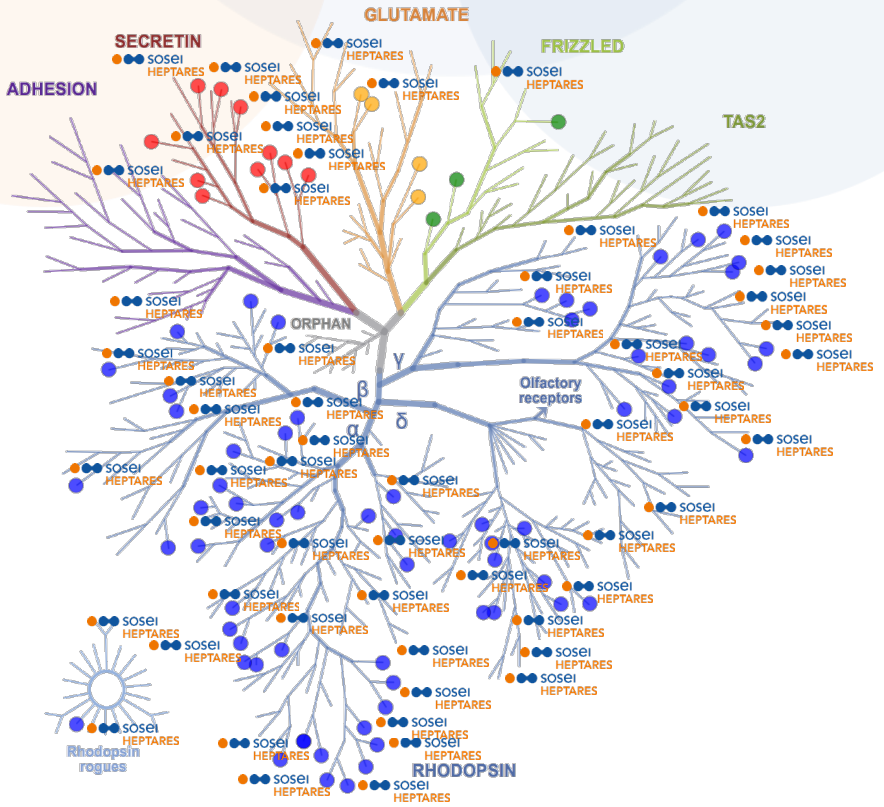
We continued to expand our expertise in GPCRs, having solved our 300th high-resolution structure from 30th GPCR drug target



Solved **300+** molecular structures from **30+** different receptors / **60+** StaRs

Highest resolution GPCR structure to date. Average resolution of **2.5Å** – higher than the average resolution reported globally.

Significant untapped GPCRome opportunity for years to come – **StaR® technology** is enabling us to unlock the potential of GPCRs



~400 GPCR targets

~75% Not yet drugged

Antagonist / Agonist bound

Small molecule / Antibody / Peptide discovery

Multiple indications

Source: "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, Protein Data Bank

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

Receptors for which Sosei Heptares has developed a StaR®

Our StaR® technology and SBDD platform enables productive drug discovery and generates multiple high quality candidates

LAST 10 YEARS (StaR® / SBDD GENERATED)

DRUG DISCOVERY

Generated

24

high quality novel preclinical candidates

EARLY DEVELOPMENT

Produced

8

IND[1] clinical candidates that have entered human trials

TODAY

LEAD OP

4 compounds

PRECLINICAL

13 candidates

CLINICAL

8 candidates

MEDIUM TERM OUTLOOK

TECHNOLOGY

Deliver at least

4

new programs to lead optimization stage every 2 years

DRUG DISCOVERY

Generate on average

2

new preclinical candidates every year

One of the most productive GPCR drug discovery teams in the world over the past 10 years

Note: [1] IND = Investigational New Drug

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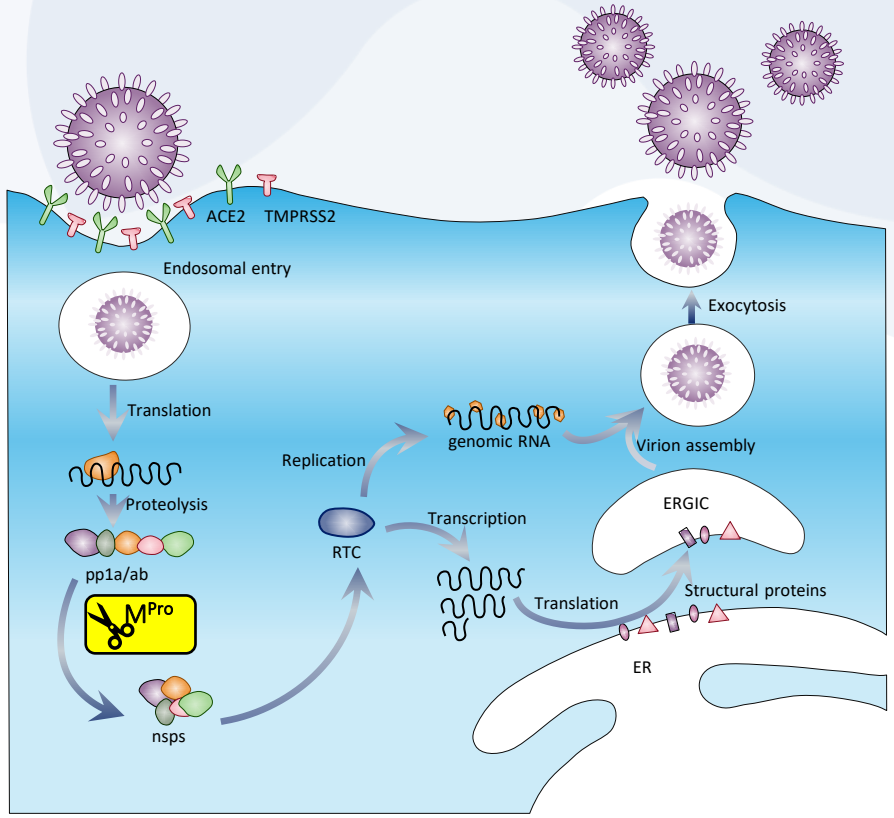
We leveraged our SBDD platform to support COVID-19 research in 2020, discovering a potent series of broad spectrum anti-virals

- Program focused on inhibitors of **SARS-CoV-2 main protease**, a highly conserved protein essential for viral replication
- Structure-based design approach has identified potent compounds for further development as **oral treatments** for SARS-CoV-2 infection and future coronavirus variants
- Program has advanced rapidly under an international collaboration of companies led by Sosei Heptares as part of its **commitment to socially responsible investing**



Now seeking partners with expertise in antiviral development for rapid progression of identified molecules for this important global fight against SARS-COV-2 and future coronavirus variants

We added multiple new partnered and in-house programs to our deep pipeline, which will drive more collaborations and value creation

	Pre-Disc. / Discovery (20+)	Preclinical development (13)			Phase 1 (7)	Phase 2 (2)	Marketed (4)
Out-licensed	Multi-target Multiple Genentech	Single target Metabolic Pfizer	GPR35 ag. IBD gsk	CGRP ant. Neurology biohaven	A_{2A} ant. Solid tumors AstraZeneca	A2a ant. combo(s) mCRPC AstraZeneca	Ultibro® Breezhaler® COPD NOVARTIS
	Multi-target Multiple Pfizer				GLP-1 ag. T2DM/Obesity Pfizer		Seebri® Breezhaler® COPD NOVARTIS
	Multi-target GI and other Takeda				CCR6 ant. IBD Pfizer		Enerzair® Breezhaler® Asthma NOVARTIS
	Single target Inflammatory abbvie						Oravi® Mouth candidiasis FUJIFILM
Co-dev / Profit share	Captor Therapeutics® TPD	metrion biosciences Ion channel		CXCR4 mAb Immuno-oncology SANOFI kymab			
	PeptiDream PAR2 peptide	PHARMENABLE AI					
Co-owned companies	OX1/OX2 ag. Narcolepsy Orexia INEXIA				$mGlu_5$ NAM Substance Use Tempero Bio		
In-house / Not yet partnered	SARS-CoV-2 MPro Coronaviruses	GLP-2 ag. peptide Intestinal failure	H4 ant. Atopic Dermatitis	PAR2 mAb Atopic Dermatitis	$SSTR_5$ ag. peptide Endocrine	M_1 ag[1] HTL'318 DLB	
	10+ programs Neurology GI / Inflammation Immunology	GLP1 ant. peptide[2] Endocrine	EP4 ant. Immuno-oncology	M_4 ag. Backup Neurology ★	M_4 ag. HTL'878 Neurology ★		
		GPR52 ag. Neurology	M_1M_4 ag. Neurology ★	M_1 ag. Backup Neurology ★	M_1 ag. HTL'936/'318 Neurology ★		

Partnered Program

In-house Program

★ Recently regained program

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Note: Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG. [1] Phase 2 trial of HTL0018318 for DLB in Japan has been withdrawn. The Group may resubmit a new clinical trial notification for HTL0018318 (or another novel M_1 agonist) to the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in the future. [2]The option to license GLP1 antagonist peptide was not exercised before 31 December 2020 and therefore the program is currently wholly in-house.

We continued to make excellent progress in collaborative drug discovery, adding three new pharma partnerships in 2020

Partner	Active Partnered Program	Therapeutic Area	UF / Near Term Payments	Potential deal value[1]
gsk	2020 Collaboration and Licensing Agreement for GPR35 agonist	Gastrointestinal, immunology	$44m	$480m+
biohaven pharmaceuticals	2020 Collaboration and Licensing Agreement for CGRP antagonist	Neurology	$10m	$380m+
abbvie	2020 Discovery Collaboration and Option to License[2]	Inflammatory and Autoimmune	$32m	$400m+
Takeda	2019 Multi-target Collaboration	Multiple; Initial focus on Gastrointestinal	$26m	$1.2bn+
Genentech A Member of the Roche Group	2019 Multi-target Collaboration	Multiple	$26m	$1.0bn+
Pfizer	2015 Multi-target Collaboration	Multiple	Nil	$1.8bn+
AstraZeneca	2015 Collaboration and Licensing Agreement for A_{2a} antagonist	Immuno-oncology	$10m	$500m+
TOTAL			**$148m**	**$5.9bn+**

[1] Potential option fees, development, regulatory and commercial milestone payments, plus royalties on global commercial sales;
[2] AbbVie has the option to expand the collaboration by an additional three targets

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We created Tempero Bio, an exciting co-owned investment with the global pharma industry leaders at Aditum Bio

Tempero Bio to advance the clinical development of **mGlu5 NAM** program in neurological diseases

Tempero Bio – a new company created to develop the mGlu5 NAM program, including candidate HTL14242 (TMP-301), to develop therapies targeting **substance use disorders and anxiety**.

Aim of co-investment to combine **high quality mGlu5 NAM pharmacotherapy with digital devices** to support patient treatment, improve adherence and ultimately create better patient outcomes.

Tempero Bio plans to bring TMP-301 into a **Phase 2** clinical trial within 12 months, utilizing **TrialSpark** – a tech-enabled platform – as the innovative clinical research engine.

Sosei Heptares received $5 million upfront payment and **strategic equity stake** in Tempero Bio, and is eligible to receive development and commercial milestone payments plus tiered royalties.

Tempero Bio

Nov 2020

Aditum Bio

Co-founded by industry veterans:

Joe Jimenez

NOVARTIS

Former CEO

Mark Fishman

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH

Founding President

Paul Sekhri

LYCERA

Former CEO

"We created Aditum Bio to select and develop clinical assets using a novel approach combining data, software and technology to speed development." – Joe Jimenez

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Strategic growth plan driving corporate value expansion

Adding new revenues, and accessing new technologies, to expand our future-proof our capabilities

✓ Collaborations in FY20 ✓ Collaborations in FY21 (See Appendix)

We have taken our first step into the exciting area of Targeted Protein Degradation via a strategic collaboration with Captor

Strategic technology collaboration with **Captor Therapeutics** focused on **targeted GPCR degradation**

Explores the potential of our unique combination of technologies to **develop a novel GPCR degraders platform**, opening up so far intractable drug targets for us to address.

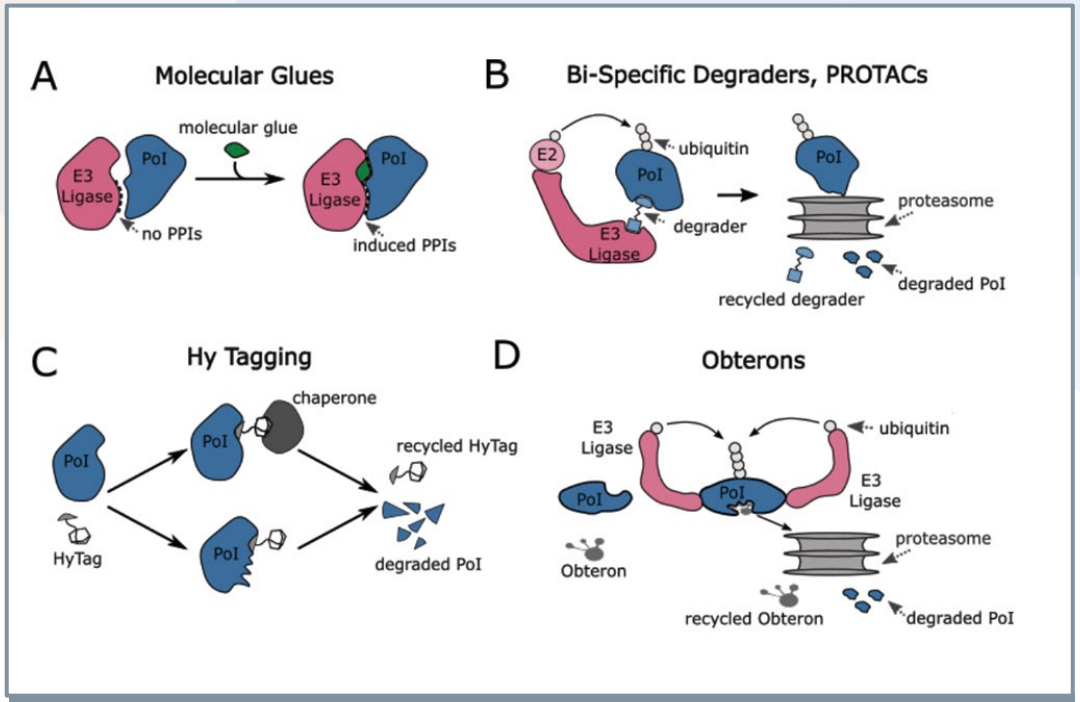
Targeted protein degradation – **novel approach to drug discovery** where the body's natural process for degrading proteins is diverted using small molecule drugs to eliminate disease-causing proteins.

Expected to have **multiple advantages over classical drugs** such as inhibitors and antibodies for the development of novel therapeutics against a broad range of diseases.

Initial focus to identify small molecules targeting a GPCR with a key role in a strongly validated signalling pathway implicated in **gastrointestinal disorders**.

Captor Therapeutics®

Dec 2020



- ✓ The Captor platform includes Molecular Glues, Bi-Specific Degraders and Obterons
- ✓ Each approach has different characteristics and may be better suited to different targets or diseases

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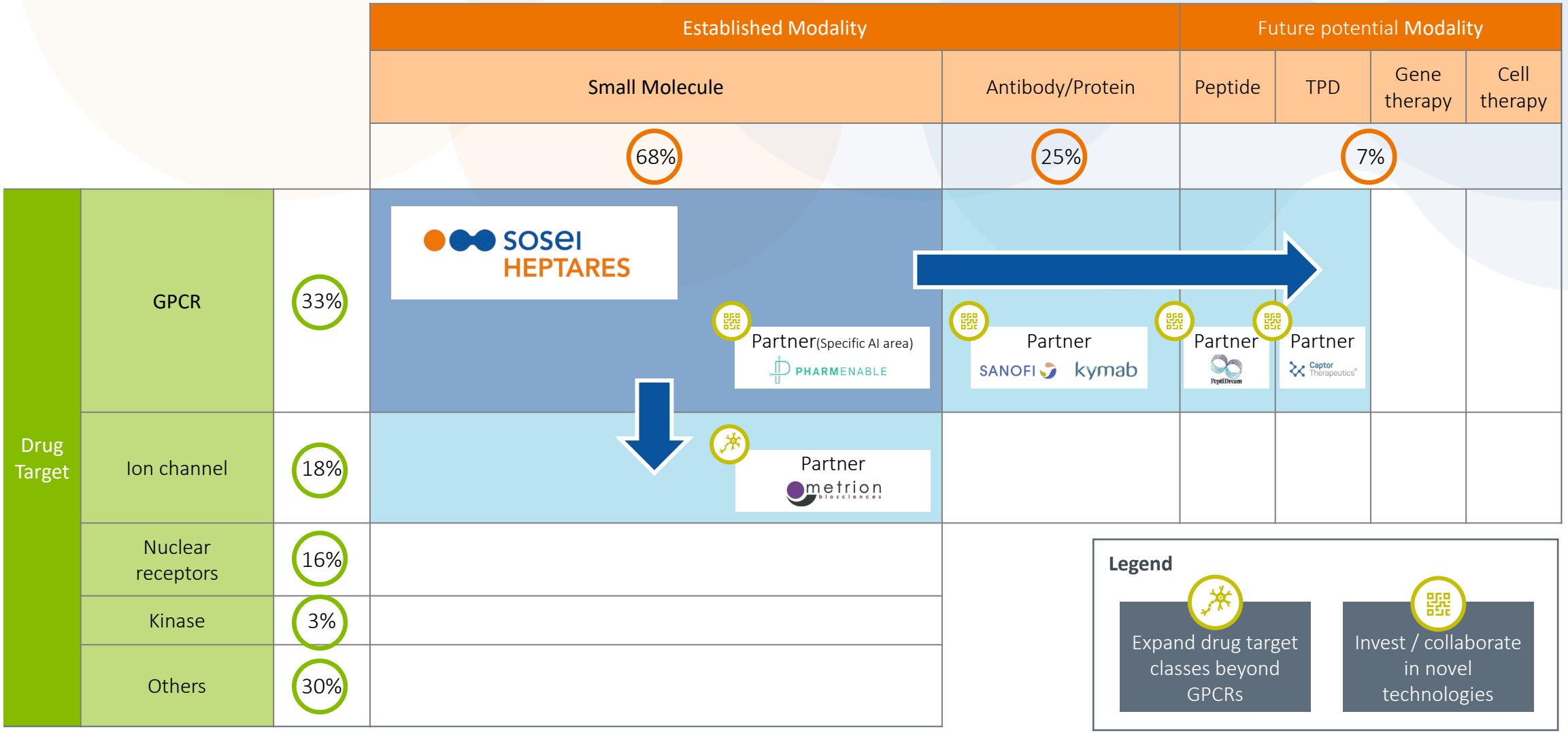
We are covering ~50% of the drug discovery landscape through the tactical expansion of our strategic collaborations



○ : Proportion of small–molecule drugs that target major families (Nature Reviews Drug Discovery volume 16, pages19–34(2017))

○ : Proportion of new drugs approved by FDA (2015-2019) by modality

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3

Key themes for the future

- Addressing challenges in drug discovery
- Being an ESG leader

Shinichi Tamura, Chairman and CEO

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)

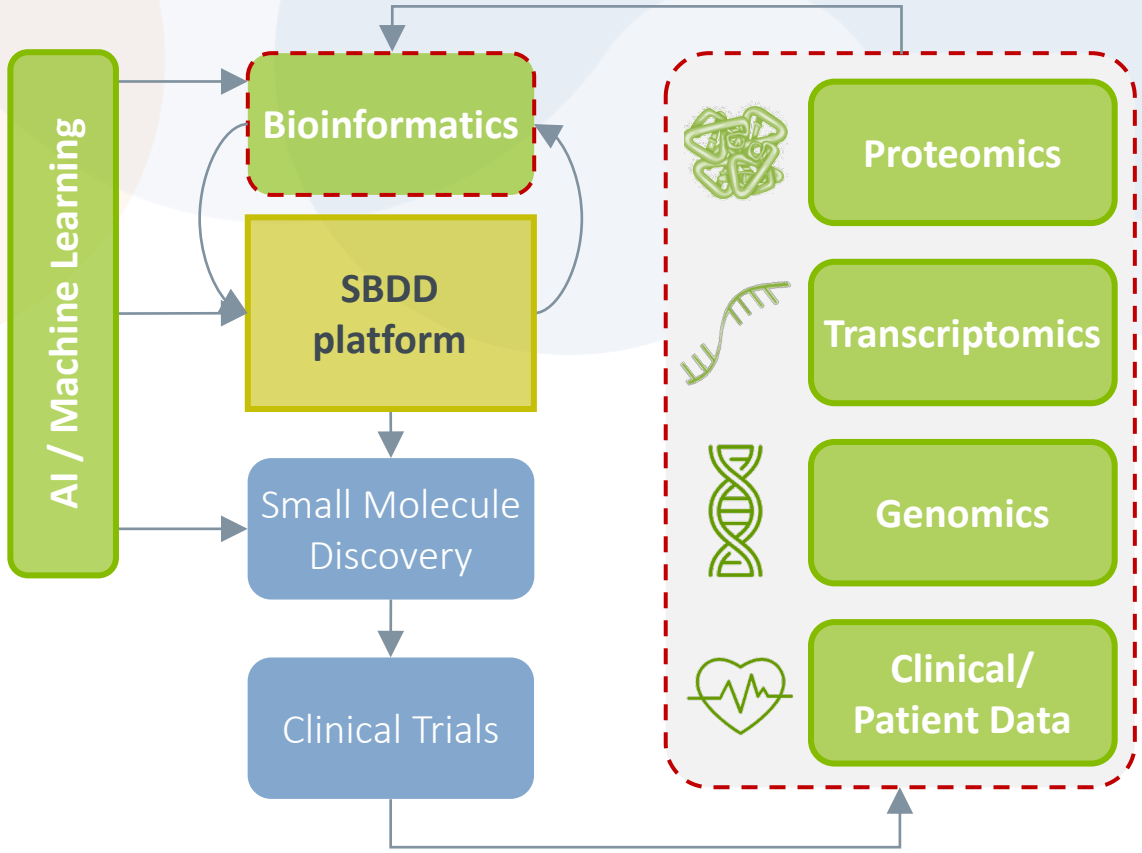
Conducting
the right patient studies

- 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

We have created the new target ID and validation (TIV) framework to accelerate our quest to **choose the right** 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

New TIV Framework - mid-term plan to pursue investments and external collaborations to hunt novel first-in-class drug targets

2021	2022	2023	2024

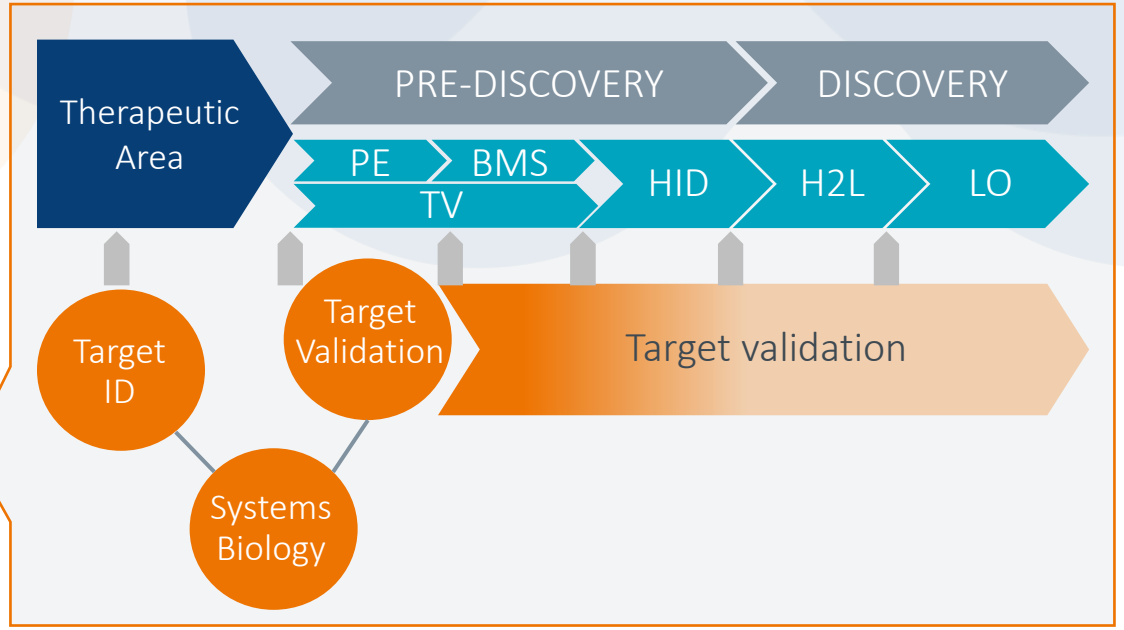
INTERNAL THERAPEUTIC AREA INITIATIVES

MAXIMIZE EXISTING COLLABORATIONS

NEW EXTERNAL COLLABORATIONS / ALLIANCES

- To support our Therapeutic Areas of Interest (GI/Immunology/Neuroscience)

Investing in the next wave of future targets



mAb PLATFORM BUILD

- Identify strategic partner to maximise platform capability

Commencing 2021 we will aggressively expand our external technology collaborations and alliances

Note: PE = Protein Engineering; BMS = Biomolecular Structure; TV = Target Validation; HID = Hit Identification; H2L = Hit-to-Lead; LO = Lead Optimization

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Our commitment to ensure a sustainable future for all

Sustainable Development Goals adopted by the United Nations (Sep-15)

Sosei Heptares is undertaking initiatives focused on 10 of the 17 Sustainable Development Goals

E SUSTAINABILITY COMMITTEE

- Promoting efficient energy use and renewable energy sources
- Reducing waste and water usage
- Promoting efficiency in drug discovery

S CHARITY COMMITTEE

- Hosting events to raise monetary donations for multiple dementia-related charities
- Equipment donations to local educational institutions

G GOVERNANCE STRUCTURE

- Board of Directors –6 members (incl. 5 external independent)
- Investment Committee and Scientific Advisory Board provide recommendations to the Board

Source: United Nations
LINK: https://soseiheptares.com/uploads/Sustainability/Sustainability_20201214_JP.pdf

4

FY2021 Strategic Outlook

Shinichi Tamura, Chairman and CEO

Priority objectives for FY2021

Being an ESG leader

- **Promote sustainable ESG practices and policies across global business**
- Establish collaborations with industry partners to further develop candidates as oral treatments for human coronaviruses

Progress the organic growth plan

- Extend technology / platform leadership
- **Generate high quality Preclinical-stage candidates**
- Advance discovery and development pipeline
- **Execute 2-3 new high value collaborations and/or co-investments**

Execute on the strategic growth plan

- **Seek out revenue-generating opportunities**
- **Invest / collaborate in novel technologies and expand drug target classes beyond GPCRs**
- In-license late-stage assets for Japan market

Thank you for continued investment and interest!

1. Maintain **technology and platform leadership** in our chosen field
2. Enter new high value drug discovery and development **partnerships with pharma /biotech**
3. Achieve **important milestones** on existing partnered programs
4. Seed multiple **new in-house drug candidates** in strategic areas for future high value partnering
5. **Advance selected in-house programs** in early-stage clinical studies for higher value partnering
6. Create new **asset-centric spin-out companies** backed by venture capital and retain equity holding

FY2020 Achievements

Orexin agonist scientific breakthrough (Orexia, INEXIA)	Inflammatory and Autoimmune Collab (abbvie)	Launch of Enerzair® Breezhaler® for Asthma in EU and Japan (NOVARTIS)	Nomination of H4 ant. candidate for Atopic Dermatitis (sosei HEPTARES)	CGRP ant. advanced to Phase 1 ready and out-licensed to Biohaven	Created Tempero Bio with Aditum Bio to advance mGlu5 NAM program targeting substance use disorders and anxiety (Tempero Bio)
Tech collaboration for Targeted Protein Degradation (TPD) (Captor Therapeutics®)	CGRP ant. Out-licensing and Collaboration (biohaven pharmaceuticals)	Phase 1 start of CCR6 ant. for inflammatory bowel disease (Pfizer)	Nomination of EP4 ant. candidate for Immuno-oncology (sosei HEPTARES)	mGlu5 NAM advanced through Phase 1 and out-licensed to Tempero Bio (Tempero Bio)	
	GPR35 ag. Out-licensing and Collaboration (gsk)		Nomination of GPR35 ant. candidate and out-licensed (gsk)		

Note: Enerzair® and Breezhaler® are registered trademarks of Novartis AG

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5A

Appendix

Significant events post FY2020 close

Bolstered drug discovery capabilities with technology collaborations

Collaborate in novel technologies

Collaboration with **PharmEnable** to leverage its proprietary **artificial intelligence-enabled** and medicinal chemistry technologies to identify novel, highly specific drug leads for future development.

PharmEnable's approach **identifies 3D drug candidate hits** with improved specificity compared with traditional screening methods, enabling the company to tackle challenging biological targets.

Initial focus to apply these technologies on a **peptidergic GPCR target associated with neurological diseases** that has proved particularly difficult to drug.

Sosei Heptares and PharmEnable will **jointly conduct** and share the costs of the discovery and development program and will **co-own** any resulting products.

PHARMENABLE

Jan 2021

Expand drug target classes beyond GPCRs

Collaboration with **Metrion Biosciences** to explore the potential of Sosei Heptares' SBDD technologies to address **disease-associated ion channels** in a similar way it has succeeded with GPCRs.

Ion channels – regulate the flow of ions across the cell membrane and represent a **large and established but under-exploited class of drug targets** beyond GPCRs.

Initial focus to identify novel, highly specific drug leads for further development against a single ion channel that is well-validated in **neurological diseases**.

Sosei Heptares will have **exclusive, full global rights** to all molecules identified and directed to the targets for development by Sosei Heptares.

metrion biosciences

Feb 2021

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We regained a larger and strengthened selective muscarinic agonist portfolio following over $55m of investment from Allergan

Sosei Heptares receives all programs under development, together with the associated IP and preclinical and clinical data generated from the partnership with Allergan

Includes a pipeline of next-generation selective muscarinic agonists with newly developed chemistry

StaR® and SBDD precision-design platform has delivered a patent estate of chemically diverse M_4, M_1 and M_1/M_4 muscarinic agonist back-ups in preclinical development

Program	Compound	Stage
M_4 agonist	**HTL'878**	**Ph 1**
	Undisclosed	Preclinical
M_1 agonist	HTL'318	Ph 1
	HTL'936	Ph 1
	Undisclosed	Candidate Selection
	Undisclosed	Discovery
	Undisclosed	Discovery
M_1 / M_4 dual agonist	Undisclosed	Candidate Selection

We have completed our internal review of the Muscarinic programs and will now **increase our investment of the M_4 agonist program** while maintaining investment in the other portfolio programs

Potential to deliver transformative new treatments for patients

Muscarinic M_4 and M_1 receptors are validated targets for psychosis and cognition

Muscarinic M_4 and M_1 receptors represent validated targets for the treatment of psychosis and cognition, respectively

Selective orthosteric agonists have been very challenging despite over 25 years of effort by major global pharma

~20M
SCHIZOPHRENIA


GLOBAL SUFFERERS

~50M
DEMENTIA

$818BN
SOCIETAL COST


COST OF DEMENTIA

1.1%
GLOBAL GDP

Xanomeline, the M_4/M_1 preferring agonist, achieved human Proof of Concept in double-blind, placebo-controlled trials in SZ and AD patients

Selective muscarinic receptor agonist xanomeline as a novel treatment approach for schizophrenia

Anantha Shekhar [1], William Z Potter, Jeffrey Lightfoot, John Lienemann, Sanjay Dubé, Craig Mallinckrodt, Frank P Bymaster, David L McKinzie, Christian C Felder

Effects of xanomeline, a selective muscarinic receptor agonist, on cognitive function and behavioral symptoms in Alzheimer disease

N C Bodick [1], W W Offen, A I Levey, N R Cutler, S G Gauthier, A Satlin, H E Shannon, G D Tollefson, K Rasmussen, F P Bymaster, D J Hurley, W Z Potter, S M Paul

Muscarinic M_4 and/or M_1 receptor agonists **with selectivity** over peripheral muscarinic M_2 and M_3 receptor subtypes have the **potential to be transformative treatments**

Source: World Health Organization

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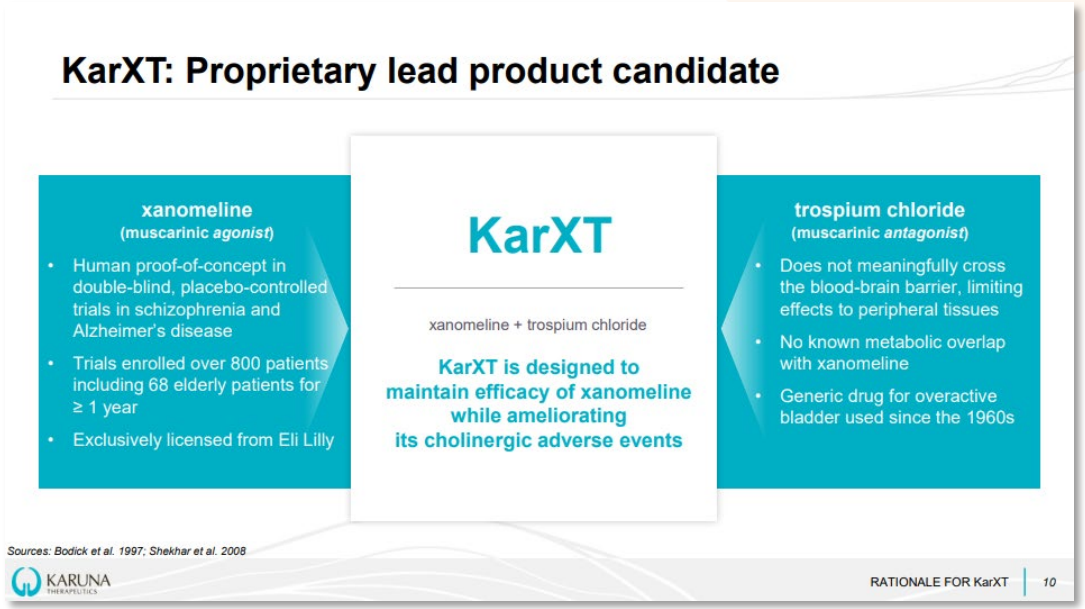
Potential to deliver transformative new treatments for patients

Karuna Therapeutics and Cerevel Therapeutics are advancing supportive muscarinic stories

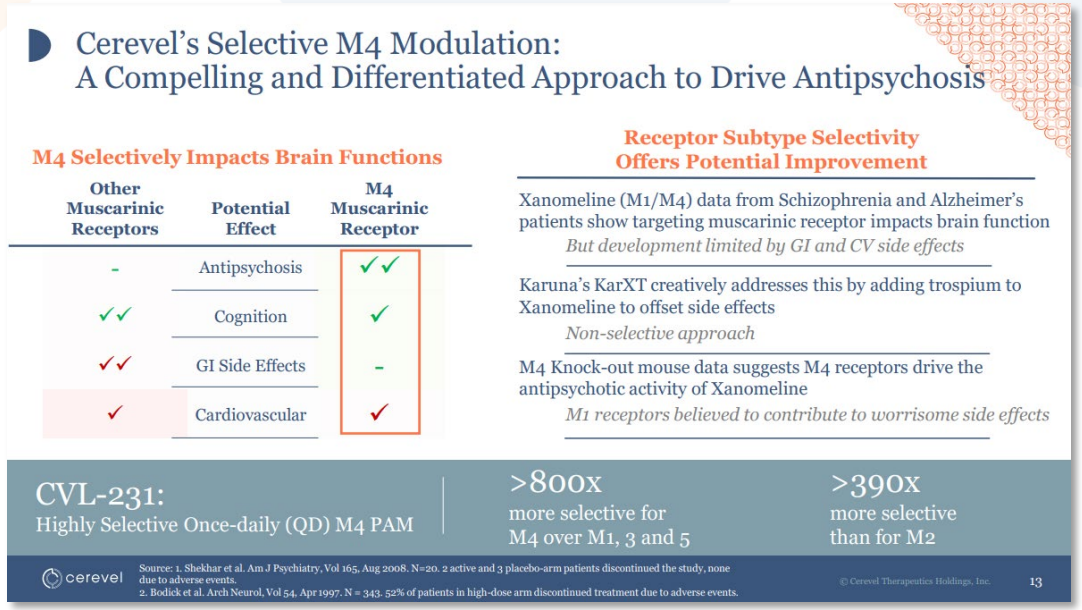
KARUNA THERAPEUTICS

cerevel

KarXT (M_1/M_4 agonist, M_2/M_3 antagonist)



CVL-231 (M_4 PAM)



Karuna Therapeutics' KarXT[1] and Cerevel Therapeutics CVL-231[2] have reawakened investors and the pharma industry to the potential of muscarinic programs for the treatment of psychosis and cognition

1. KarXT is combination of xanomeline (muscarinic M_1/M_4 preferring agonist) and trospium chloride (muscarinic M_2/M_3 antagonist). Source: Karuna Therapeutics Company Presentation (December 2020) LINK
2. CVL-231 is a selective muscarinic M_4 positive allosteric modulator (PAM). Source: Cerevel Therapeutics Company Presentation (November 2020) LINK

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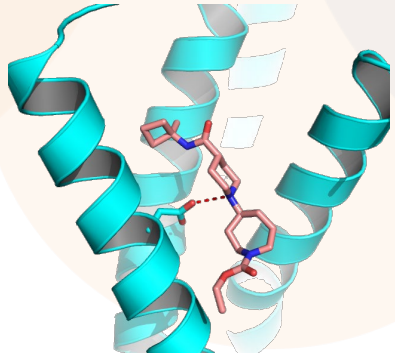
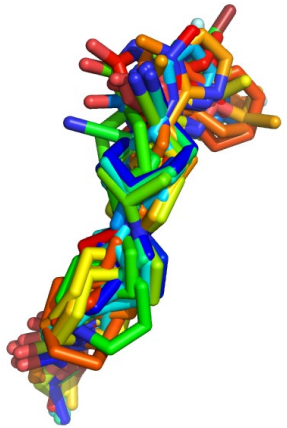
Potential to deliver transformative treatments for patients

M_4 agonist program a potential next-generation, first-in-class treatment for SZ

Using our proprietary StaR® technology, we have developed crystallography systems for Muscarinic receptors stabilized in agonist forms

Details obtained from structures of a compound series enable tuning of interactions and affinities across receptor sub-types





HTL'878

Highly selective M_4 receptor agonist for the treatment of psychosis in schizophrenia and dementias

- Potent orthosteric agonist of the M_4 receptor
- Highly selective vs other muscarinic receptor subtypes
- Highly selective vs other GPCRs and other drug targets
- Excellent CNS penetration and good druglike properties to ensure access to the target (target engagement)

Our StaR® / SBDD precision designed M_4 agonist program is **highly selective for the muscarinic M_4 receptor subtype**, offering a differentiated approach versus the competitors in development

Potential to deliver transformative treatments for patients

SZ remains a huge unmet medical need

Large market with blockbuster sales profiles…

~20M — SZ patients worldwide

Blockbusters sales profiles despite limited efficacy and severe side effects

$10BN+ (2020) → $13BN+ (2026)

Zyprexa Olanzapine · Seroquel quetiapina · Abilify (aripiprazole) 2, 5, 10, 15, 20, 30 mg Tablets

…Despite no innovation in 70 years

Current treatments use the same MOA 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 HTL'878

- ✓ Selective M_4 agonist
- ✓ Potential First in Class therapy with a novel MOA
- ✓ Improved tolerability
- ✓ Significant need for new treatment options in SZ

The severe side effect profile of Atypicals continues to drive high relapse rates, disease progression and discontinuation of treatment – **there is a significant need for new treatment options**

Source: World Health Organization; EvaluatePharma

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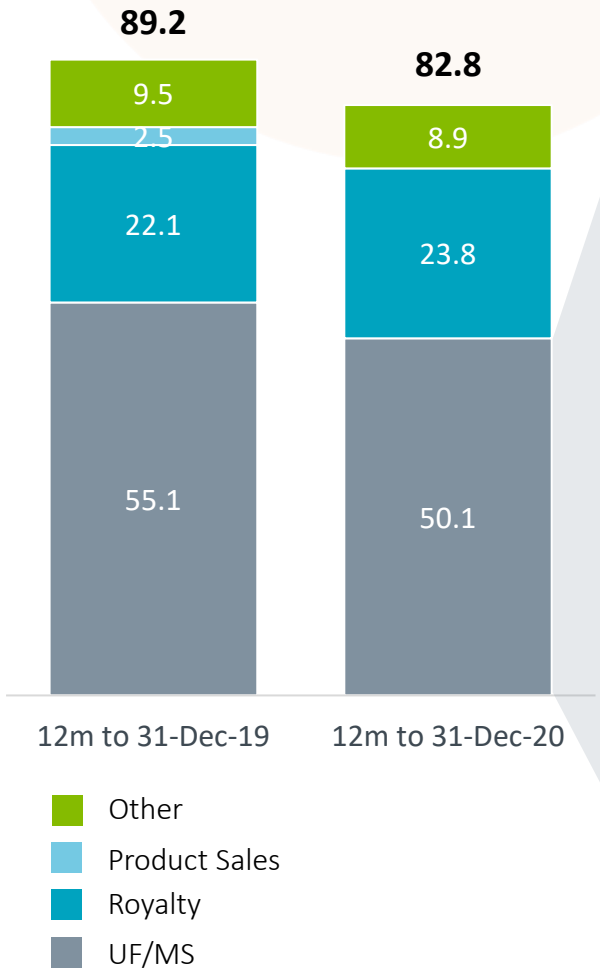
5B

Appendix

Revenue and Pipeline progression

Revenue breakdown by type (IFRS)

USD (M)



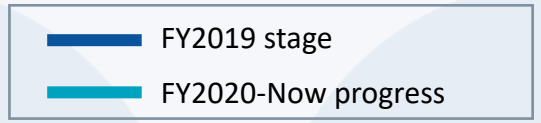
Upfront (UF)/Milestone (MS) revenue recognized in the full Financial Year[1]

Date	FY19 UF/MS Event	Revenue (USDm)
Jan-19	AZD4635 Phase 2 start	15.0
Feb-19	Inexia collab upfront	0.3
Feb-19	Fair value of shares in Orexia and Inexia	2.3
Feb-19	Daiichi Sankyo structure solved	0.5
Feb-19	Fujifilm Oravi payments	1.8
May-19	Pfizer candidate nomination	3.0
May-19	Novartis Enerzair® Breezhaler® EMA filing	2.5
May-19	Pfizer candidate nomination	3.0
Jul-19	Genentech collab upfront	7.6
Aug-19	Takeda collab upfront	10.0
Sep-19	Genentech target nomination	0.8
Dec-19	Pfizer Phase 1 start	5.0
Dec-19	Pfizer candidate nomination	3.0
	Selected revenue	0.8

Date	FY20 UF/MS Event	Revenue (USDm)
Feb-20	Daiichi Sankyo lead identified	1.5
Jun-20	AbbVie collab upfront	2.5
Jun-20	Novartis Enerzair® Breezhaler® Japan approval	1.3
Jul-20	Novartis Enerzair® Breezhaler® EU approval	5.0
Aug-20	Takeda structure solved	0.3
Sep-20	Pfizer Phase 1 start	5.0
Nov-20	Tempero Bio collab upfront	5.0
Nov-20	Fair value of shares in Tempero Bio	2.0
Nov-20	Biohaven collab upfront	5.0
Nov-20	Biohaven share consideration	4.7
Dec-20	AbbVie StaR® structure solved	0.7
Dec-20	Takeda StaR® structure solved	0.3
Dec-20	GSK collab upfront	12.5
	Selected revenue	4.3

Note: [1] Values relate to revenue recognized in the full financial year per accounting measures, as opposed to cash received in the full financial year.

Progression of 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	Fujifilm
Imaradenant	Adenosine A2a ant. combo	SME	mCRPC	AstraZeneca
Imaradenant	Adenosine A2a antagonist	SME	Solid tumors	AstraZeneca
PF-07081532	GLP-1 agonist	SME	T2DM / Obesity	Pfizer
PF-07054894	CCR6 antagonist	SME	Inflammatory bowel disease	Pfizer
Not disclosed	Single target	SME	Metabolic and other	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
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
Co-owned investments				
TMP301	mGlu5 NAM	SME	Substance use disorders	Tempero Bio
Not disclosed	OX1/OX2 agonist	SME (Oral)	Narcolepsy	Orexia
Not disclosed	OX1/OX2 agonist	SME (Intranasal)	Narcolepsy	Inexia

Note: Seebri®, Ultibro®, Enerzair® and Breezhaler® are registered trademarks of Novartis AG.

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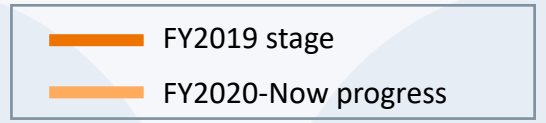
Progression of In-house Pipeline



Compound	Target / Mechanism of Action	Modality	Indication	Originator	Dis	PCC	Ph1	Ph2	Ph3	App	Mkt.
In-house Programs (Not yet partnered)											
HTL0016878	Muscarinic M4 agonist	SME	Neurology diseases	sosei HEPTARES							
HLT0018318	Muscarinic M1 agonist	SME	Neurology diseases	sosei HEPTARES							
HLT009936	Muscarinic M1 agonist	SME	Neurology diseases	sosei HEPTARES							
Not disclosed	Muscarinic M1 agonist (B/U)	SME	Neurology diseases	sosei HEPTARES							
Not disclosed	Muscarinic M4 agonist (B/U)	SME	Neurology diseases	sosei HEPTARES							
Not disclosed	Muscarinic M1/M4 agonist	SME	Neurology diseases	sosei HEPTARES							
HTL0030310	SSTR5 agonist	Peptide	Endocrine disorders	sosei HEPTARES							
Not disclosed[1]	GLP-1 antagonist	Peptide	Endocrine disorders	sosei HEPTARES							
Not disclosed	GLP-2 agonist	Peptide	Intestinal failure	sosei HEPTARES							
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	PAR-2 mAb	mAb	Atopic Dermatitis	sosei HEPTARES							
Not disclosed	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 (Suspended)											
HTL0018318[2]	Muscarinic M1 agonist	SME	DLB	sosei HEPTARES							

Note: [1] The option to license GLP1 antagonist peptide was not exercised before 31 December 2020 and therefore the program is currently wholly in-house. [2] Phase 2 trial of HTL0018318 for DLB in Japan has been withdrawn. The Group may resubmit a new clinical trial notification for HTL0018318 (or another novel M_1 agonist) to the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) in the future.

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Locations

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