



H1 FY2022 Financial Results

Six-month period ended June 30, 2022

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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.

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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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Financial Results

Hironoshin Nomura, CFO

Financial Summary for H1 2022

Successful execution of strategy with continuing investment in R&D

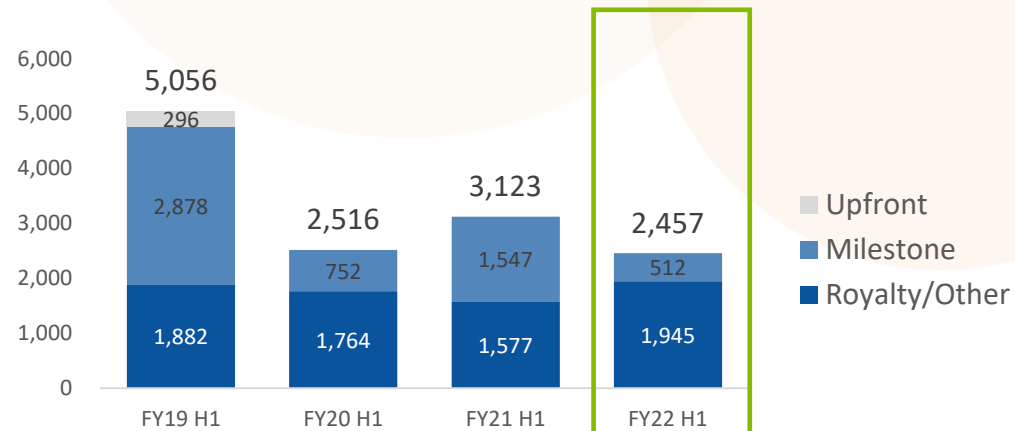
- 1** **H1 Revenue of ¥2,457m (\$20m)** vs. ¥3,123m (\$29m) in the prior comparative period. H1 2022 includes two milestone events vs. five in the prior comparative period.
- 2** **H1 Operating Loss of ¥3,804m (\$31m)** vs. ¥1,849m (\$17m) in the prior comparative period. This reflects increased R&D expenses of ¥1,100m (\$6m) vs. the prior comparative period, in line with our strategy.
- 3** **¥54bn cash balance (\$393m)** as at June 30, 2022 - the majority of which is earmarked for acquisitions and in-licensing opportunities to accelerate our growth.
- 4** **Significant events occurring after from July 1** will be accounted for in our Q3 financial results (and afterwards) but disclosed as Subsequent Events in our Q2 financial results:
 - New collaboration with **AbbVie** announced on 2 August (\$40m upfront)
 - **Neurocrine** M4 Phase2 milestone announced on 5 August (\$30m milestone)

Note: USD:JPY FX rates used – 122.83 (Average rate YTD 2022) and 108.11 (Average rate YTD 2021)

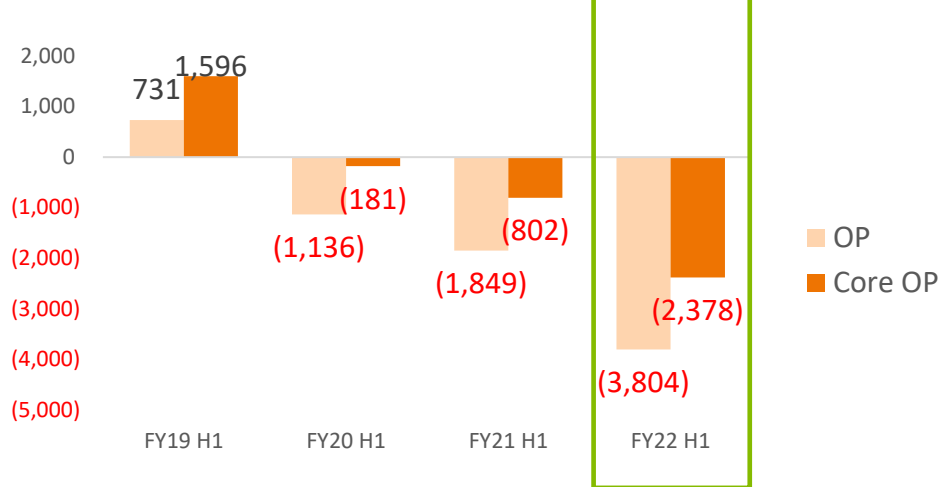
Key Financial Indicators

There were lower number of milestone events until end of June, compared with FY21

(JPY million)



(JPY million)



Revenue

- Revenue can vary significantly quarter on quarter depending on the occurrence of milestone events and the signing of new collaborations agreements with upfront fees.
- Revenue was down JPY666m / \$9m in H1 2022 vs. H1 2021 primarily due to milestone income.
- Milestone income from existing partnerships in H1 2022 included:
 - Milestones from Takeda and Genentech
 - Deferred revenue releases on AbbVie and Genentech collaborations
- There were 5 milestones in the prior comparative period.
- Royalties from Novartis were broadly flat vs. H1 2021 but slightly increased on a JPY basis due to FX rates

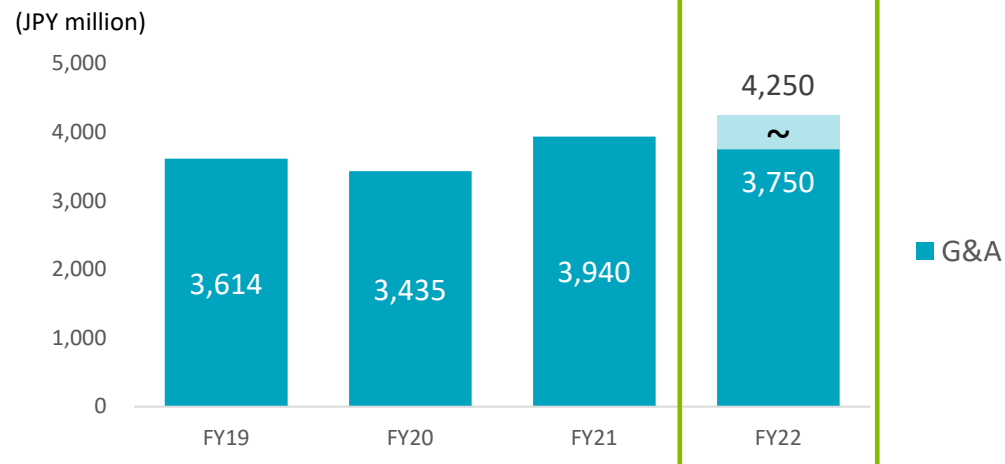
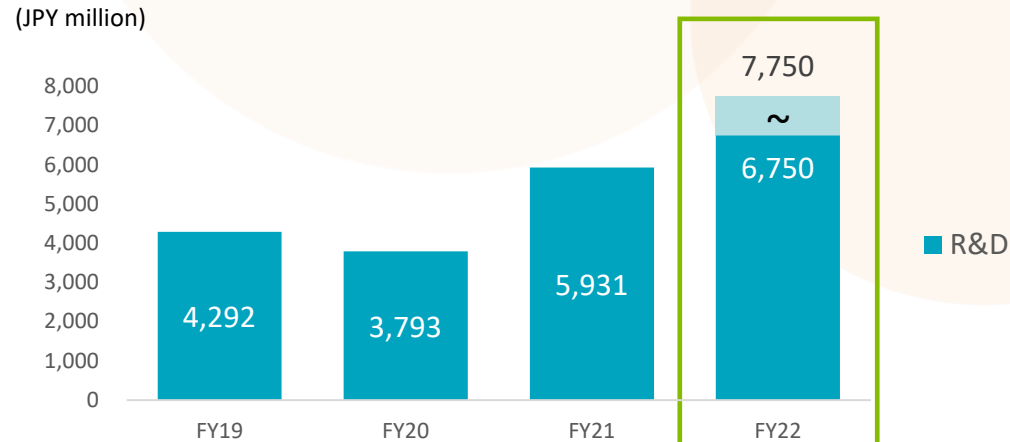
Operating Loss

- Core R&D costs increased by ¥1,003m / \$6m vs. H1 2021 primarily due to higher activity on in-house programs, participation in new co-development collaborations, the impact of a stronger GBP vs. JPY and cost inflation.
- Core SG&A costs increased by ¥329m / \$1.3m vs. H1 2021 due to a general increase in business activity owing to of lighter COVID restrictions (including travel and training) plus the impact of a stronger GBP vs. JPY and cost inflation.

Full year cost guidance (Updated)

Incremental investment designed to deliver greater returns over the medium to long term

Updated Guidance



R&D expenses (IFRS basis)

¥6,750m to ¥7,750m (up from ¥5,750m to ¥6,750m)

- Expand platform and grow discovery capacity
- Build a program-centric clinical development focus, and invest in new translational medicine capabilities
- Move priority programs into early (Phase 1b) clinical studies to deliver greater value
- Increase in full year Guidance due to:
 - i. Impact of FX rates (GBP has strengthened by 6% in the YTD vs. JPY)
 - ii. Cost inflation (UK inflation is running at circa 9%)
 - iii. Part of RSU cost reclassification from G&A to R&D for clearer presentation

G&A expenses (IFRS basis)

¥3,750m to ¥4,250m (unchanged)

- Invest in functional teams to support great science
- Enhance corporate governance
- Explore TSE PRIME listing
- No change to full year G&A Guidance:
 - i. FX rates and inflation have the effect of increasing cost
 - ii. The impact has been largely off-set by the reclassification of RSU

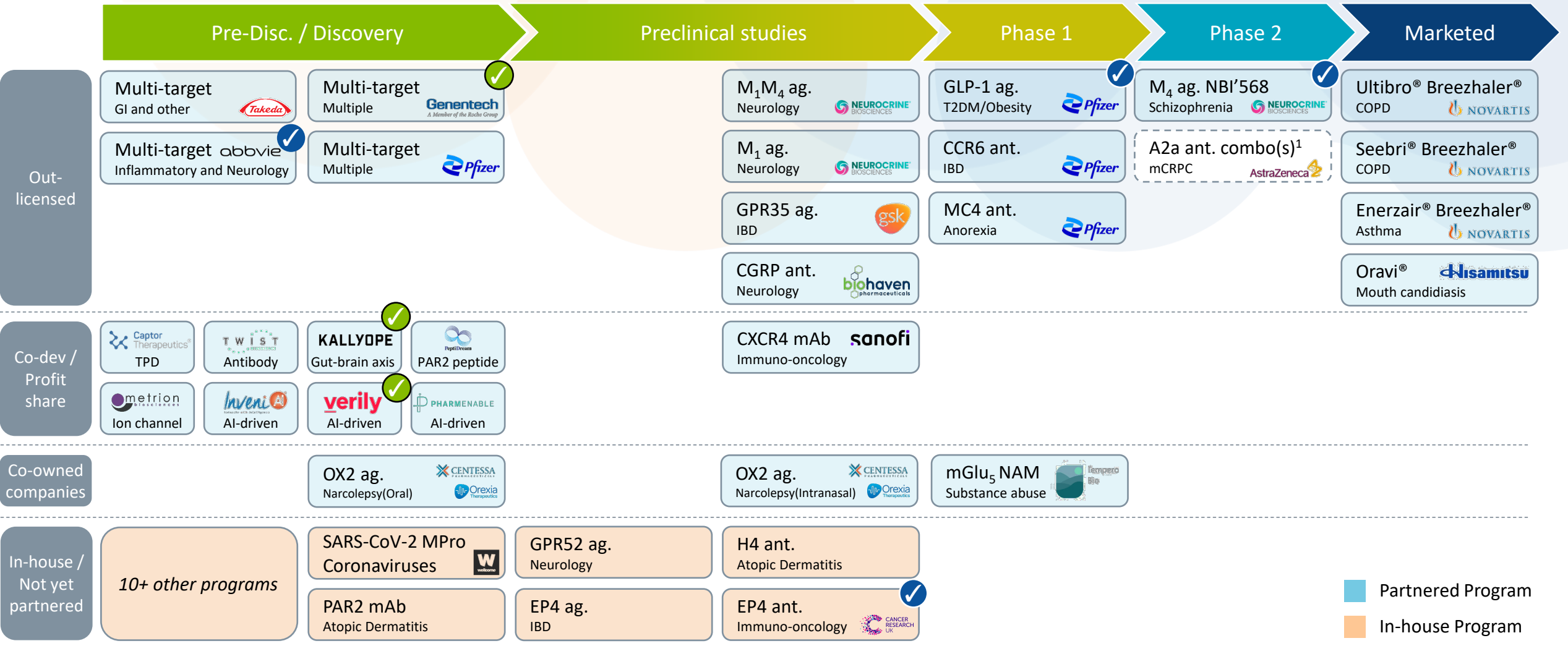
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Operational Highlights

Chris Cargill, CEO

Strong execution across all phases/collaboration types

Updates (H1)
Post H1 event



Partnered Program
In-house Program

Note: Seebri®, Ultibro®, Energair® and Breezhaler® are registered trademarks of Novartis AG. ¹AstraZeneca has removed the A2a program from its clinical pipeline as at Q3 2021

Strong execution across all phases/collaboration types (cont'd)

Discovery Research Innovation Updates



New GPCR targets already identified with AI dataset

KALLYOPE

New platform to identify novel targets



5 milestones achieved across multiple programs



New US\$1.2bn multi-target neurology collaboration



Strong GLP-1 Ph. 1 data, Ph. 2 start possible H2 2022



M4 IND accepted by FDA, Ph. 2 start possible H2 2022



New EP4 partnership to maximize cancer trials

Importantly, in addition to continuously expanding our discovery innovation, we now have two major programs, PF-070815732 (GLP-1) and NBI-1117568 (M4), expected to advance into Phase 2 trials with our partners

New multi-target Neurology collaboration with AbbVie

Post H1 event

US\$80m in upfront and near-term revenues, plus up to US\$1.2bn in future milestone revenues

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US\$40m upfront, US\$40m in near-term research milestone revenues expected over the next three years, plus up to **US\$1.2bn future milestone revenues, plus tiered royalties.**

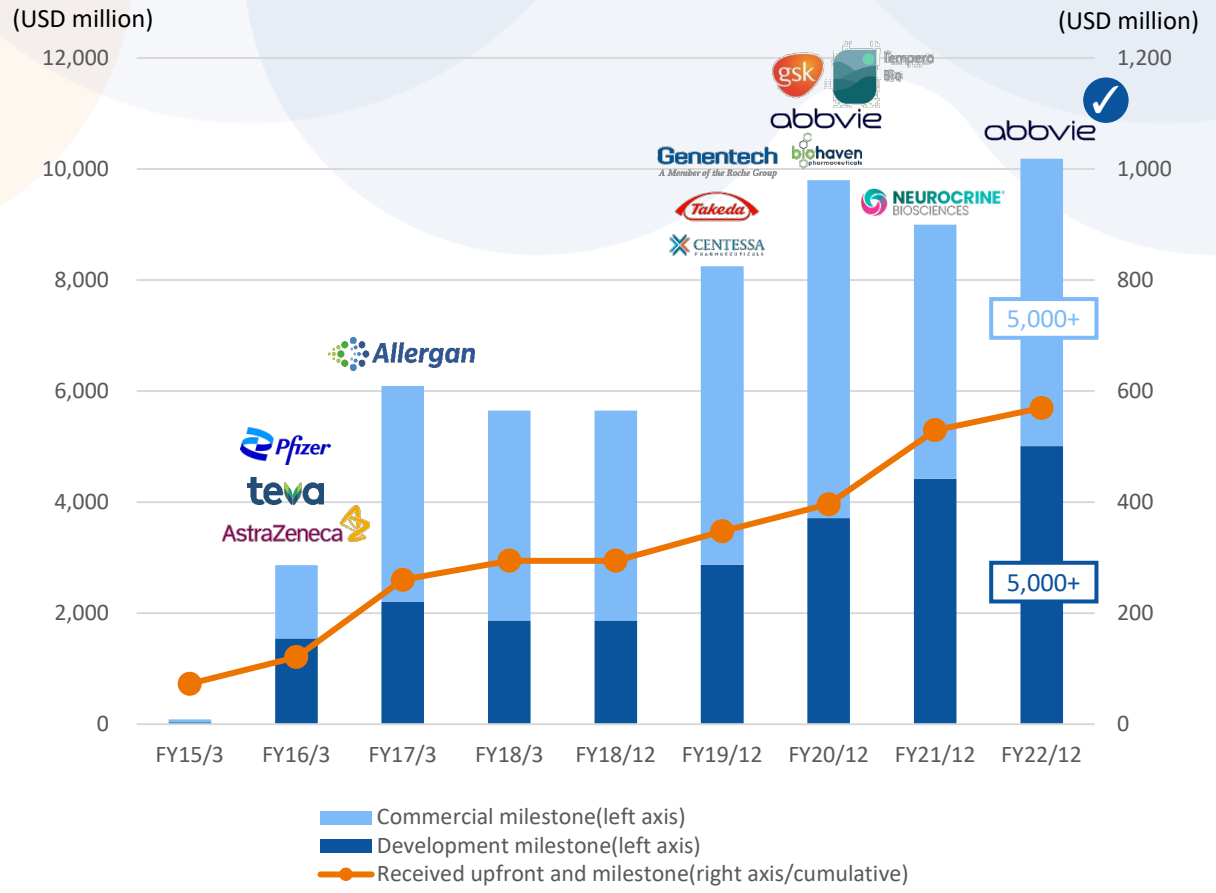
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Targeting **three** novel G protein-coupled receptor (GPCR) targets associated with **neurological disease.**

3

Highly productive working relationship with AbbVie established during initial collaboration in 2020, enables us to get off to a quick start.

Balance of potential milestone income from existing license agreements¹



¹ Balance as of the end of the fiscal year of only those currently under contract. TEVA and AbbVie (formerly Allergan), for which compounds were returned, are excluded from the balances from FY2018 and FY2021, respectively

EP4 antagonist (HTL0039732)

New collaboration with CRUK to advance clinical trials for this promising cancer therapeutic

Best access - unrivalled network of world-leading scientists and clinicians

World-class infrastructure - multi-center trials delivered across 20 clinical centers in the UK

Shared costs and risks - co-development project, coordinated and managed by CRUK, with joint funding and shared risk reward

Win-win for cancer drug development - Sosei Heptares retains the license to clinical trial results and collaboration IP, CRUK receives a share of future revenue if the drug successfully developed






27 PARTNERSHIPS TO DATE	11 (+1) PARTNERSHIPS CURRENTLY ACTIVE	8 ACTIVE LICENCES
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Cancer is an extremely complex area for development. We are partnering with CRUK who have a proven track record having delivered 6 agents as registered medicines alongside world-leading corporate partners

Source: Cancer Research UK, Center for Drug Development

Advancing four wholly-owned programs

Advancing priority programs into early clinical studies, including collaboration with CRUK

				
Indication and target	Schizophrenia and Psychosis	Atopic Dermatitis	Immunosuppression in solid tumors	Inflammatory Bowel Disease
	GPR52 agonist	H4 antagonist	EP4 antagonist	EP4 agonist
Target Product Profile	<ul style="list-style-type: none"> Once daily oral small molecule 24hr target engagement 	<ul style="list-style-type: none"> Once daily oral small molecule To be used as a monotherapy or in combination 	<ul style="list-style-type: none"> Once daily oral small molecule To be used in combo with checkpoint inhibitors Collaboration with CRUK 	<ul style="list-style-type: none"> Oral GI restricted Good potency and selectivity Minimal GI systemic exposure
Clinical start target	H1 2023	H1 2023	H1 2023 	End of 2023

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R&D Progress

Dr. Matt Barnes, President of Heptares
and Head of UK R&D

Muscarinic M4 agonist (NBI-1117568)

Collaboration with Neurocrine, announced IND of Ph2 study trigger \$30 million milestone

Novel Muscarinic Receptor Agonists Collaboration with Sosei Heptares

Neurocrine Biosciences Initiating Clinical Studies for Muscarinic Portfolio

Initiating clinical studies, including:

- **Phase 2 placebo-controlled study** of NBI-1117568*, a selective M4 orthosteric agonist, as a potential treatment for schizophrenia scheduled to start in 2022
 - ✓ NBI-1117568 offers the potential for an improved safety profile:
 - ❑ Without the need of combination therapy to minimize side effects
 - ❑ Avoids the need of cooperativity with acetylcholine when compared to non-selective muscarinic agonists and positive allosteric modulators in development
- **Phase 1 study** of a dual M1 / M4 orthosteric agonist in 2023
- **Phase 1 study** of a selective M1 orthosteric agonist in 2023



*In-licensed from Sosei Heptares, formerly HTL-0016878. NBI-1117568 is investigational and not approved in any country

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GLP-1 agonist (PF-07081532)

Pfizer highlights potentially best-in-class data to be presented at EASD (19-23 September)

PF-07081532: Potential Best-In-Class Once-Daily Oral GLP-1 Profile

Upcoming EASD Phase 1 data show rapid, robust reduction in glucose and body weight¹

99 mg/dL Reduction in Mean Daily Glucose after 6 weeks¹

Group	Reduction (mg/dL)
Placebo	-29
PF-07081532	-99

5kg Reduction in Body Weight after 6 weeks¹

Group	Reduction (kg)
Placebo	-2
PF-07081532	-5

- Similar changes in body weight observed in participants with non-diabetic obesity
- Safety and tolerability profile consistent with GLP-1 RA class, further titration optimization in planned Phase 2 Study
- Three presentations² across oral GLP-1 RA franchise at EASD Annual Meeting, September 2022

EASD = European Association for the Study of Diabetes; T2DM = Type 2 Diabetes Mellitus; GLP-1 = Glucagon-like Peptide-1; RA = Receptor Agonist
 Results from Clinicaltrials.gov identifier: NCT04305587, Randomized, double-blind, placebo-controlled, multiple ascending dose Phase 1 Study in adults with T2DM and non-diabetic obesity

⁽¹⁾ Abstract #114, 58th Annual Meeting - Once-Daily Oral Small Molecule GLP-1R Agonist PF-07081532 Robustly Reduces Glucose and Body Weight within 4-6 Weeks in Adults with T2DM and Non-Diabetic Adults with Obesity, Modelled means presented, Mean baseline daily glucose 212 mg/dL, Mean baseline bodyweight in T2DM participants 90kg

⁽²⁾ Abstracts #114, 588, 589







Second Quarter 2022 Earnings

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Multi-target Collaboration Partners

Making excellent progress with new and long-term partnered programs

Updates (H1)
Post H1 event

Partner	Execution	Therapeutic Area	Stage	Progress
	November 2015	Multiple	Phase 1	x3 clinical stage assets achieved in 6 years and clinical development is ongoing
 <small>A Member of the Roche Group</small>	July 2019	Multiple	Discovery	x5 milestones achieved in 3 years with  targets for small and large molecule drugs
	August 2019	Multiple (Initial focus on Gastrointestinal)	Discovery	Early Discovery milestones achieved
	June 2020 August 2022 	Inflammatory, Autoimmune and Neurology	Discovery	

Strategic collaboration landscape

Adding complementary approaches to increase discovery opportunities



Choosing the right target

Our Core Technologies


- StaR®
- CryoEM
- Protein Binder Toolkit
- SBDD
- DEL Screening

Discovering a therapeutic agent

Strategic collaboration partners

Identification and validation of novel GPCR targets for new discovery programs

2021~




AI drug discovery (Target)

- 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

Immunology/Multi-target

2022~




AI drug discovery (Target)

- 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

Immunology/Multi-target

2022~



Gut-brain axis platform (Target)

- Strategic research collaboration leveraging Sosei Heptares capabilities with Kallyope's gut-brain axis platform
- Collaboration aims to identify, prioritize and validate novel GPCR targets with a goal of creating new drug discovery programs in the area of gastrointestinal (GI) diseases

Gastroenterology/Multi-target

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Objectives for FY2022

Chris Cargill, CEO

Priority objectives for FY2022

Excellent progress YTD across our business

FY2022 OBJECTIVES

UPDATES



Organic Growth

- 1 Execute at least one new high value collaboration and/or co-investment
- 2 Generate at least one new preclinical candidates
- 3 Further enhance R&D productivity



Strategic Growth



- 1 Continue to search for opportunities to acquire companies that will bring new sources of revenue
- 2 Collaborate/invest in new technologies with synergies
- 3 In-license late-stage products for clinical development and commercialization in Japan



abbvie
US\$80m in upfront and near-term milestone revenues, plus up to US\$1.2bn in the future



Weatherden
Strategic collaboration to drive R&D transformation and growth and to build Translational Medicine

World-class clinical trial partner for cancer

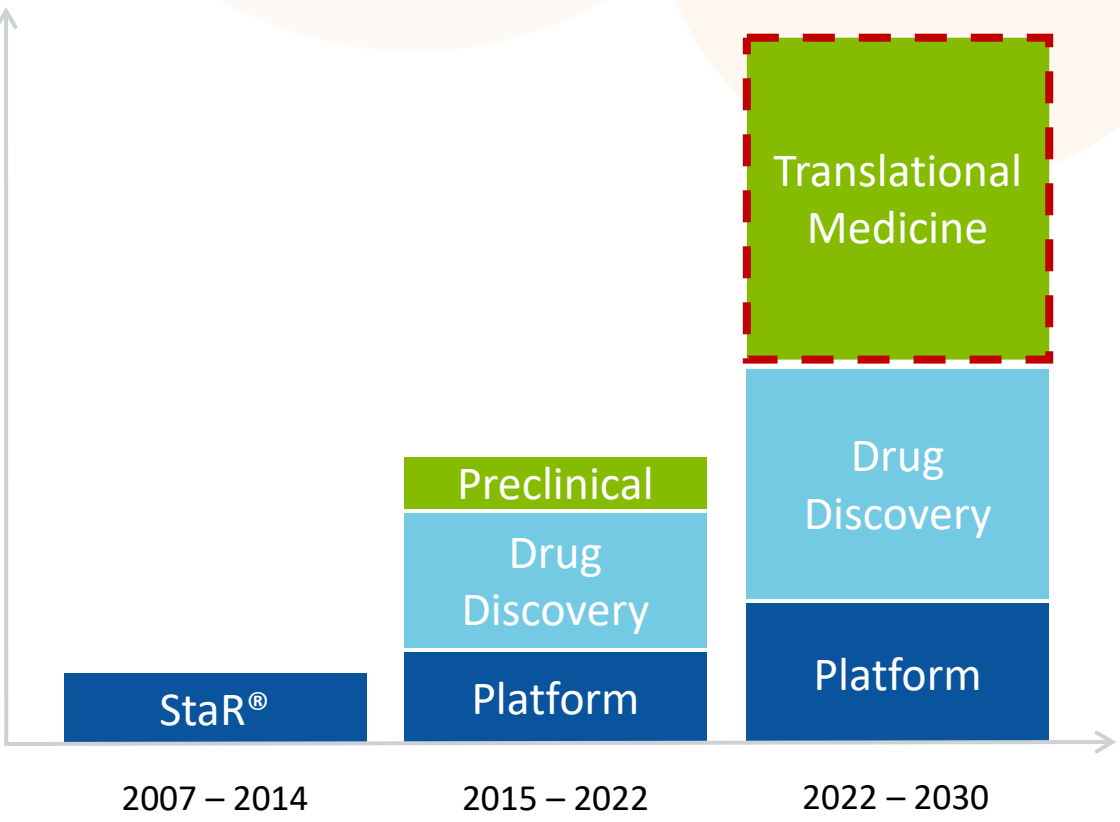


verily KALLYOPE
Aiming to deliver the next wave of data-driven, innovative drug targets

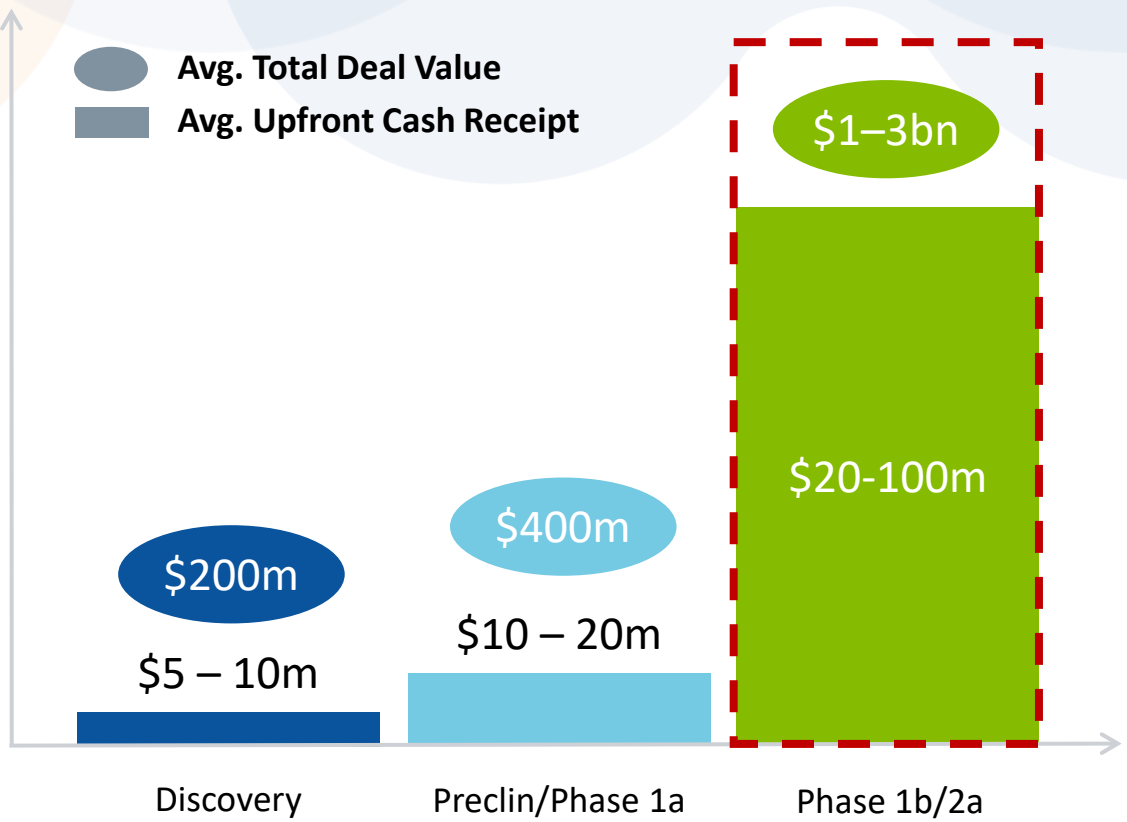
Mid to long-term direction for accelerating our growth

World-class science and Translational Medicine expansion to build long-term value

Historic and planned corporate value expansion



Example of partnership value versus stage of progress





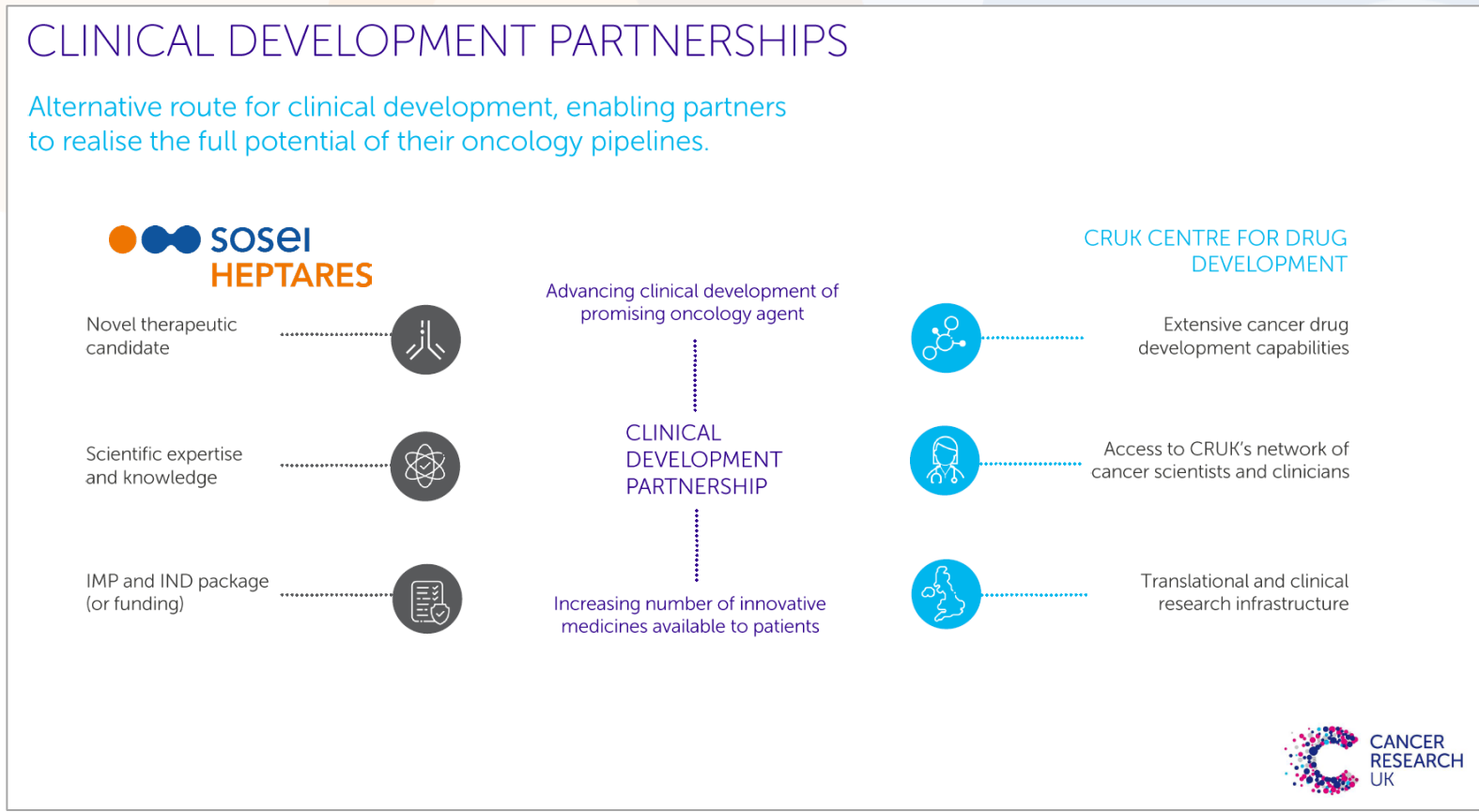
Q&A

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Appendix

EP4 antagonist (HTL0039732)

Clinical Development Partnership with CRUK to advance potential best-in-class therapeutic



Partnership enables us to cost effectively access the most advanced cancer drug development capabilities – and bring potentially innovative medicines to patients faster than we could do by ourselves

Source: Source: Cancer Research UK, Center for Drug Development

Introduction of ‘Core Operating Profit’

Core Operating Profit – the financial indicator closer to the reality of our business

Operating Profit
“IFRS”

- Financial results recorded and prepared in accordance with International Financial Reporting Standards (IFRS)

+ Material Non-cash Costs

(Depreciation, Amortization, Share based payments, Impairment...etc.)

+ Material Non-recurring Costs

(Restructuring costs and Other material one-off items...etc.)

Operating Profit
“Core”

- Core Operating Profit is a new key financial indicator that highlights the underlying recurring cash generating capability of the business.
- Core Operating Profit is defined as IFRS Operating Profit + material Non-cash costs + material non-recurring costs
- Material Non-cash Costs include depreciation, amortization, share based payments and impairment.
- Material Non-recurring Costs include restructuring costs and other material one-off items.
- Core Operating Profit = Cash Earnings + material Non-recurring Costs

	Cash	Non-cash (Material)
Recurring	Costs under “Core”	
Non-recurring (Material)		Costs under “IFRS”

Partnered pipeline

Updates (H1)
Post H1 event

Compound	Target / Mechanism of Action	Modality	Indication	Partner	Disc.	PCC	Ph1	Ph2	Ph3	App	Mkt
Out-licensing Collaborations											
Seebri® Breezhaler®	LAMA	SME	COPD	NOVARTIS	█	█	█	█	█	█	█
Ultibro® Breezhaler®	LAMA+LABA	SME	COPD	NOVARTIS	█	█	█	█	█	█	█
Energair® Breezhaler®	LAMA+LABA+ICS	SME	Asthma	NOVARTIS	█	█	█	█	█	█	█
ORAVI®	Antifungal agent miconazole	SME	Oropharyngeal candidiasis	DAISAMITSU	█	█	█	█	█	█	█
Imaradenant ¹	Adenosine A2a ant. combo	SME	mCRPC	AstraZeneca	█	█	█	█	█	█	█
NBI'568	Muscarinic M4 agonist	SME	Schizophrenia	NEUROCRINE BIOSCIENCES	█	█	█	█	█	█	█
Not disclosed	Muscarinic M1 agonist	SME	Neurology diseases	NEUROCRINE BIOSCIENCES	█	█	█	█	█	█	█
Not disclosed	Muscarinic M1/M4 agonist	SME	Neurology diseases	NEUROCRINE BIOSCIENCES	█	█	█	█	█	█	█
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	█	█	█	█	█	█	█
Not disclosed	CGRP antagonist	SME	Neurology diseases	biohaven pharmaceuticals	█	█	█	█	█	█	█
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 <small>A Member of the Roche Group</small>	█	█	█	█	█	█	█
Not disclosed	Multi target	SME/LME	Gastrointestinal and other	Takeda	█	█	█	█	█	█	█
Not disclosed	Multi target	SME	Inflammatory diseases / CNS	abbvie	█	█	█	█	█	█	█

Note: SME = small molecule. LME = large molecule. Seebri®, Ultibro®, Energair® and Breezhaler® are registered trademarks of Novartis AG. ¹ AstraZeneca have removed the A2a program from their clinical pipeline as at Q3 2021






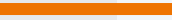















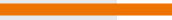






Partnered pipeline (cont'd)

Updates (H1)
Post H1 event

Compound	Target / Mechanism of Action	Modality	Indication	Partner	Disc.	PCC	Ph1	Ph2	Ph3	App	Mkt
Co-development											
KY1051	CXCR4 mAb	mAb	Immuno-oncology		████████████████████						
Not disclosed	PAR-2	Peptide	Inflammatory diseases		████████████████						
Not disclosed	Targeted Protein Degradation	SME	Gastrointestinal disorders		████████████████						
Not disclosed	AI-Augmented Drug Discovery	SME	Neurology diseases		████████████████						
Not disclosed	Ion Channel Drug Discovery	SME	Neurology diseases		████████████████						
Not disclosed	Multi target AI-powered	SME/LME	Immune diseases		████████████████						
Not disclosed	Antibody Discovery	mAb	Disease-relevant GPCR targets		████████████████						
Not disclosed	Multi target AI-powered	SME/LME	Immune diseases		████████████████	✓					
Not disclosed	Gut-brain axis drug discovery	SME	Gastrointestinal disorders		████████████████	✓					
Co-owned companies											
TMP301	mGlu5 NAM	SME	Substance use disorders		██						
Not disclosed	OX2 agonist (Intranasal)	Peptide	Narcolepsy		████████████████						
Not disclosed	OX2 agonist (Oral)	SME	Narcolepsy		████████████████						

Note: SME = small molecule. LME = large molecule

In-house pipeline

Compound	Target / Mechanism	Modality	Indication	Originator	Disc.	PCC	Ph1	Ph2	Ph3	App	Mkt
In-house Programs											
Not disclosed	H4 antagonist	SME	Atopic Dermatitis								
HTL0039732	EP4 antagonist	SME	Immuno-oncology								
Not disclosed	GPR52 agonist	SME	Neurology diseases								
Not disclosed	EP4 agonist	SME	Inflammatory bowel disease								
Not disclosed	PAR-2 mAb	mAb	Atopic Dermatitis								
Not disclosed	SARS CoV-2 Mpro	SME	Coronaviruses								
Multiple programs	Not disclosed	SME/LME	Neurology diseases								
Multiple programs	Not disclosed	SME/LME	GI and Inflammatory diseases								
Multiple programs	Not disclosed	SME/LME	Immunology diseases								
In-house Programs (No longer internally funded. Targeting academic / industrial partnership)											
HTL'310	SSTR5 agonist	Peptide	Hypoglycaemic disorders								
HTL'097	GLP-1 antagonist	Peptide	Hypoglycaemic disorders								
HTL'023	GLP-2/GLP-1 agonist	Peptide	Intestinal failure / NASH								
Not disclosed	Apelin agonist	Peptide	Pulmonary Arterial Hypertension								
HTL'641	Dual orexin antagonist	SME	Insomnia and sleep disorders								

Note: SME = small molecule. LME = large molecule

Our partnered candidates target significant market opportunities

Multi-billion USD annual peak sales potential for our post-pre-clinical pipeline

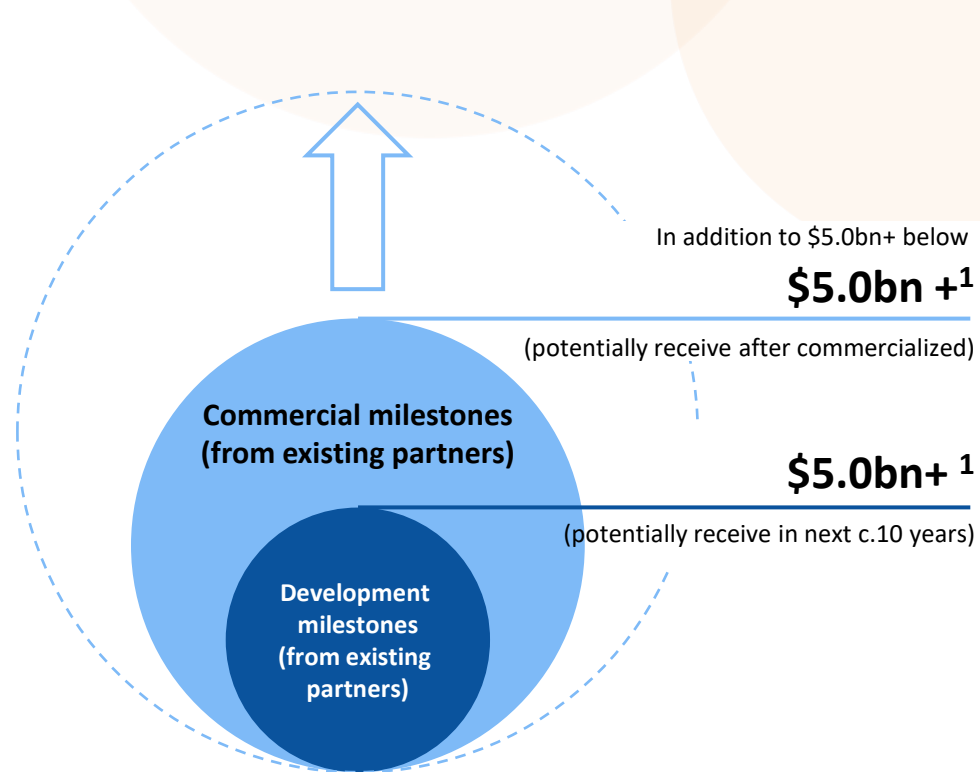
Category	Indication ²	Number of Patients	Peak Sales(USD million)		Our Candidates	
			Market Size	Individual Products		
Neurological disorders	Dementia	~55 million	\$7.3 billion (2010)		M1 agonist, M1/M4 agonist	
	Schizophrenia	~20 million	\$20.7 billion (2011)		M4 agonist, M1/M4 agonist	
	Substance use disorders	~10.4 million ¹	-	-	-	mGlu5 NAM
	Narcolepsy	~3 million	\$2.2 billion (2021)		\$1.7 billion (2020/Xyrem)	OX2 agonist
	Other	-	-	-	-	CGRP antagonist, GPR52 agonist
Immunological disorders	Cancer	~42 million	\$168.7 billion (2021)		\$17.2 billion (2021/Keytruda)	A2a antagonist, EP4 antagonist, CXCR4 mAb
	IBD	~10 million	\$22 billion (2021)		\$8.3 billion (2021/Humira)	CCR6 antagonist, GPR35 agonist, EP4 agonist
	Atopic Dermatitis	~13.3 million	\$6 billion ³ (2021)		\$5 billion (2021/Dupixent)	H4 antagonist, PAR2 mAb
Other	T2DM/Obesity	~420 million	\$55.5 billion (2021)		\$6.6 billion (2014/Lantus)	GLP1 agonist
	Anorexia	~10 million	-	-	-	MC4 antagonist
Total			~\$282 billion/year		~\$49 billion/year	

Source (Number of patients): World Health Organization, Evaluate Pharma, The European Federation of Crohn's & Ulcerative Colitis Associations (EFCCA), Narcolepsy Network, Inc., GBD 2015 Disease and Injury Incidence and Prevalence Collaborators (October 2016). "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015". Lancet. 388 (10053): 1545-1602 ¹The number of patients with drug addiction
Source (Peak Sales):Sales of each indications are extracted form Evaluate Pharma's data of sales by disease and sales by individual products (as of 30 June. 2022). ²Sosei Heptares may target one segment in the market for specific diseases. ³ Since there is no applicable indication category, the market size of "Eczema" is stated. Current market size for Atopic Dermatitis may be larger than stated above.

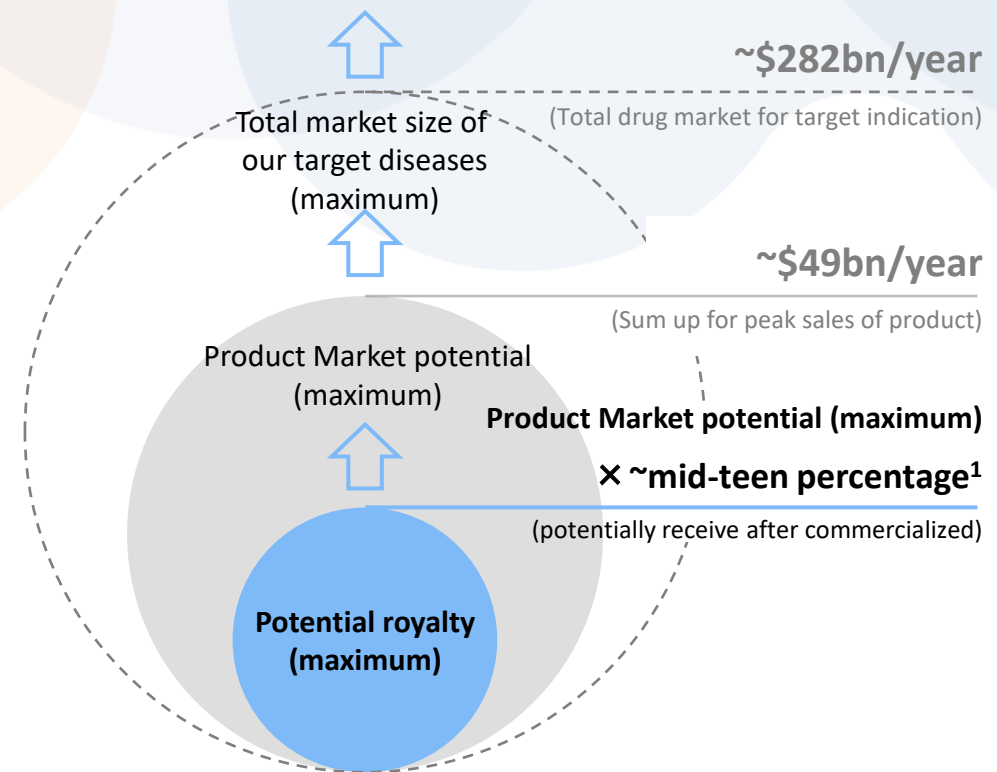
Potential revenues from existing partnerships




Securing stable revenues in the short to medium term from existing partnerships

Potential milestones from existing partners



Potential royalties from existing partners












 Short to medium term revenue potentially received in next 10 years	 Mid to long term revenue potentially received after commercialization	 Expand by executing new collaborations
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¹ All of these are the maximum values if all existing programs are successful. Note that the probability of success in drug discovery is not relatively high, and realistically not all programs will be successful. Source: Total market size of our target diseases and Product Market potential is stated in the previous page

Major licensing transactions

New multi-target collaboration for Neurological disorders with AbbVie signed in August 2022

Partner	Execution	Program	Therapeutic Area(s)	Upfront and Initial Milestones	Potential Total Milestone ¹
	August 2022	Multi-target Collaboration	Neurological disorders	\$80m	\$1.2bn
	November 2021	Collaboration and license agreement for M ₄ , M ₁ and M ₁ /M ₄ dual agonist	Neurological disorders	\$100m	\$2.6bn
	December 2020	Collaboration and license agreement for GPR 35	Gastrointestinal, immunology	\$44m	\$480m
	December 2020	Collaboration and license agreement for CGRP portfolio	Neurology	\$10m	\$380m
	June 2020	Discovery Collaboration and Option to License ²	Inflammatory and Autoimmune	\$32m	\$400m
	August 2019	Multi-target Collaboration	Multiple; Initial focus on Gastrointestinal	\$26m	\$1.2bn
 <small>A Member of the Roche Group</small>	July 2019	Multi-target Collaboration	Multiple	\$26m	\$1bn
	November 2015	Multi-target Collaboration	Multiple	-	\$1.8bn
	August 2015	Collaboration and license agreement for A _{2a} antagonist ³	Immuno-oncology	\$10m	\$500m

¹Potential option fees, development, regulatory and commercial milestone payments. Sosei Heptares is also eligible to receive tiered royalties ranging from high single digit to mid-teen percentage on future net sales of any products developed under the partnership. ² AbbVie has the option to expand the collaboration by an additional three targets. ³ AstraZeneca have removed the A2a program from their clinical pipeline as at Q3 2021

Glossary

Basic Terminology/Technology		
GPCR	G Protein-Coupled Receptor	There are about 800 types of GPCRs in the human body. While 400 of them are known to be potential drug targets, about 300 of them are not yet drugged
StaR	Stabilized Receptor	Sosei Heptares' proprietary technology to stabilize a GPCR by engineering a small number of single point mutations outside of the ligand-binding site. It enables to identify the structure of GPCRs to be used for SBDD drug discovery as well as antibody drug discovery as antigens
SBDD	Structure-Based Drug Design	A method to design drugs on a computer base based on the analysis of the three-dimensional structure of the drug target (e.g., protein receptor)
TPD	Targeted Protein Degradation	Drugs that promote the degradation of target proteins (e.g., receptors) in cells and aim for therapeutic effects by reducing disease-causing proteins
PAM	Positive Allosteric Modulator	A regulator that binds to unusual active sites (allosteric sites) on the receptor to increase the affinity and effect of the agonist
NAM	Negative Allosteric Modulator	A regulator that binds to an unusual active site on the receptor (allosteric site) and reduces the affinity and effectiveness of the agonist
Ag	Agonist	A therapeutic drug that binds to a receptor and activates an intracellular signaling system similar to biological substances
Ant	Antagonist	A therapeutic drug that suppresses biological reactions by binding to receptors and preventing them from binding to biological substances
PK	Pharmacokinetics	Research and testing on the relationship between drug dosage and blood concentration. Mainly describes the rate process of ADME
PD	Pharmacodynamics	Research and testing on the relationship between drug concentration and pharmacological effects
ADME	Absorption, Distribution, Metabolism and Excretion	A series of process in the absorption of drugs into the body, distribution within the body, metabolism in the liver and other organs, and excretion in the kidneys and other organs
POM	Proof of Mechanism	Proof of mechanism of action, mainly through biomarkers. It can suggest the possibility of efficacy in fewer cases than POC
POC	Proof of Concept	Proof of a therapeutic concept, primarily through clinical efficacy and safety
Ach	Acetylcholine	A neurotransmitter released from the peripheral parasympathetic and motor nerves to transmit nerve stimuli
IND	Investigational New Drug	Information packages for development candidates to be submitted to the U.S. Food and Drug Administration (FDA) at the time of initiation of clinical trials
Ph1	Phase1	A study in humans. The main purpose is to confirm the safety of the drug candidate mainly by healthy volunteers.
Ph2	Phase2	A study in humans. The main purpose is to confirm the efficacy of the drug candidates on a small scale (however, the number of patients varies greatly depending on the disease)
Ph3	Phase3	A study in humans. The main purpose is to determine the efficacy of the drug candidates on a large scale (however, the number of patients varies greatly depending on the disease)
NDA	New Drug Application	An application to the U.S. Food and Drug Administration (FDA) for approval to market a new drug
Disease/Drug		
LAMA	Long Acting Muscarinic Antagonist	An inhalant that dilates bronchial tubes and improves respiratory function by inhibiting the action of acetylcholine receptors (M3), which increase parasympathetic nerves.
LABA	Long Acting Beta2-Agonist	An inhalant that improves respiratory function by stimulating sympathetic beta2 receptors to dilate the bronchi.
ICS	Inhaled Corticosteroid	An inhalant that suppresses airway inflammation to prevent coughing attacks and other symptoms caused by asthma, also promotes the action of beta 2 stimulants and improve airway hyperresponsiveness.
mCRPC	Metastatic Castration-Resistant Prostate Cancer	Cancer that has spread (metastasized) beyond your prostate gland and for which hormone therapy is no longer effective in stopping or slowing the disease.
COPD	Chronic Obstructive Pulmonary Disease	A group of diseases that causes damage to the bronchi and lung due to smoking or inhalation of toxic substances, resulting in breathing problems.
AD	Alzheimer's Disease	Alzheimer's disease is a progressive neurologic disorder that causes the brain to shrink (atrophy) and brain cells to die, the most common cause of dementia .
DLB	Dementia with Lewy Bodies	Protein deposits, called Lewy bodies, develop in nerve cells in the brain regions involved in thinking, memory and movement (motor control), the second most common type of dementia.

Glossary (cont'd)

Drug discovery target		
M1	Muscarinic M1 Receptor	One of the five subtypes M1 to M5 of muscarinic acetylcholine receptors, known to be involved in learning and memory.
M4	Muscarinic M4 Receptor	One of the five subtypes M1 to M5 of muscarinic acetylcholine receptors, known to be involved in behavior and dopamine release.
CGRP	Calcitonin Gene-Related Peptide	CGRP is thought to be involved in vasodilation, decreased heart rate, and increased myocardial contractility via receptors.
A2A	Adenosine A2A receptor	One of the four subtypes of adenosine receptors, A1, A2A, A2B, and A3. It is expressed in many tissues and has multiple functions such as neural activity, vasodilation, and immune regulation.
GLP-1	Glucagon-like Peptide 1	GLP-1 is secreted by gastrointestinal cells when we eat, and is involved in insulin secretion from the pancreas and appetite regulation in the central nervous system.
CCR6	Chemokine Receptors 6	A type of B chemokine receptor that responds to chemokines generated during inflammation. It is believed to be involved in inflammation and immunity mainly by it's regulating the migration activity of leukocytes into inflamed tissues.
MC4	Melanocortin 4 Receptor	MC4 is expressed in the central nervous system and is the main receptor that mediates the appetite suppressing effect of alpha-melanocyte stimulating hormone.
GPR35	G Protein-Coupled Receptor 35	Orphan receptors - expressed mainly in immune and gastrointestinal tissues and is thought to be involved in areas of gastrointestinal tract, cardiovascular, inflammation, and central nervous system.
CXCR4	CXC Motif Chemokine Receptor 4	CXR4 induces migration of cancer cells and is known to be important in metastasis process.
mGlu5	Metabotropic Glutamate Receptor 5	One of the metabolic glutamate receptors expressed in the central nervous system. Glutamate is known to be the most abundant excitatory neurotransmitter in the human nervous system.
OX1, OX2	Orexin 1 Receptor, Orexin 2 Receptor	Orexins are a class of neuropeptides that are known to play a role in stabilizing wakefulness and inhibiting sleep.
GPR52	G Protein-Coupled Receptor 52	An orphan receptor that is highly expressed in the striatum- may play a role in the regulation of frontal lobe-striatal and limbic dopamine in psychiatric and neurological disorders.
H4	Histamine H4 Receptor	H4 is particularly expressed in immune system cells and is known to be involved in inflammation and allergy.
EP4	Prostaglandin EP4 Receptor	EP4 suppresses innate and acquired immunity and is known to induce tumor progression
PAR2	Protease-Activated Receptor 2	PAR2 is known to be associated with many physiological and pathophysiological processes such as inflammation, tumor metastasis, gastrointestinal motility, pain, and itching
SSTR5	Somatostatin Receptor 5	SSTR is expressed mainly on small intestinal endocrine cells and pancreatic beta cells, inhibits the secretion of gastrointestinal hormones such as GLP-1 and PYY by binding somatostatin.
GLP-2	Glucagon-like Peptide 2	Intestinal GLP-2 is secreted together with GLP-1 during nutrient intake, and repairs and protects the intestinal tract.
Mpro	SARS-CoV-2 Main Protease	An enzyme essential for the replication of Sars-CoV-2(COVID-19 cause virus). One of the target proteins for the development of antiviral drugs.
D2	Dopamine Receptor D2	Dopamine is a neurotransmitter in the brain involved in motor control, motivation, and learning - known to be associated with Parkinson's disease and schizophrenia.
5-HT	5-Hydroxytryptamine Receptor	5-hydroxytryptamine (serotonin), as a transmitter in the central nervous system, is thought to play an important role in the regulation of brain function.
Orphan receptor		A receptor whose existence is known based on genetic analysis, but for whom no ligand has been identified.
Ligand		A ligand is a molecule that binds to a specific receptor in vivo, such as hormones, neurotransmitters. For example, the ligand for muscarinic receptors is acetylcholine.

Locations

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