Sosei Group Corporation

FY2014 Results
Conference Call

13 May 2015

www.sosei.com

Director and CEO	Shinichi Tamura
Executive Vice President CFO	Hidetoshi Torami
Heptares Therapeutics CSO	Fiona Marshall
Executive Vice President CSO	Akinori Mochizuki

FY2014 Highlights

Pipeline

Future Prospects and Strategy

FY2014 Achievements

✓ Achieved revenue goals

Dec 2014 Milestone revenue triggered by US submission of NVA237 and QVA149

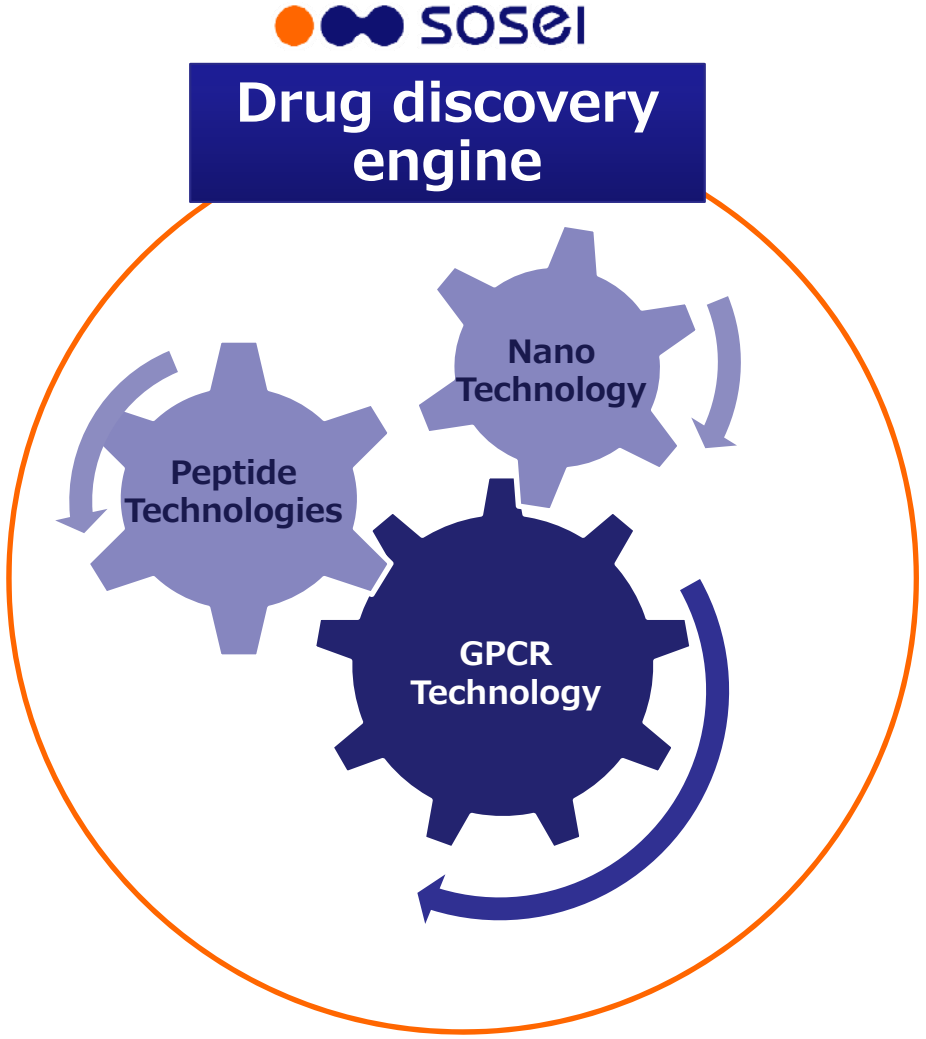
✓ Created powerful product engine through M&A

Dec 2014 Acquisition of Jitsubo

Feb 2015 Acquisition of Heptares Therapeutics

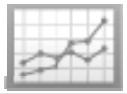
M&A Adds Powerful Product Engine

- ☑ Driving sustainable pipeline of new product opportunities
- ☑ Continued strategy to partner around platform and pipeline
- ☑ World-class UK R&D team
- ☑ Synergy with existing Sosei Group platform technologies



Sosei Group – Acquired New Strengths

Continuing revenue stream



Profitable, sustainable revenue structure

Innovative drug discovery engine

Sustainable pipeline replenishment through innovative drug discovery engine

High-profit potential pipeline

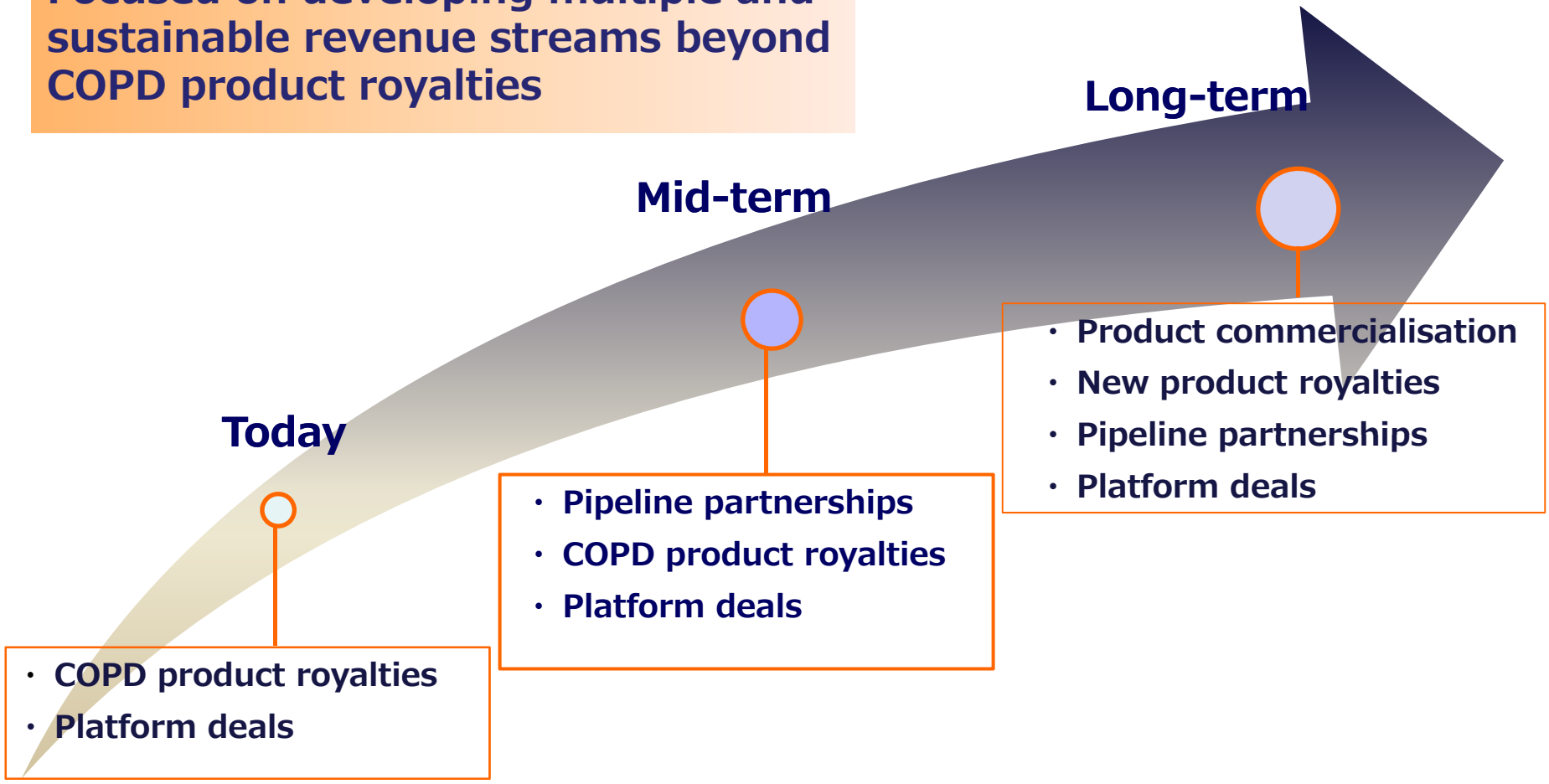
Number of first-in-class/ best-in-class candidates

Global management

Exceptional leadership team, strong corporate governance system

Business Strategy

Focused on developing multiple and sustainable revenue streams beyond COPD product royalties



FY2014 Financial Highlights

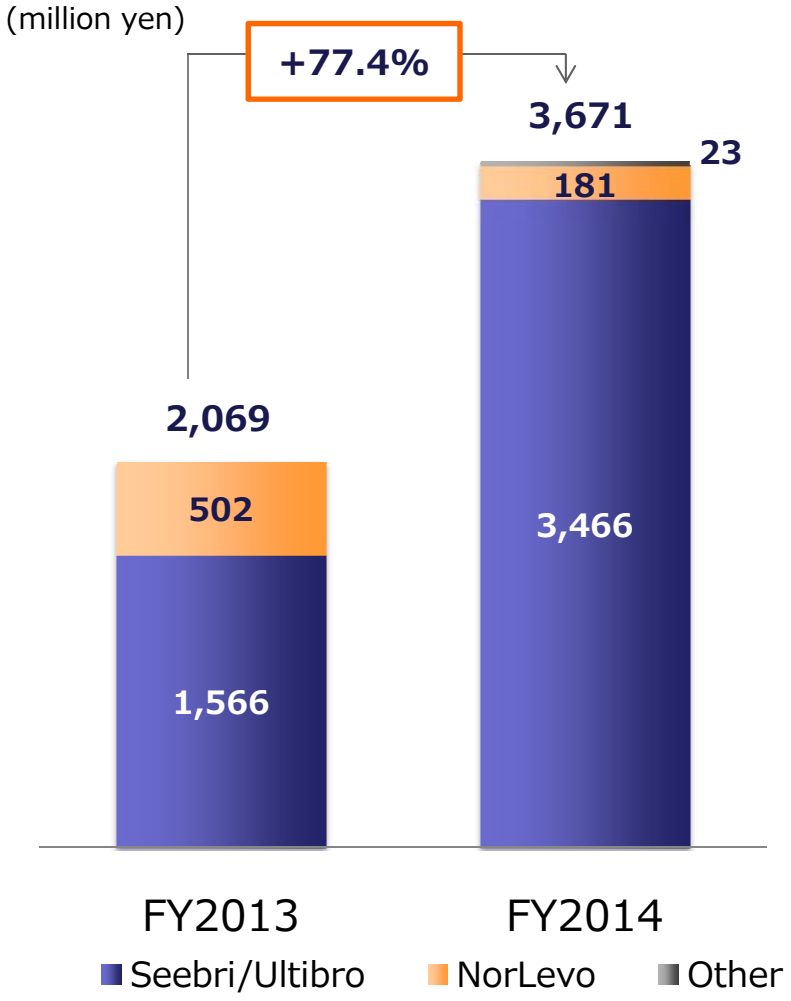
(million yen)

	FY2013	FY2014	Change (%)
Revenue	2,069	3,671	77.4%
Gross margin	1,818	3,602	98.1%
R&D expenses	305	557	82.9%
SG&A expenses	882	1,946	120.6%
Operating income	756	1,108	46.6%
Net income	1,526	562	-63.1%
Net income attributable to owners of the parent company	1,526	568	-62.8%

(million yen)

	FY2013	FY2014	Change
Cash and cash equivalents	7,214	5,573	-1,641

Revenue Driven by Strong Performance of Seebri® and Ultibro®



- **Seebri® and Ultibro®**
  - US submissions of NVA237 and QVA149 triggered USD 20m milestone payment
  - Royalties from sales of both products
- **NorLevo®**
  - Royalties from sales in Japan and Australia
- **Other**
  - Heptares milestones

* Seebri® Breezhaler® and Ultibro® Breezhhaler® are the registered trademarks of Novartis

Continuing Revenue Stream from Seebri®・Ultibro®

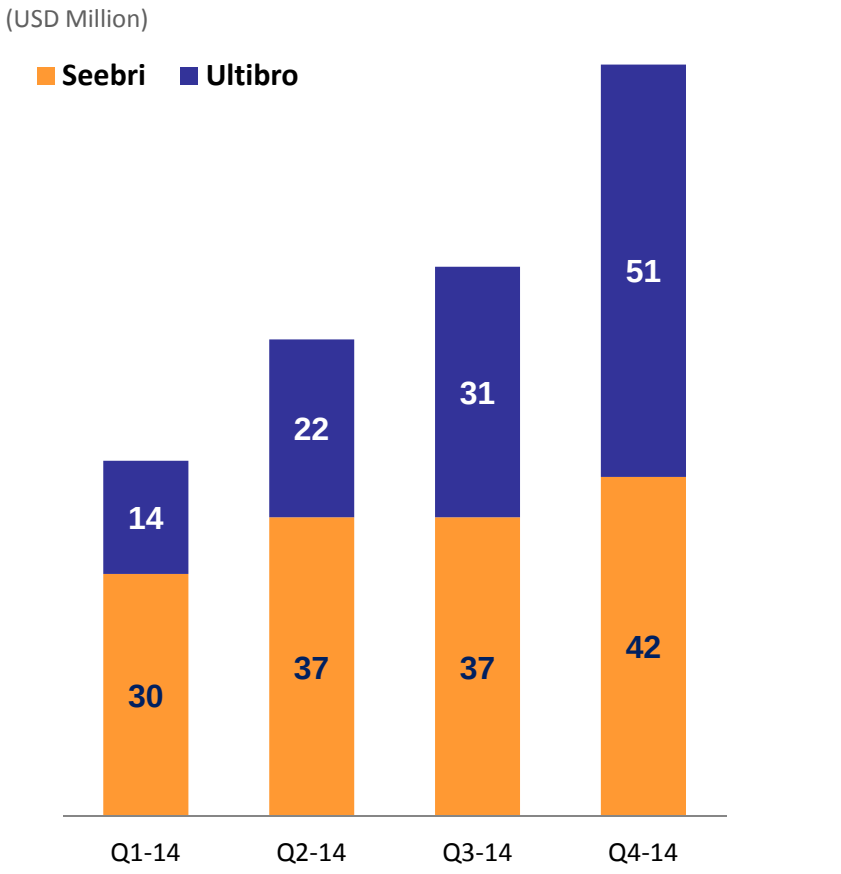
Seebri®* (LAMA)

- Approved in over 80 countries
- NVA237 submission to FDA completed (Dec 2014)

Ultibro®* (LAMA/LABA)

- Approved in over 50 countries
- QVA149 submission to FDA completed (Dec 2014)

Seebri・Ultibro Novartis Sales (Actual)

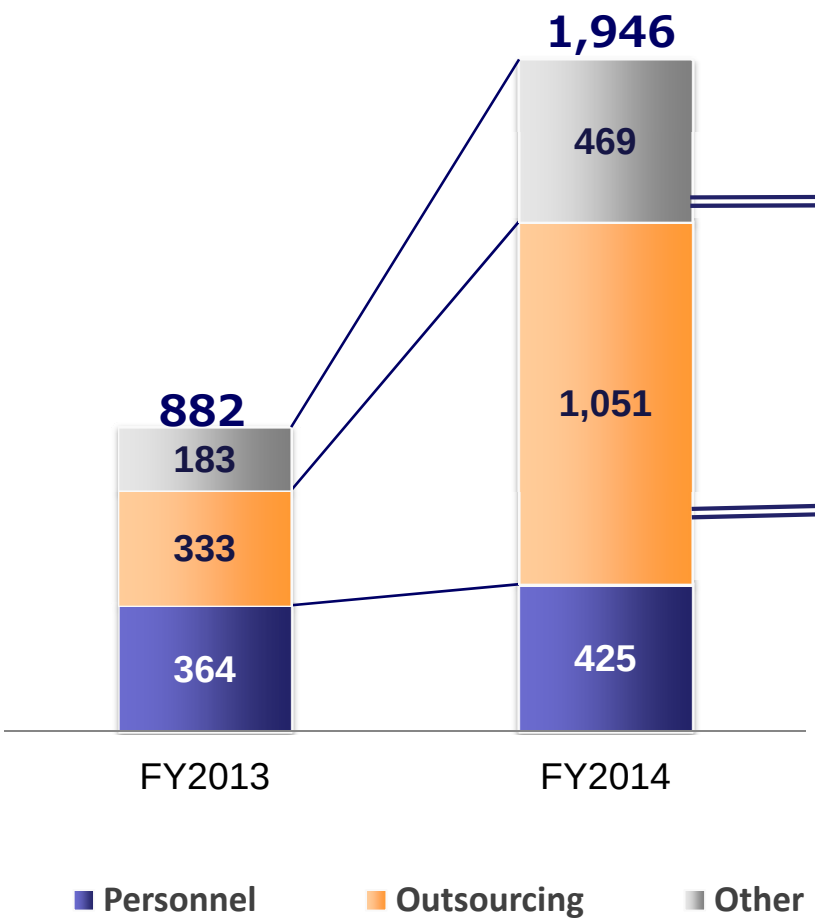


Source: Novartis presentation material

* Seebri® Breezhaler® and Ultibro® Breezhhaler® are the registered trademarks of Novartis

SG&A Expenses

(million yen)



- **Increased by 1,064 million mainly due to incurred costs related to Heptares acquisition**

- **Increased mainly due to the payment of UK stamp clause for Heptares acquisition**

- **Increased mainly due to the payment of advisory fees for Heptares acquisition**

FY2015 Financial Forecast

(million yen)

	FY2014 (Actual)	FY2015 (Budget)
Revenue	3,671	11,732
Operating income	1,108	5,899
Income before tax	1,366	5,915
Net income attributable to owners of the parent company	568	6,047
R&D expenses	558	4,003
SG&A expenses	1,945	1,824

Revenue

- Seebri and Ultibro US approval milestones, and royalties
- Initial payments and milestones related to Heptares product candidates

R&D expenses

- Increase investment in development of high-potential products

FY2014 Highlights

Pipeline

Future Prospects and Strategy

Heptares Therapeutics Ltd.
GPCR Drug Discovery and Development

Heptares Therapeutics Snapshot

HEPTARES therapeutics

Building the world's leading GPCR therapeutics company

Exceptional pipeline of clinical candidates

- Diversified pipeline across neuroscience, metabolic, orphan diseases
- Multiple Phase 1 & Phase 2 clinical programmes reporting data during 2015-2017

Unique, proprietary GPCR structure-based drug discovery platform

- Breakthrough chemistry for validated, yet previously hard-to-drug, biology
- Enables small molecule, peptide, and biologics discovery

Multiple platform deals – potential for sustainable revenues

AstraZeneca, morphosys, CUBIST PHARMACEUTICALS, MedImmune, Inc., Takeda, NOVARTIS

Experienced global leadership team (Most with megapharma/biopharma experience)

Heptares Corporate Deals

- **Key strategy to partner around pipeline and platform**
- **Provides strong validation, cash and sustainable long-term revenue potential**
  - More than $30 million generated in upfront and milestone payments
  - Potential to generate more than $1 billion in future milestones and royalties

Partner	Focus
AstraZeneca	Small molecule & antibody drugs in multiple therapeutic areas
MedImmune, Inc.	StaR® antigens for antibody discovery, multi-target alliance
CUBIST / MERCK	Up to 2 GPCR drug targets for undisclosed indications in acute care
morphosys	StaR® antigens for antibody discovery, multi-target alliance
Takeda	Small molecules targeting single GPCR linked to CNS disorders
NOVARTIS	Small molecules targeting a single GPCR nominated by Novartis

The Heptares Pipeline

Programme	Indication	Discovery	Preclinical	Phase 1	Phase 2
M_1 agonist	AD/Sz Cognition				
M_4 agonist	Sz/AD Psychosis				
M_1M_4 dual agonist	Sz/AD Psych / Cog				
A_{2A} antagonist	ADHD		IND open		
CGRP antagonist	Migraine				
Orexin OX_1 antagonist	Addiction				
GLP-1 antagonist	Congenital hyperinsulinism				
Multiple targets	Multiple indications				
Partnered programmes	Multiple indications	Progress confidential			

AD: Alzheimer's disease; Sz: schizophrenia;
ADHD: attention deficit hyperactivity disorder

- **Highly validated targets, low biology risk**
- **All first-in-class or superior next-generation therapeutics; multiple shots on goal**
- **Leading in neuroscience, next wave of orphan (eg GLP-1 antagonist)/other therapeutic areas**

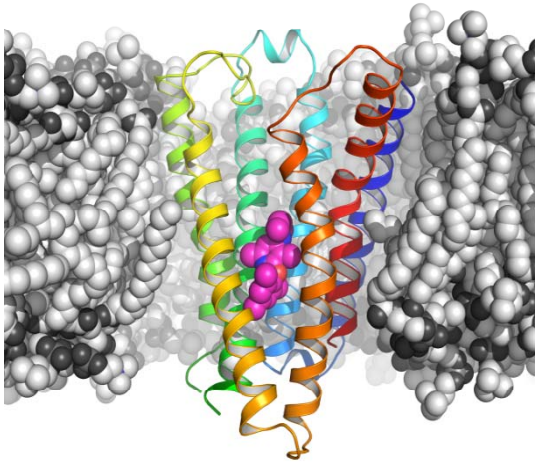
Value Potential from Heptares Platform/Pipeline

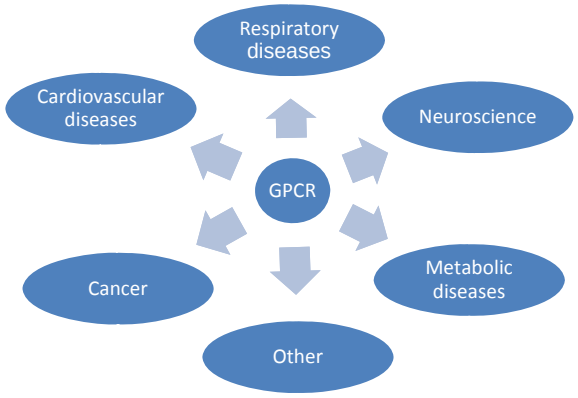
Candidate	Target product profile	Patient population US/5EU [1]	Market value (est) [1]	Projected peak sales (est) [2]	Reference product peak sales
M1 agonist	Well-tolerated pro-cognitive for AD and first-ever for cognitive impairment in Sz, PDD	AD 5-8.5M Sz 2.8M (85% of patients)	$7bn precedent for AD + new Sz, PD	$3-5 bn	Aricept $3.9 bn
M4 agonist	Well-tolerated anti-psychotic for Sz and first-ever for AD	AD psychosis 1.5-2.3M Sz 3.5M	$6.5 bn Sz $13bn total	$3-5 bn	Abilify $5.7 bn in all indications
Dual M1/M4 agonists	Dual anti-psychotic and pro-cognitive for AD, Sz, other	AD 2-3.5M Sz 3.3M	$20 bn	$5-10 bn	New paradigm in AD and Sz
A2A antagonist	Effective, safe non-stimulant for ADHD	31M pediatric and adult	$5-8 bn	$0.5-1.5 bn	Strattera $0.7 bn Vyvanse $1.4 bn
CGRP antagonist	First-in-class SME for Migraine Treatment and Prophylaxis	US: 36M, 12.6M eligible for prophylaxis, 30-40% triptan failures, 5EU: 47M	$2-3 bn (Rx)	$0.5-2 bn	Levadex $0.5bn (est) AMG-334 $2.6bn (est)
Orexin OX1 antagonist	First-in-class new mechanism for craving/addiction	Smoking: c70M US: 1.3M on Chantix Opioid: 4.2M	$2.7-3.7 bn	$1-3 bn	Chantix $0.9 bn Suboxone $0.9 bn

[1]Sources: Decision Resources, Defined Health, LEK, GBI, analyst reports and company financial reports and presentations
[2]Estimate based on market size and differentiation versus standards of care and competitor pipeline

G Protein-Coupled Receptor (GPCR) Super Family

- **Most important family of drug targets in industry**
  - Seven transmembrane protein with crucial role in many biological processes
  - 375 GPCRs in 3 major subfamilies (Class A, B, C)
  - 225 with known ligands, 150 orphan targets
- **Clinical validation and compelling biology across a wide range of diseases**
- **Source of approx. 40% of approved drugs***





Respiratory diseases
Advair®
OxyContin®
Breo™ Ellipta™
Anoro®
Seebri®
Ultibro®
Ventolin® HFA
Singulair®
Spiriva®
Tudorza® Pressair®

Neuroscience
Zyprexa®
Abilify®
Seroquel®
Suboxone®

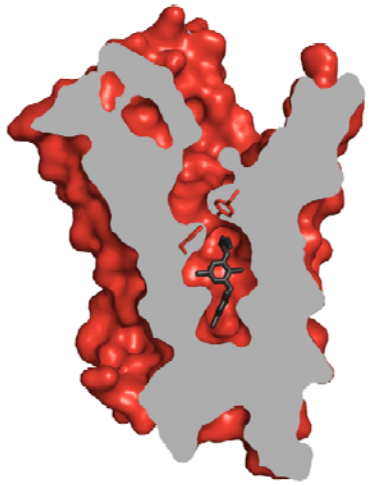
Metabolic diseases
Belviq®
Byetta®
Myrbetriq®
Signifor®

Cardiovascular diseases
Opsumit®
Diovan®
Benicar®
Tracleer®
Zioptan™
Plavix®

Cancer
Erivedge®

Major Opportunity Targeting GPCRs

- **GPCRs are not optimally drugged**
  - Limited potency and selectivity
  - Metabolic and safety liabilities
  - Inadequate route of administration
- **Many high-value targets remain untapped or intractable**
  - First-in-class and superior medicines required
  - Dynamic area with new biology constantly emerging
  - Small molecules and biologics
- **GPCRs inaccessible to many conventional discovery approaches**
  - Native GPCR spans cell membrane – highly unstable when removed



Allosteric binding pocket in a Class B GPCR

➔ **Stable GPCRs and 3D structures form the key to unlocking GPCR discovery**

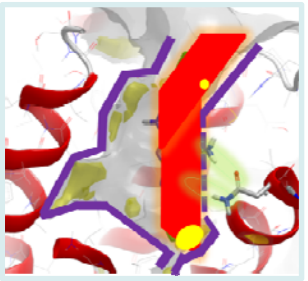
Revolution in GPCR Drug Discovery

Traditional Approach

1M compounds randomly screened by HTS

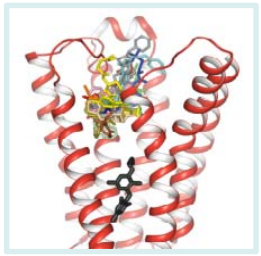
Low hit rate – poor quality
No information on mechanism

Resource-intensive empirical chemistry programme



Sub-optimal drug candidates

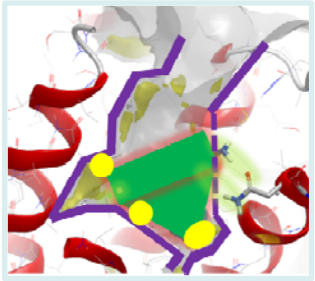
Heptares Approach



>10M compounds screened 'in silico' to fit protein pocket

High hit rate – precise information on ligand/protein interactions

Structure-based design rapidly generates optimised candidates



Optimised drug candidates 'perfect fit'

Reduced attrition

Heptares Holds Key to GPCR Structure-based Design

Heptares StaRs® → Stable Protein → Structural Information → SBDD

- **Heptares StaR® Technology**
  - Stabilises GPCRs for structure determination and antibody discovery
- **Transformative for discovery**
  - Yields drugs with increased selectivity, safety and greatly reduced clinical attrition
- **Strong scientific validation**
  - Extensive publication record in high impact journals
- **StaR® proteins for all families of GPCRs**
  - 10+ world-first receptor x-ray structures
- **7 novel first/best-in-class candidates (preclinical and Phase 1)**

StaR Technology for Antibody Discovery

- **Scarcity of GPCR mAbs: only one mAb approved to date**
- **StaR technology solves key problem:**
  - stable, quality antigen in specific conformation
- **>100 untapped mAb GPCR targets across range of diseases**
- **Heptares pipeline development via partnerships**

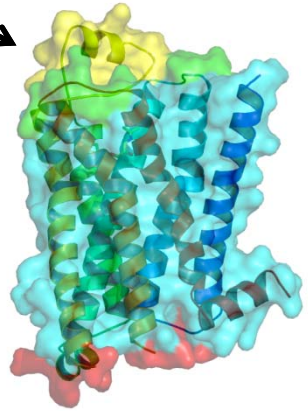
Antibody Partners

MedImmune, Inc.

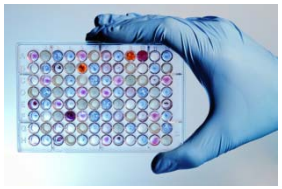
morphosys

Unique Structural Insights

mAb epitope



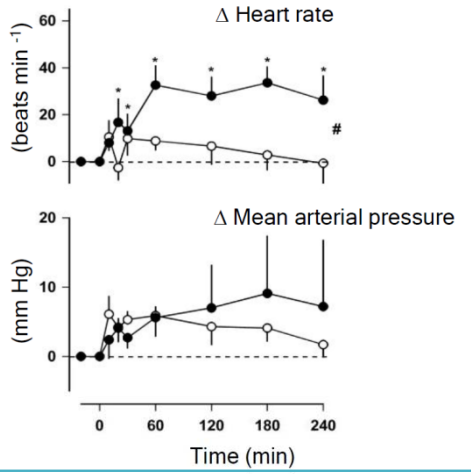
Broad Utility in Ab Discovery



In vitro eg Phage screening

In vivo Immunisation

Activity in Disease models

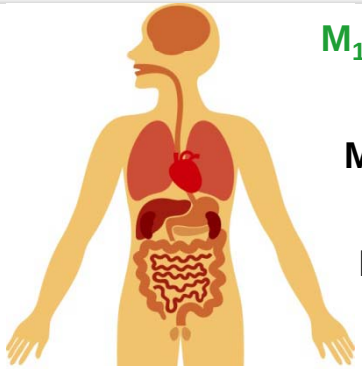


Design of Selective Muscarinic Agonists

M_4 brain – behaviour, dopamine

M_2/M_3 lung – bronchoconstriction

$M_{2>3}$ bladder – contraction

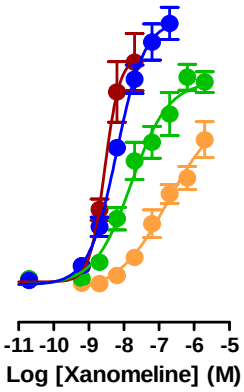


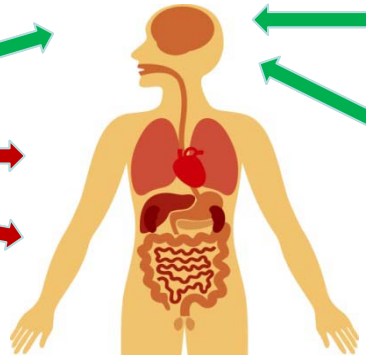
M_1 brain – learning and memory

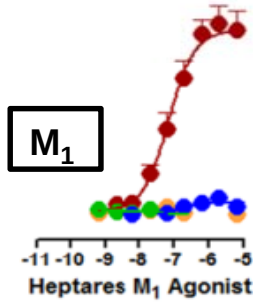
M_2 heart – HR and BP

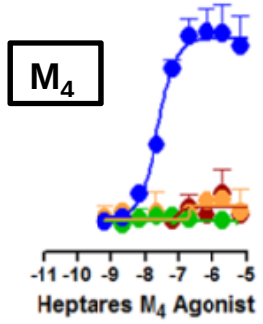
$M_{2/3}$ stomach – gastric emptying

$M_{2/3}$ gut – gut transit







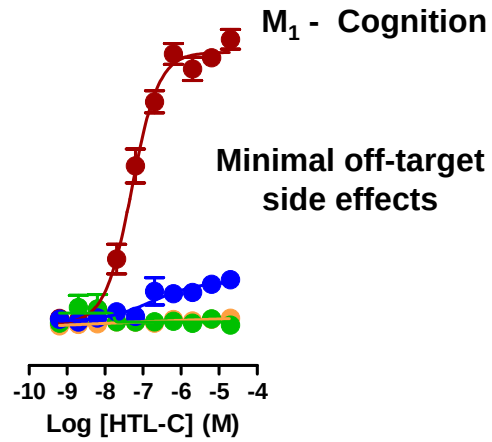


Older Muscarinic Agonists

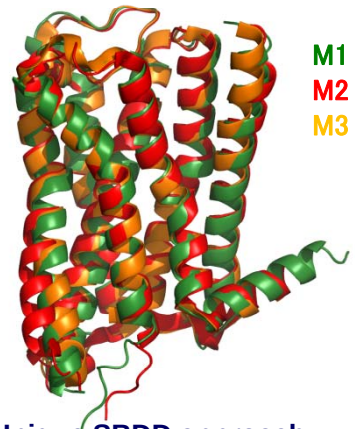
Heptares Muscarinic Agonists

Heptares Muscarinic Programmes

- **M_1 agonists – Cognitive impairment in AD and SZ**
  - Highly selective M_1 agonists with optimised level of activity
  - Phase 1a complete
  - Clinical Proof-of-concept (PoC) trials in elderly subjects (readout 2015/2016), and AD patients (readout 2016/2017)
- **M_4 agonists – Psychosis and behavioural disturbance**
  - Potential in SZ and Alzheimer's disease
  - Highly selective for M_4, optimised pharmacology
  - Phase 1 likely to commence in 2016, clinical PoC in Sz psychosis likely readout in 2017/2018
- **Dual M_1/M_4 agonists – Cognitive impairment & Psychosis**
  - Initiation of Phase 1 clinical study in 2016/2017, and Phase 2a in 2017/2018
- **Addresses high unmet medical needs in AD and SZ**



Heptares Muscarinic M_1 agonist



Unique SBDD approach

M_1 Selective Agonist HTL-9936

THE FIVE MOST PROMISING DRUGS ENTERING PHASE I TRIALS

DRUG	DISEASE	COMPANY
HTL-9936	Cognitive impairment	Heptares Therapeutics
BIOD-531	Type 2 diabetes	Biodel
SGN-LIV1A	LIV-1-positive metastatic breast cancer	Seattle Genetics
PulmoXen™	Cystic fibrosis	Xenetic Biosciences/Pharmasynthez
ESN-364	Female sex-hormone related disorders	EuroScreen

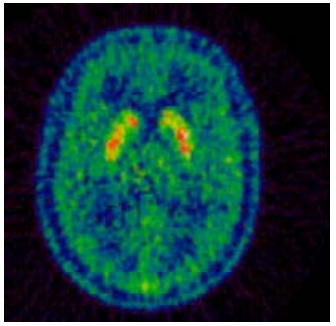
The Ones To Watch, Thomson Reuters, Feb. 2014

- **Previous non-selective M_1 agents showed good efficacy but had poor safety/tolerability, thought to be due to lack of selectivity over M_2 / M_3**
- **Phase 1 study of HTL9936 ongoing to evaluate efficacy, tolerability and safety in cognitively impaired elderly people**
- **Designed to provide early Proof of Concept**

A_{2A} Antagonist as Novel Non-Simulant for ADHD

- **Principal unmet need in ADHD: more effective/better tolerated non-stimulants**
- **A_{2A} mechanism provides opportunity for effective non-stimulant with excellent safety**
  - Efficacy comparable to amphetamine and methylphenidate (standard stimulant therapy) in preclinical models
  - No appetite suppression, growth retardation, insomnia, or CV risk
  - Clinical validation with caffeine, natural non-selective A_{2A} antagonist (use limited by weak target inhibition and off-target side effects)
- **Heptares A_{2A} antagonist – First-in-class for ADHD, best-in-class chemistry**
  - Rapid acting, no titration, daily, excellent tolerability
  - Phase 1 clinical study to commence in 2015
  - Proof of CNS target engagement 2016, clinical PoC 2016/2017

Most common childhood psychiatric disorder

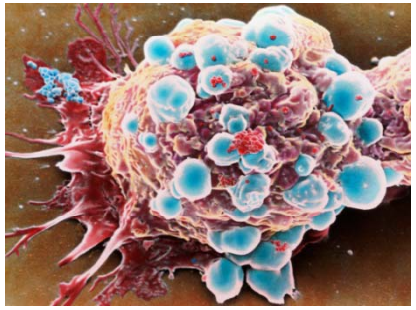


A_{2A} antagonists target brain areas linked to ADHD*

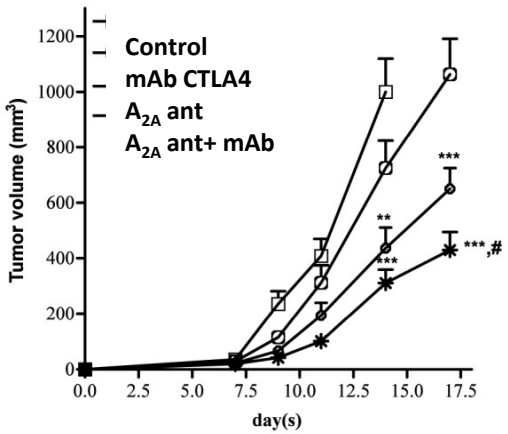
*Source: *Journal of Diagnostic Imaging in Therapy. 2014; 1(1): 20-48 Grachev et al.*

A_{2A} Antagonist for Cancer Immunotherapy

- **Immunotherapy is a revolutionary way to treat cancer**
  - Dramatic efficacy seen with antibodies to CTLA4 (Yervoy) and PD1 (Optivo, Keytruda)
  - Tumours have many mechanisms to evade immune system – including production of adenosine
- **Adenosine A_{2A} antagonists have potential to increase efficacy of immunotherapies by blocking action of adenosine on T cells**
  - Potential to combine with multiple immunotherapy approaches e.g. checkpoint inhibitors, cancer vaccines, CAR-T
- **Opportunity in a wide range of tumour types**
- **Ability to select patients based on biomarkers of elevated adenosine e.g. CD73**
- **Heptares uniquely positioned with X-ray structures of multiple adenosine receptors**
  - Discovery of first A_{2A} antagonists specifically optimised for cancer indications



T cell killing a cancer cell. Blocking A_{2A} receptors on T cells prevents tumours evading the immune system

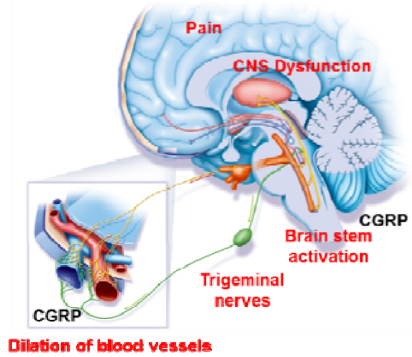


A_{2A} antagonists enhance the efficacy of other immunotherapies, e.g. CTLA4 and PD1 mAbs*

*Modified from *Fig. 1, Ioannone, et al. Am. J. Cancer Res. (2014)*

Small Molecule CGRP Antagonists: Migraine

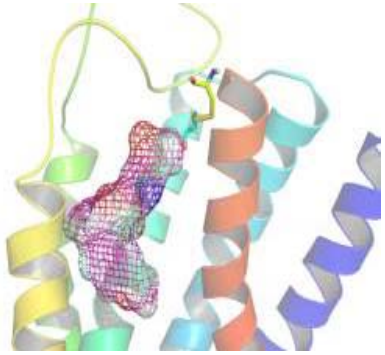
- **CGRP antagonism is a new clinically validated approach in migraine**
  - Opportunity for rescue therapy and prophylaxis
  - CGRP antibodies progressing in clinic have validated opportunity
  - Need for well tolerated small molecule drug – non-invasive, easily reversible
- **Opportunity to address significant unmet medical needs**
  - Triptan use limited (refractory patients and those with CV risk)
  - Current prophylaxis treatment has <50% response rate, poorly tolerated
- **Heptares CGRP antagonists**
  - Highly potent small molecules optimised by structure methods
  - Readout of Phase 1 proof of mechanism in 2016/2017 and Phase 2 PoC in 2017/2018
- **Intranasal product for both prophylaxis and rescue use**
- **Auto-injector for emergency rescue in severe attacks**



Selective Orexin OX_1 Antagonists for Addiction

- **First-in-Class agent for treatment of addiction disorders**
  - Superior relapse prevention in broad spectrum of substance addictions, e.g. nicotine, cocaine, alcohol, prescription drugs
  - First treatment for various compulsive disorders (binge eating, gambling)
- **High unmet need for agents that are not replacement therapies**
  - High relapse rate with current therapies
- **Novel GPCR mechanism to directly inhibit craving and relapse in addiction**
- **Heptares Orexin 1 Antagonist Project**
  - Heptares has crystal structures of OX1 & OX2 receptors
  - First-in-class industry position with highly potent & selective leads

Orexin pathway regulates arousal, reward and motivated behaviours that underlie addiction and craving



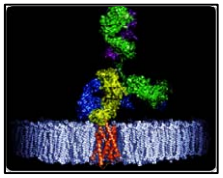
OX_1 structure with novel Heptares lead agent

Heptares vision for the next five years

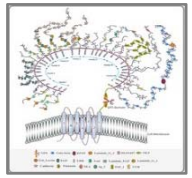

Clinical pipeline

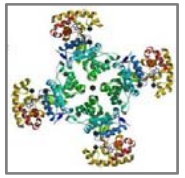

Rare diseases


Oncology


Biologics


Oral agonists


New GPCRs*


All membrane proteins

- **Clinical Proof of Concept on first wave of neuroscience products 2015-2017**
- **Transformative partnerships**
  - Additional discovery alliances and clinical-stage product deals
- **Next wave of product candidates into clinic, including orphan/rare diseases, oncology, metabolic**
  - Potential to take to market independently in selected cases
  - Leverage capabilities of Sosei Group to advance/differentiate product opportunities
- **Science and technology leadership**
  - New GPCRs, transporters, ion channels, biased agonists

* Source: **Lagerström & Schiöth *Nature Reviews Drug Discovery* 7, 339-357 (2008).**

Jitsubo Peptide Technology

Jitsubo Snapshot

Vision

- To contribute to human development through technology innovation
- To contribute to welfare of society through development of peptide products

Established:	**April 2005**
Representative:	**Yusuke Kohno, CEO**
Business overview:	**1. Development of peptide generics** **2. Licensing of intellectual property** **3. Development of improved peptide products**

Tokyo University of Agriculture and Technology, Venture Port

Jitsubo's Strengths

1 Development of high-quality peptide at low costs

➢ **Molecular Hiving™**

- Development of high-purity peptide API at low costs
- Technology enables supervision during the manufacturing process
- Highly reactive, enables synthesis of specialized peptides that was difficult using pre-existing technologies.

2 High-value adding novel peptide modification technology

➢ **Peptune™**

- Improves functions of peptides without changing their original pharmacological features
- By optimizing existing peptides, new IP and product candidates can be developed
- Enables peptide binding to small-molecule compounds

Peptide therapeutics market potential

Sales	2012	2020	Growth
Japan	USD 1.4 bn	**USD 2.4 bn**	71%
W-W	USD 16 bn	**USD 23 bn**	44%
Generic market	USD 1.2 bn	**USD 3.8 bn**	217%

Source: Seed Planning, Inc. Market Research & Consulting,「2014年版 世界のペプチド医薬品開発の現状と将来展望」

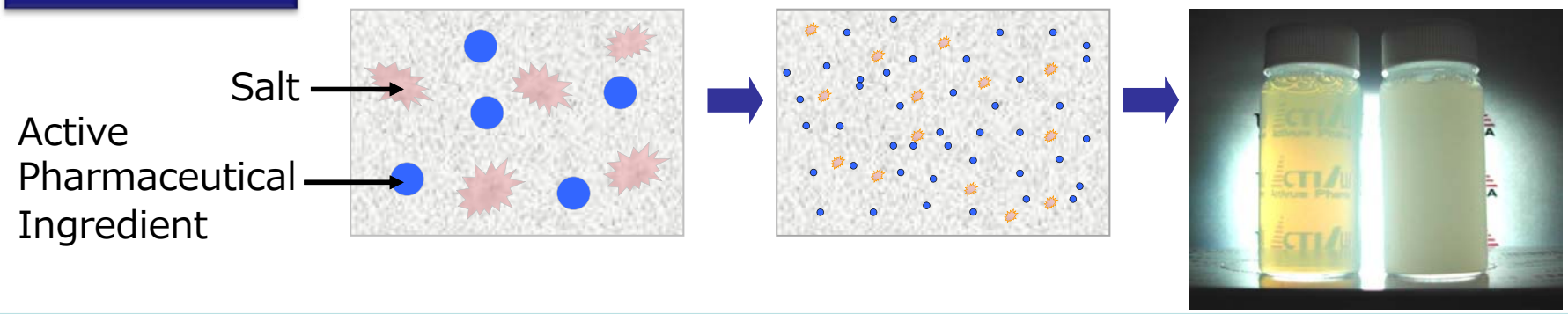
Novel peptide compounds	➢ **Peptide therapeutics market is expected to grow** • Discovery of novel peptide compounds in collaboration with Heptares (StaR® technology)
Generic peptide market	➢ **Generic peptide market to grow subsequent to the patent expiration of blockbuster peptides** • Alliances expected in generic field based on high-effeciency synthesis

APNT
(Activus Pure Nano-particle Technology)

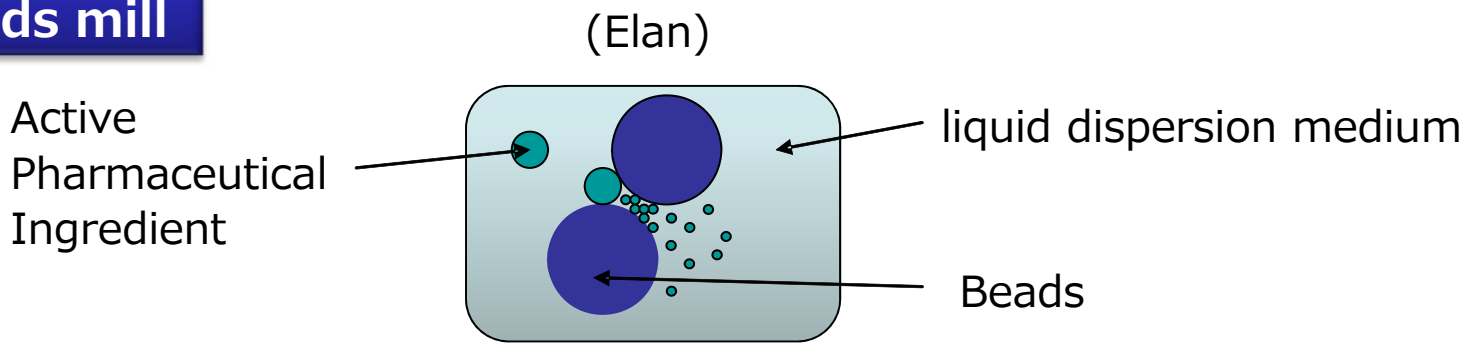
APNT (Activus Pure Nano-particle Technology)

- **APNT does not use metal or ceramic beads and therefore avoids contamination derived from beads' chip. APNT utilizes salt for milling, which is completely washed away from the final product**

APNT



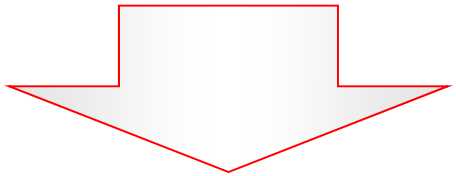
Beads mill



Contributing to drug development with unique technology

➢ Technology with high usability in drug development

- Over 90% of pharmaceutical products and candidate compounds with promising efficacy and safety profiles have poor solubility, which causes low bio-availability and increased doses, and inhibits drug development.
- Pharmaceutical companies have been investigating the potential of life-cycle management



✓ **Activus offers a solution by using its own unique nanotechnology**

✓ **Development of novel but poorly soluble candidate compounds from Heptares StaR® technology discovery platform**

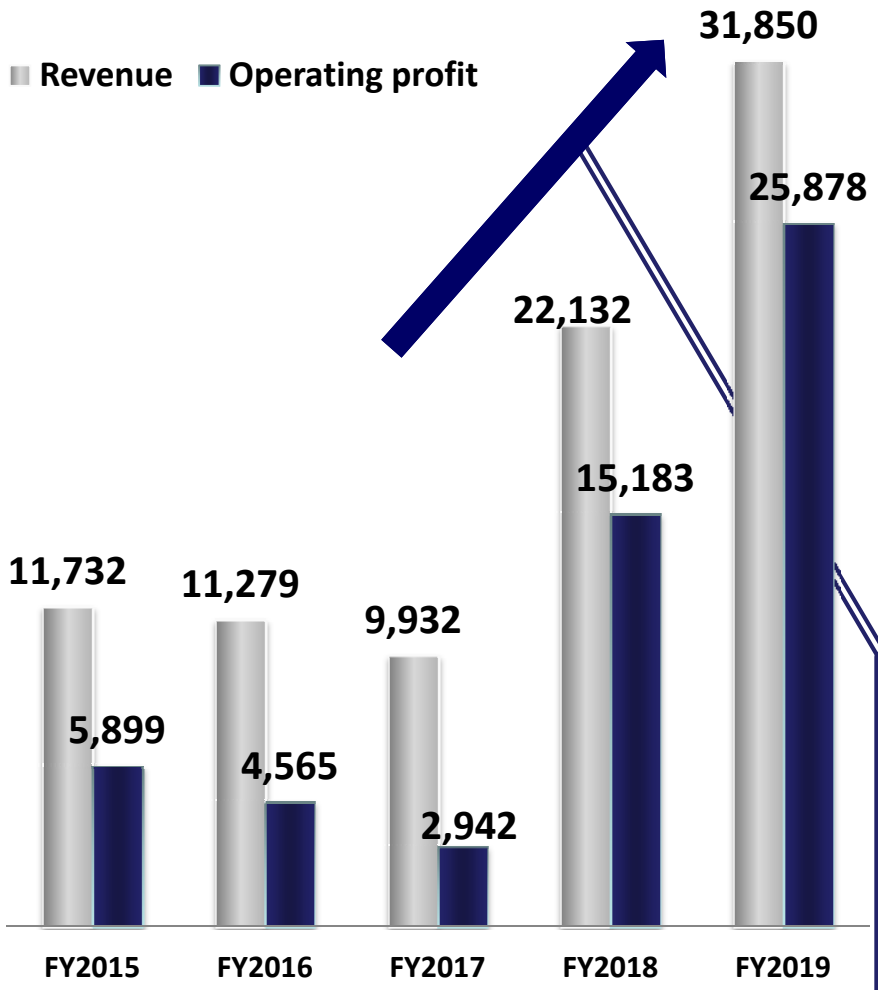
FY2014 Highlights

Pipeline

Future Prospects and Strategy

Mid-term Projections (before Heptares acquisition)

(million yen)



Revenue

- Milestones and royalties from Seebri and Ultibro
- Initial payments and milestones related to outlicensing product candidates from Heptares pipeline
- Initial payments from new partnerships based on Heptares screening technology

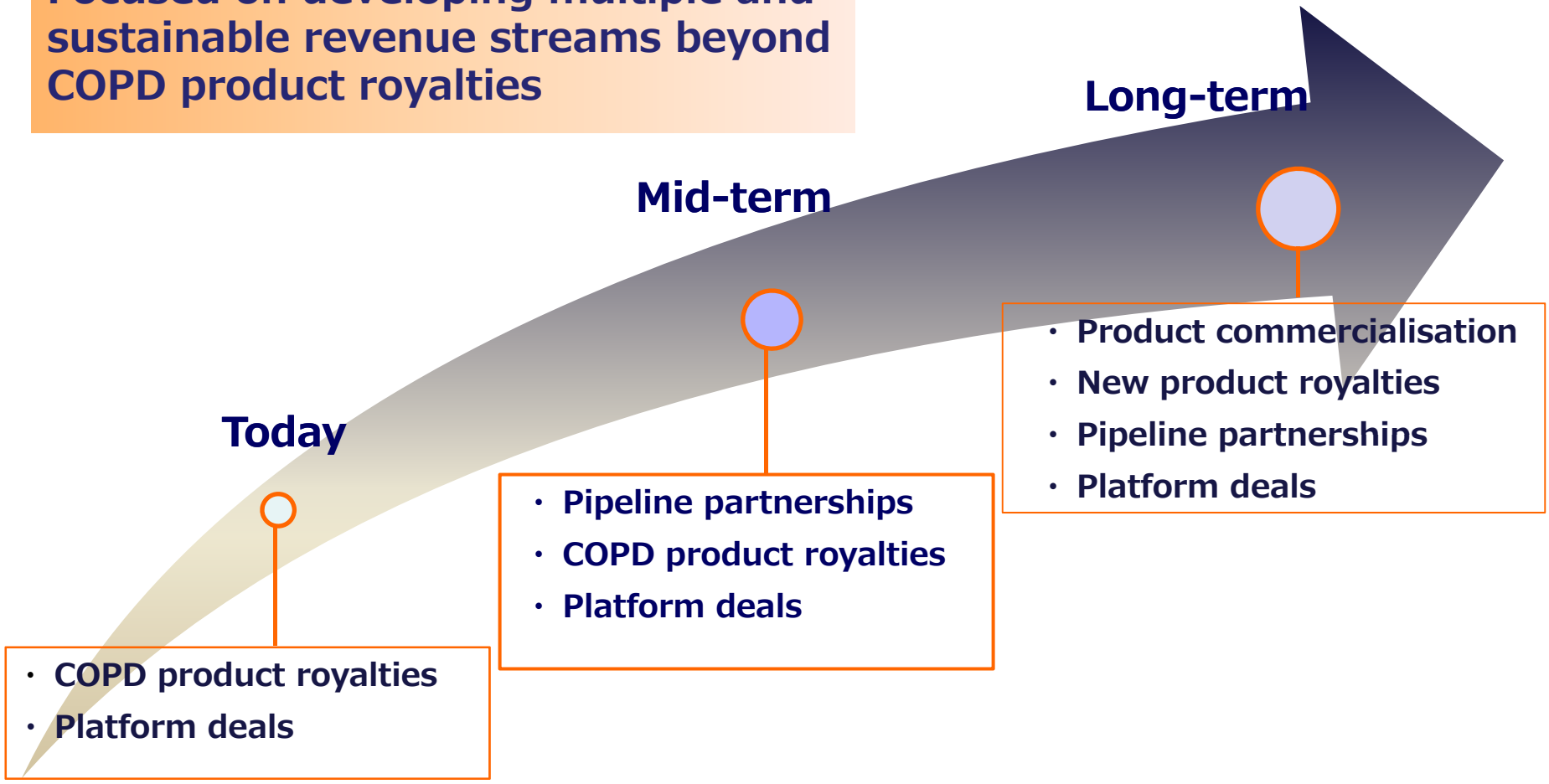
Operating profit

- R&D expenses: c. 4 billion yen annually
- SG&A: c.2 billion yen annually

- Heptares milestones payments from outlicensing product candidates are expected to increase
- US launch of Seebri and Ultibro, as well as increased awareness of COPD is expected to stimulate market expansion from FY2017

Business strategy

Focused on developing multiple and sustainable revenue streams beyond COPD product royalties



Q&A

Disclaimer

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