



AdAlta
next generation protein therapeutics

Introducing AD-214

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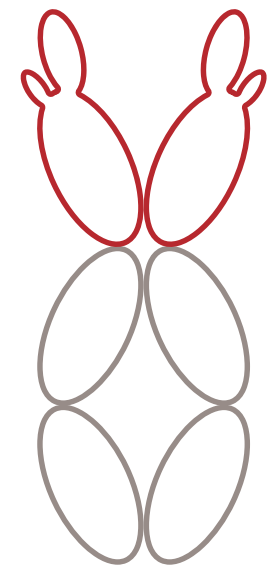
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AdAlta Limited (ASX:1AD) is a drug discovery and development company using its powerful technology platform to generate a promising new class of protein therapeutics, known as i-bodies, for treating a wide range of human diseases.

AdAlta (1AD) investment summary

- ▶ Initial focus on treating fibrosis – high unmet medical need
- ▶ Advanced lead fibrosis drug candidate AD-214 with significant pre-clinical validation
- ▶ New molecule, AD-214 leverages all work from AD-114 to deliver enhanced activity and significantly improved half-life
- ▶ New process to manufacturing drug is well understood by AdAlta and global pharma
- ▶ AdAlta will progress AD-214 to phase 1 development as lead fibrosis drug, while retaining Orphan Drug Designation from US FDA
- ▶ New molecule expected to be more attractive to patients and potential pharma partners
- ▶ Developing i-body pipeline to further expand opportunities for partnering of novel i-body platform
- ▶ Experienced team with strong track record of drug development and ability to deliver



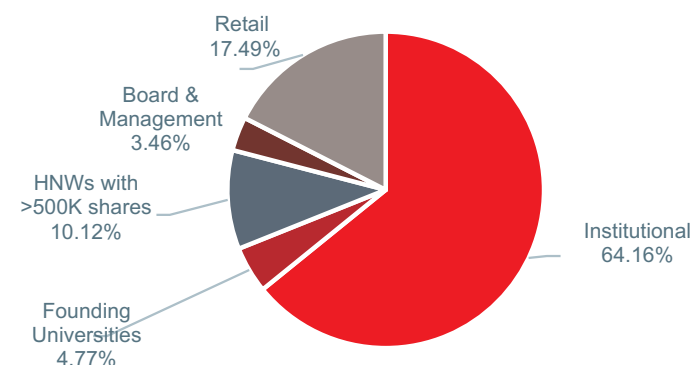
AD-214

Financial position

Key financial details	
ASX code	1AD
Share price (10 th April 2018)	AU\$0.325
Market capitalisation	AU\$33m
Shares on issue*	101,845,845
Escrowed shares (August 2018)	24,000,000
Options on issue	4,090,866
Current cash (31 March 2018)	AU\$3.63m
Trading range (last 12 months)	AU\$0.20 to \$0.40
Average daily volume	36,533

Major shareholders	%
Yuuwa Capital LP	53.08
Platinum Asset Management	8.00
Citycastle Pty Ltd	5.22
La Trobe University	2.99
National Nominees Limited	2.08
Other shareholders	28.63
Total	100%

Share performance (last 12 months)



Extensive support from institutional investors and HNWs

- ▶ Top 20 shareholders 83%
- ▶ 64% institutional shareholders
- ▶ 10% HNWs with >500K shares each
- ▶ 5% founding academic institutions
- ▶ 3.46% Board and Management and 4,090,866 Options issued from 25cents-\$1 under Employee Share Option Plan



Australian based venture capital \$40m fund



\$27b under management, global equities investor



Australian and international equities investor



ASX micro and small cap investor

Management and Board in place to deliver strategy



Sam Cobb: Founding CEO and Director

Extensive experience in raising equity, contract and grant funding

15 years of commercialisation and management experience



Dr John Chiplin: Independent Director

CEO of investment Company NewStar Ventures

Managing Director of acquired antibody company Arana Therapeutics (acquired by Cephalon Inc. for US\$200 million)



Dr Paul MacLeman: Chairman

Director of CMAX Clinical Research Pty Ltd, Livac and Protec Groupe

Founded biologics companies, experienced ASX listed executive



Liddy McCall & Dr James Williams: Yuuwa Capital Directors

Founders and investment Directors of Yuuwa Capital

Founders of iCeutica Inc (acquired 2011) and Dimerix Limited

Directors of several Australian biotech and Agritech companies

Multiple FDA, CE Mark and TGA approvals



Dr Robert Peach

Founder and CSO of Receptos Inc, acquired by Celgene Corporation in 2015 for US\$7.8bn

Deep experience in research and drug development including Fc-Fusion drug Orencia



Scientific Advisory Board

Internationally recognised with proven track record of drug development



Dr Mick Foley, AdAlta CSO

Expert in phage display

NIH, NHMRC, ARC, Gates funding and over 70 scientific publications



John Westwick: pulmonary drug discovery and development

Over 14 years experience at Novartis, head of respiratory drug discovery

Five product launches and 13 positive proof of concepts in respiratory, including a number of antibodies which are now in phase III.



Brian Richardson: drug discovery and development expert

Ex-Sandoz and Novartis (40+ years), including Head of Pre-clinical Research

Over 60 original peer reviewed research papers



David McGibney: pre-clinical and clinical advisor

20 years with Pfizer, including Head of European R&D

Ex Pfizer Ltd board member

Developed Viagra, and 10+ blockbuster drugs



Steve Felstead: clinical advisor

Ex-Pfizer (25 years), including Head of Clinical Research, Pharmatherapeutics Division

Developed Zithromax, Vfend, Celsentri, Viagra



Hausi Kocher: manufacturing expert

Ex Sandoz and Novartis involved in the development of a number of biopharmaceuticals, including three marketed therapeutic antibodies

From single domain antibody to AD-214

When combined, the i-body and Fc Fragment create a superior drug, with improved therapeutic benefit for patients and for potential commercial partners

Monoclonal Antibody



AD-114

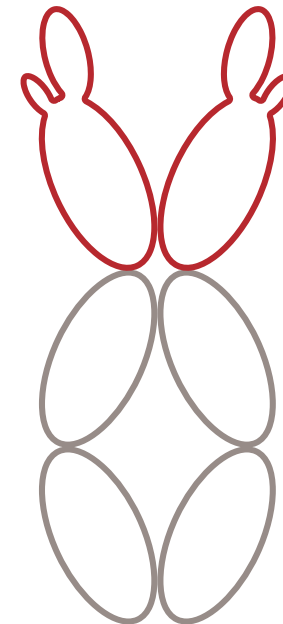
Binds to CXCR4 on the cell surface and has anti-fibrotic activity



Fc Fragment

Binds to cells expressing the Fc receptor (FcRn) to extend the half life and create a molecule with great therapeutic potential

AD-214

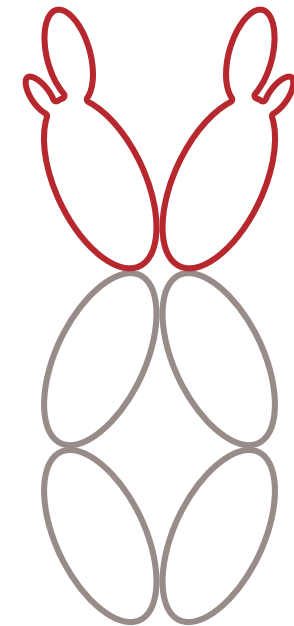


i-body binds to CXCR4 to have anti-fibrotic activity

Fc Fragment binds to extend half life

Fc Fusion – well understood, high value drugs

- ▶ Fc-Fusion proteins join the fragment (Fc) domain of an antibody with another protein domain or peptide to create a unique molecule with great therapeutic potential
- ▶ 11 Fc-Fusion based products approved by the FDA
- ▶ Straightforward, well understood manufacturing process
- ▶ Expected to lead to significantly reduced cost of goods for commercial drug due to ease of manufacturing



\$2.6b sales 2017



\$23.1b sales 2017



\$6.3b sales 2017

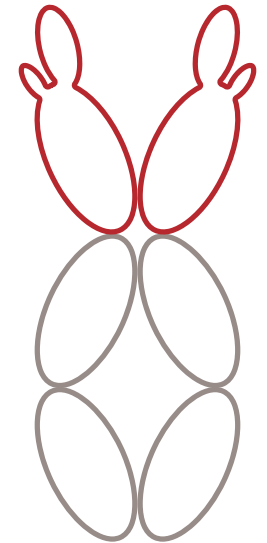
AD-214: superior drug candidate

► Enhanced binding

- Due to dual binding of two i-body molecules, enhanced binding to drug target CXCR4
- No change to proposed mechanism of action; i-body binds to CXCR4 with unique activity compared to other CXCR4 antagonists
- Same active molecule which has demonstrated broad anti-fibrotic and anti-inflammatory effects in several models of disease



► Improved half life

- Half-life duration or the time in which a drug stays in the body significantly improved (Approved Fc-Fusion $\frac{1}{2}$ life in humans range from 4-25 days)
- Less frequent dosing required and suitable for a wider range of fibrotic conditions



New molecule expected to be significantly more attractive to patients and potential pharma partners

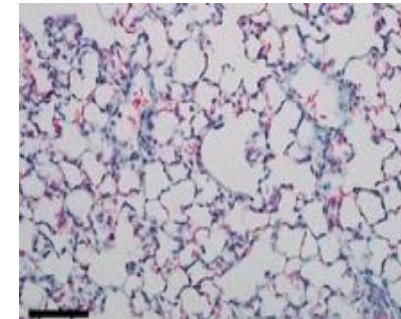
Leveraging AD-114 for a superior molecule

	AD-114 	AD-214 
High affinity binding to CXCR4	✓	✓✓✓
Specificity to CXCR4	✓	✓
Unique pharmacology compared to other CXCR4 antagonists	✓ No stem cell mobilisation	✓ No stem cell mobilisation
Half-life	24hrs in non human primates	Significantly improved from AD-114 (Approved Fc-Fusions ½ life in humans range from 4-25 days)
Dosing	Daily, subcutaneously	Less frequent IV or subcutaneous dosing required due to more potent and improved half life
Partnering	Suited to IPF	Suited to a range of fibrotic diseases, including IPF, NASH & wet AMD

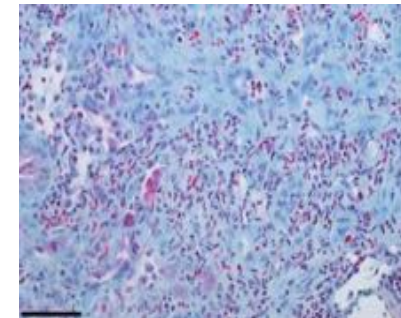
AD-214 for the treatment of IPF

Extensive pre-clinical data package with i-body demonstrates positive *in vitro* and *in vivo* in models of IPF

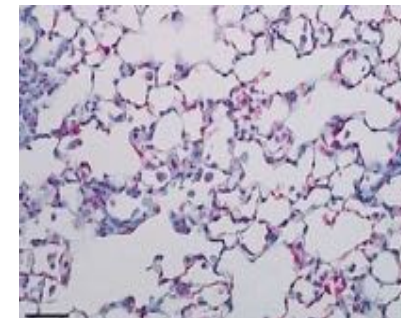
- ▶ In the bleomycin mouse model of fibrosis the anti-CXCR4 i-body has several effects in both therapeutic and prophylactic modes:
 - Inhibits fibrocytes migrating to the lungs
 - Significantly reduces Ashcroft Score and collagen deposition
 - Demonstrates anti-inflammatory and anti-fibrotic gene expression
- ▶ With human IPF tissue the anti-CXCR4 i-body demonstrated unique activity compared to existing IPF treatments Pirfenidone and Nintedanib:
 - Reduces migration of IPF patient fibroblasts and has no effect on normal lung fibroblasts
 - Reduces collagen production and fibrotic gene expression



**Normal
lung tissue**



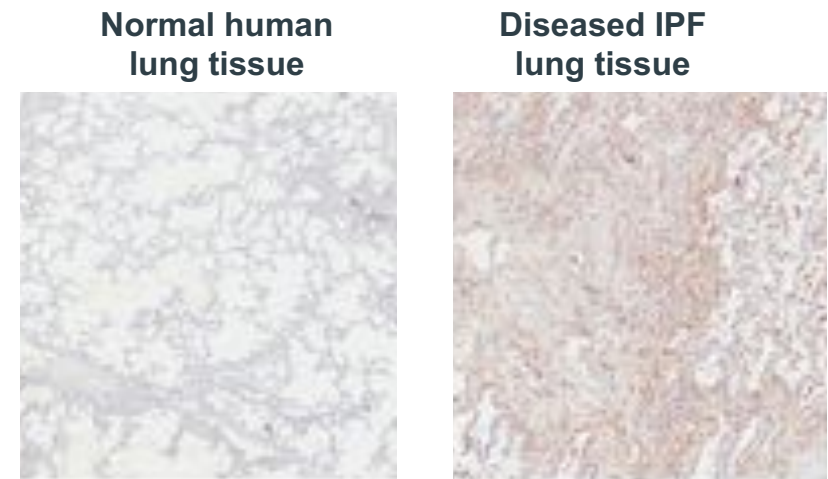
**IPF lung
tissue**
(lung disease
mouse model)



**IPF lung
tissue + i-
body dosed
for 21 days**
(lung disease
mouse model)

CXCR4 novel target for treatment of IPF

- ▶ Significant literature to support hypothesis of the involvement of CXCR4 in fibrosis
- ▶ IPF diseased lung tissue has increased CXCR4 expression compared with normal lung tissues
- ▶ AD-214 has unique activity compared to other CXCR4 binders with no stem cell mobilisation
- ▶ AD-214 has been granted orphan drug status by US FDA for treatment of IPF
- ▶ Data recently published in ***Nature Scientific Reports (2018) 8:3212*** supports anti-CXCR4 i-body AD-214 in treatment of pulmonary fibrosis



SCIENTIFIC REPORTS

OPEN Anti-fibrotic Effects of CXCR4-Targeting i-body AD-114 in Preclinical Models of Pulmonary Fibrosis

Received: 8 November 2017
Accepted: 24 January 2018
Published online: 16 February 2018

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Market opportunity for IPF

Idiopathic Pulmonary Fibrosis (IPF) is an irreversible, unpredictable and incurable disease

THE STATISTICS

People living with IPF

300,000

People die from IPF every year

40,000

Median length of survival after IPF diagnosis

3.8 years



Causes



The cause is unknown but risk factors may include: smoking, environmental exposures, chronic viral infections, abnormal acid reflux and family history of the disease.

Pathology



Resultant scarring/honeycombing in the lung restricts breathing and oxygen exchange.

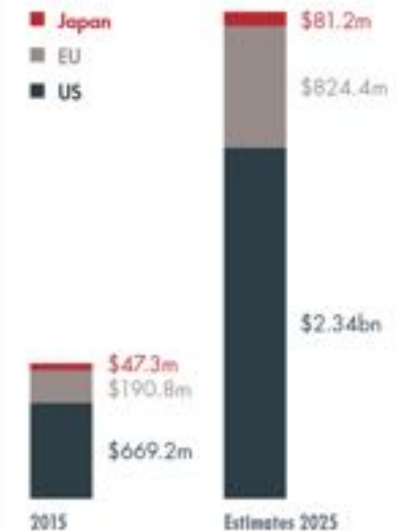
Current IPF treatments

Pirfenidone

Nintedanib



IPF Therapy Sales (US\$)



Source: GlobalData IPF Forecast 2016

Global market interest in fibrosis treatments

Fibrosis assets acquired at an early stage – typically based on Phase I results

Date	Company	Target	Acquired by	Deal value (US\$)	Deal commentary
Sep-15	Adheron Therapeutics	SDP051	Roche	\$105M upfront, plus \$475M in milestones	SDP-51 at end of Phase I for IPF
Aug-15	Promedior	PRM-151	BMS	\$150m upfront + \$1.25B	Phase II IPF and myelofibrosis
Nov-14	Galecto Biotech AB	TD139	BMS	\$444M	Option to acquire at end of clinical POC (no later than 60 days following Ph 1b for IPF completion)
Aug-14	Intermune	Esbriet / Pirfenidone	Roche	\$8.3B	Approval in Europe / Japan, phase III in the US
Jun-13	MicroDose Therapeutx	MMI0100	Teva Pharmaceuticals	\$40M upfront \$125M milestones	MMI0100 was in pre-clinical development
Mar-12	Stromedix	STX100	Biogen Idec	\$75M upfront \$487.5M milestones	End of phase I for IPF
Jul-11	Amira / BMS	BMS-986020	BMS	\$325M upfront \$150M milestones	End of phase I for IPF

Source: Medtrack Pharma Intelligence, Informa (all IPF deals since 2011)

IPF Phase II readouts generate \$1.4 billion market value

FibroGen

- ▶ (NASDAQ:FGEN)
- ▶ \$869 million added to its market cap on announcement (7 August 2017) of meeting primary endpoint in Phase IIb study
- ▶ Pamrevlumab (FG-3019) 103 patients 48 weeks

Galápagos

- ▶ (Euronext:GLPG; NASDAQ:GLPG)
- ▶ \$555 million added to market cap on announcement (9 August 2017) exploratory Phase IIa data
- ▶ FLORA trial had 23 IPF patients: 17 drug, 6 placebo for 12 weeks

AD-214 has broad application in treating fibrosis

AdAlta data shows that its lead anti-CXCR4 i-body candidate can improve fibrosis across a range of fibrotic diseases

- ▶ **LUNG:** Idiopathic Pulmonary Fibrosis
- ▶ **EYE:** Wet Age Related Macular Degeneration
- ▶ **LIVER:** NASH
- ▶ **SKIN:** Hypertrophic scar
- ▶ **KIDNEY:** Chronic Kidney Disease

AD-214 has broad anti-fibrotic application in several fibrotic diseases



Lung
IPF



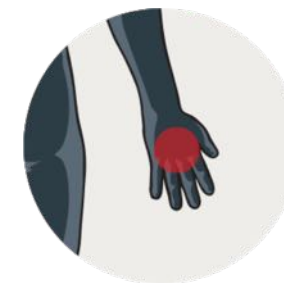
Eye
Wet-AMD & PVR



Liver
NASH & CIRRHOSIS



Kidney
RENAL FIBROSIS

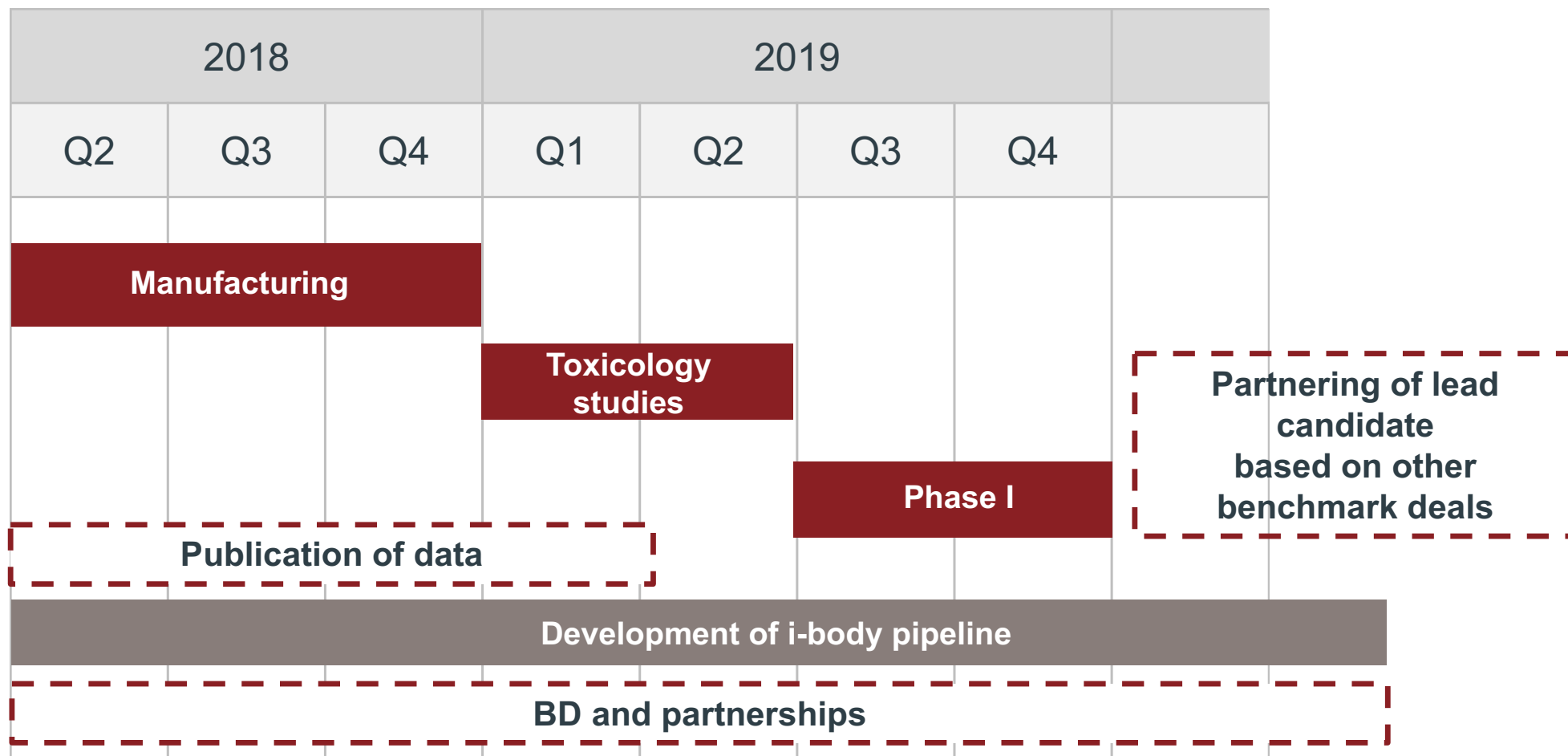


Skin
SCLERODERMA



Heart
CARDIAC FIBROSIS

AD-214 development: key milestones



i-body platform

1



Structure of **Shark** single domain antibody demonstrated unique long binding loop.

2




Two CDR loops are engineered onto the human NCAM scaffold. These enable specificity and binding affinity to a target.

A **human** protein was identified that is the same structure/shape as the shark single domain antibody. NCAM-Domain 1 is used as the backbone or scaffold protein of the i-body.

3

Each i-body has different CDR binding loops. The i-body library has 20 billion unique i-bodies.



 **AdAlta's i-body**, is the combination of a human protein that mimics the shape of the shark single domain antibody with unique long CDR binding loops.

i-bodies combine benefits of small molecules and conventional antibodies

	Small Molecule	Conventional Antibody	AdAlta i-body
High selectivity-specificity		●	●
Low toxicity: no off target effects		●	●
Cavity binding and new epitopes	●		●
Stability	●		●
Alternative routes of administration	●		●

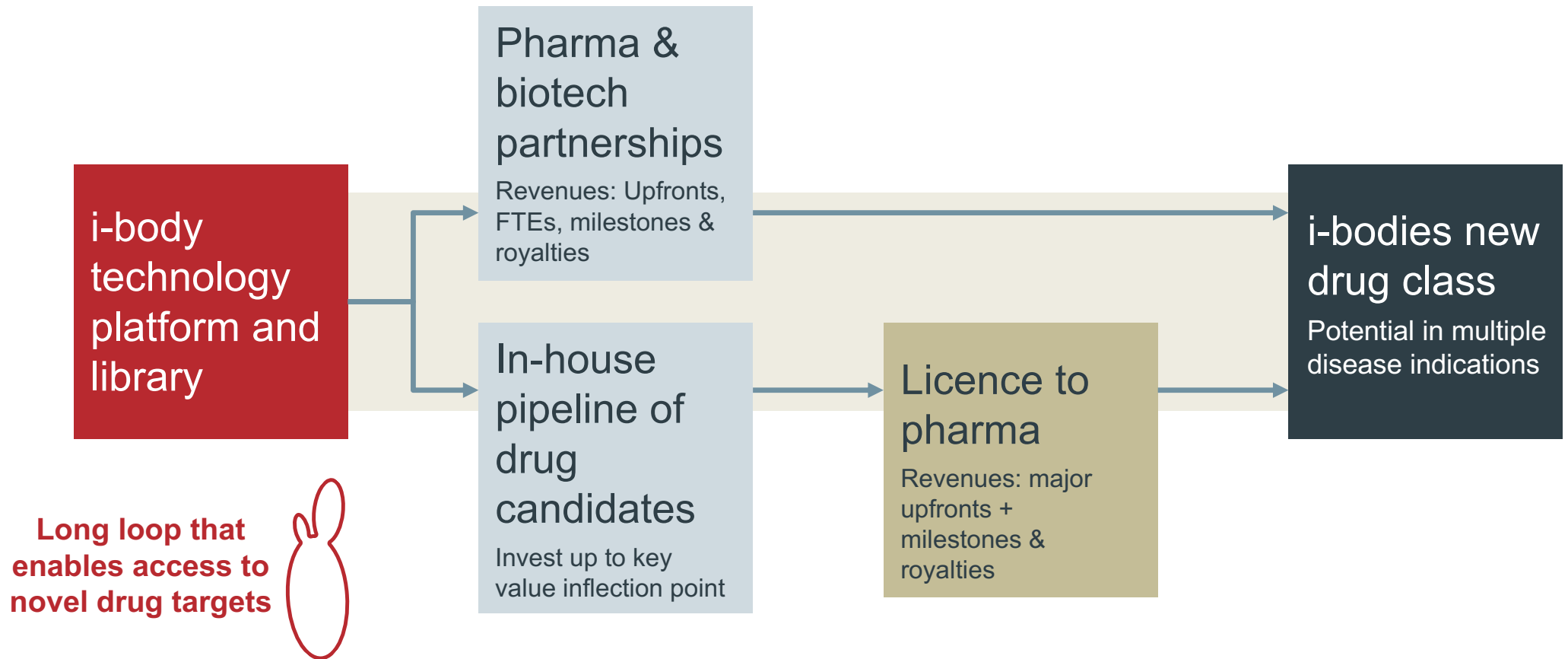
Long loop that enables access to novel drug targets



i-body human protein scaffold

i-bodies offer a new and potentially more effective approach to the treatment of a wide range of human diseases.

AdAlta business model – strategy to create value



Market benchmarks

Fibrosis lead AD-114



Sep-15 acquired by Roche
\$105m + \$475m milestones
phase I asset



Aug-15 acquired by BMS
\$150m + \$1.25b milestones
phase IIa asset

Galecto Biotech AB

Nov-14 acquired by BMS
\$444m
phase I asset

Next gen antibodies



April-16 with Abbvie
\$40m upfront + \$645m
milestones & royalties



Feb-18 with Seattle Genetics
\$30m upfront + \$1.2b
milestones & royalties



Feb-18 with Sanofi
€3.9b acquisition

GPCRs



Acquired Feb-15 by Sosei
\$400m Phase Ib asset + 7 pre-
clinical leads



Acquired by Celgene July-15
\$8b Ph III, Ph II and GPCR
platform



April-16 with Boehringer
€8m payment for Ph1 GPCR
nanobody + €125m milestones
& royalties

Significant achievements 2017/18

- ✓ Orphan Drug Designation (US FDA) of AdAlta i-body for treatment of IPF
- ✓ Completion of additional pre-clinical animal models in diseases of the lung, kidney, skin; strengthening broad anti-fibrotic data package of anti-CXCR4 i-body
- ✓ Publication of key data in *Scientific Reports* (a *Nature* publication)
- ✓ Presentation of AD-114 data at multiple fibrosis conferences including the IPF Summit
- ✓ License of Alzheimer's disease-specific shark antibodies to Crossbeta Biosciences for therapeutic and diagnostic development
- ✓ Completion of several non human primate studies demonstrating safety of AD-114 but also safety of i-body platform
- ✓ Key AU patent granted covering AD-214

Expected news flow

H1 2018

- ✓ Publication of AD-114 data in *Scientific Reports* demonstrating i-body application of pulmonary fibrosis with human tissue and animal model data
- ✓ Investor and analyst briefing detailing application of the i-body for the undruggable targets such as GPCRs and ion channels
- ▶ Commence manufacturing of AD-214

H2 2018

- ▶ Manufacturing update
- ▶ Publish i-body data in eye fibrosis
- ▶ Preliminary NHP tox data with AD-214

H1 2019

- ▶ 4 week NHP toxicology study

H2 2019

- ▶ Phase I SAD/MAD study with AD-214

AdAlta summary

- ▶ Initial focus on treating Idiopathic Pulmonary Fibrosis (IPF) and other fibrotic diseases - high unmet clinical need
- ▶ AD-214 has significant pre-clinical validation demonstrating broad anti-fibrotic and anti-inflammatory effects as well as safety
- ▶ AD-214 orphan drug designation with FDA for treatment of IPF
- ▶ Powerful proprietary technology platform to develop a pipeline of i-bodies for the treatment of a wide range of human diseases

Early commercialisation opportunity, with experienced management and Board to drive AD-214 development and secure technology platform partnerships / product licensing deals



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