



AdAlta  
next generation protein therapeutics

**i-bodies** – a new class of protein therapeutics  
to treat human disease

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**Sam Cobb, CEO and Managing Director**

s.cobb@adalta.com.au

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# Corporate and investment summary

- ▶ **AdAlta:** A drug discovery and development company focused on using its proprietary technology platform to generate a new class of protein therapeutics, known as i-bodies, for treating a wide range of human diseases
- ▶ **Investment highlights**
  - ▶ Initial focus on treating fibrosis – high unmet medical need
  - ▶ Advanced lead drug candidate AD-114 with significant pre-clinical validation
  - ▶ Early commercialisation potential
  - ▶ Team with extensive experience, track record of drug development and ability to deliver
- ▶ **IPO August 2016**
  - ▶ Raised \$10M with Offer oversubscribed
  - ▶ Pre-money valuation of \$15M (more than \$11M of funds applied to development to date)
  - ▶ IPO investment from Yuuwa Capital (\$3.1M) and institutional investors (\$3.0M)
  - ▶ IPO to fund phase I development of lead fibrosis drug and i-body pipeline

# Corporate Snapshot: 22<sup>nd</sup> August

- ▶ **ASX CODE:** 1AD
- ▶ **Market Cap (at IPO price):** \$25M
- ▶ **Cash:** ~\$11M
- ▶ **Shares on issue:** 100,000,016
- ▶ **Escrow:**
  - 83% of pre-IPO shares on issue
  - 27% 6 months from listing
  - 23% 24 months from listing
- ▶ **ESOP:**
  - 2,144,423 options on issue (1.4M escrowed 24 months)
  - ESOP capped at 5% of issued capital

Major Shareholders	%
Yuuwa Capital LP	54.06
HSBC Custody Nominees (Australia) Ltd	8.59
Citycastle Pty Ltd	5.31
La Trobe University	3.04
Robin Beaumont	1.84
Other shareholders	27.16
<b>Total</b>	<b>100%</b>

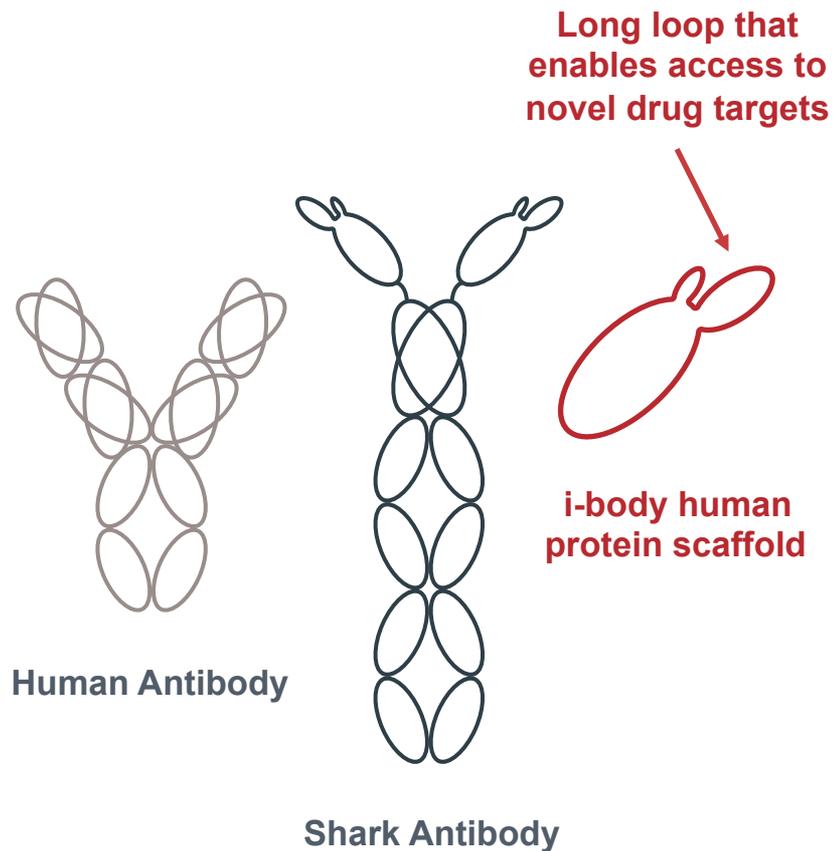
# i-body technology

AdAlta is developing a new technology platform that produces unique proteins known as i-bodies, that mimic the shape of shark antibody binding domain and engineers their key stability features into a human protein, for therapeutic intervention in disease.

The single domain antigen binding region of shark antibodies is extremely stable and has a long binding loop not present in either human or next generation antibodies.

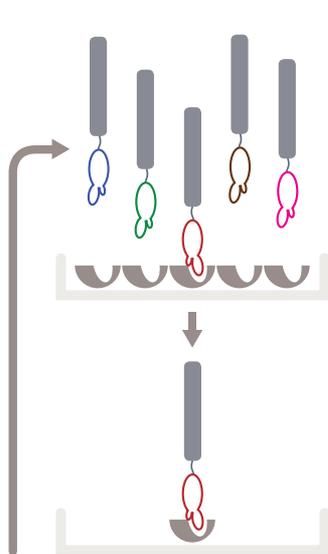
## Advantages of i-bodies

- ▶ High target specificity and high affinity for their target
- ▶ Small proteins; 10% the size of a typical human antibody
- ▶ Highly stable to proteases, high temperatures and low pH
- ▶ Long loop that can bind to a diverse range of therapeutically relevant targets including those that are difficult for current antibody therapies
- ▶ **Human protein** – reduced risk of immune response



# i-body drug discovery and manufacture

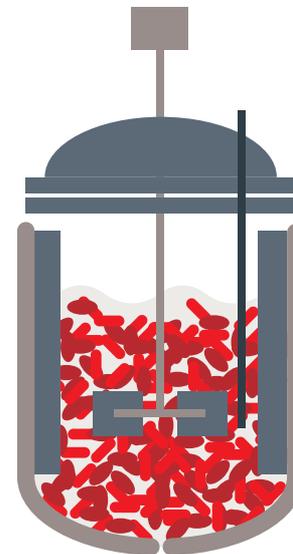
Large diverse synthetic library of 2 billion i-body protein compounds that can bind to a broad range of therapeutically relevant targets



i-body identified by rapid screening



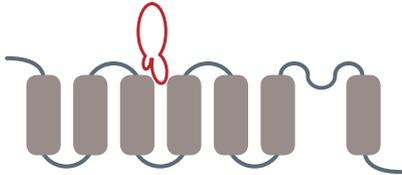
i-body affinity matured to enhance target binding and generate lead i-body candidate



Manufactured in microbial systems; more cost-effective and easier than conventional monoclonal antibodies. Potential for direct peptide synthesis

# i-body technology advantages

## Challenging targets



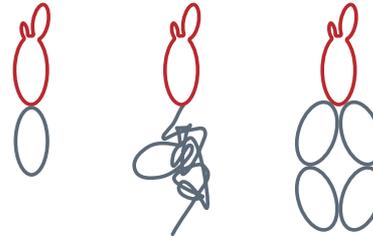
Because of the long binding loop of the i-body, that is lacking in traditional antibodies, i-bodies recognise and bind to a diverse range of different therapeutically-relevant targets including those that are difficult/intractable to access by current antibody therapies such as G-protein coupled receptors (GPCRs) and ion channels.

## Multiple delivery routes



The small physical size and stable properties of i-bodies provides advantages for tissue and organ penetration as well as multiple delivery routes.

## Customised half-life



As a result of their small size and exceptional stability i-bodies can serve as building blocks to engineer therapeutics with tailored pharmacokinetic properties.

## Multi formatting



Can easily engineer unique differentiated i-body products in a variety of formats including monospecific and bispecifics as well as i-body drug conjugates (IDCs), thus tailoring them for different therapeutic purposes.

# 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	●		●
Easy to manufacture	●		●
Speed & risk of development		●	●

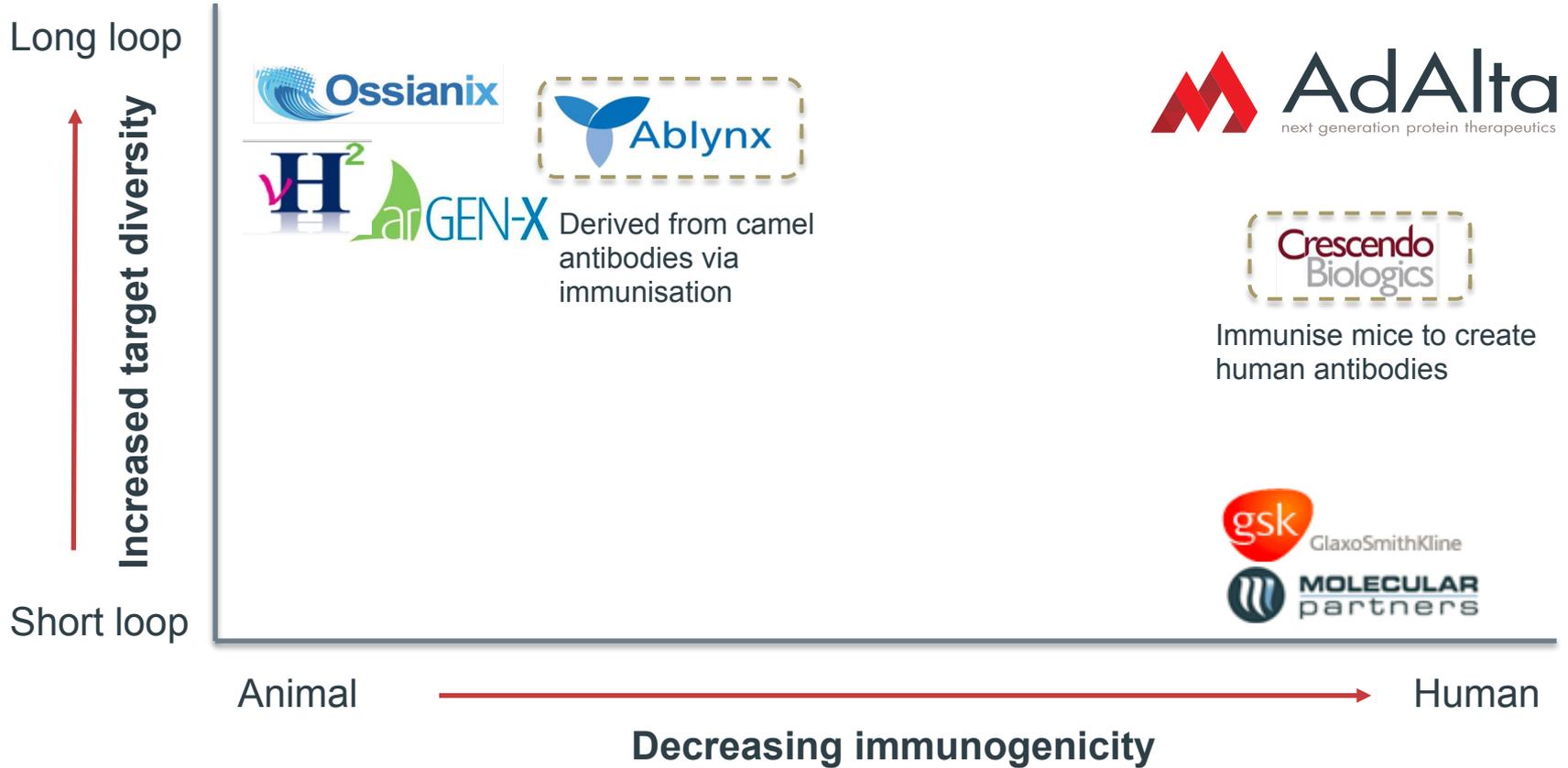
Long loop that enables access to novel drug targets



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.

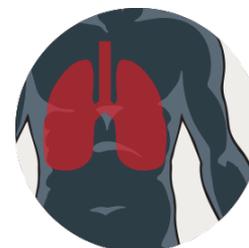
# i-body competitive differentiation



# Fibrosis: unmet medical need with multiple indications

- ▶ Developing i-bodies as improved therapies for the treatment of fibrosis
  - a condition that is prevalent in 45-50% of all diseases
- ▶ Fibrosis can occur in many tissues of the body as a result of inflammation or damage
  - it can result in scarring of vital organs causing irreparable damage and eventual organ failure
- ▶ AdAlta's initial focus is on lung fibrosis

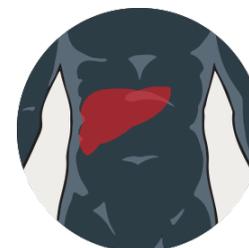
Collectively fibrosis represents a large unmet clinical need



**Lung**  
IPF



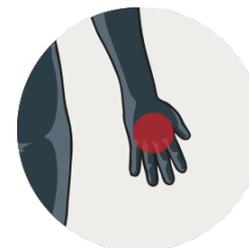
**Eye**  
Wet-AMD & PVR



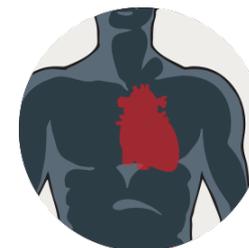
**Liver**  
NASH & CIRRHOSIS



**Kidney**  
RENAL FIBROSIS



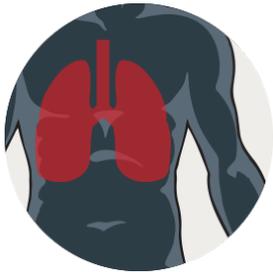
**Skin**  
SCLERODERMA



**Heart**  
CARDIAC FIBROSIS

# AD-114 lead program in Idiopathic Pulmonary Fibrosis (IPF)

- ▶ AD-114 is lead i-body candidate in pre-clinical development
  - Demonstrates both anti-fibrotic and anti-inflammatory activity in the lung
  - Important for arresting and modifying the disease and tackling the treatment of idiopathic pulmonary fibrosis (IPF); this is the primary indication



**Lung**

IPF

## **Idiopathic Pulmonary Fibrosis**

A chronic, highly lethal and rare disease.

50-70% mortality rate

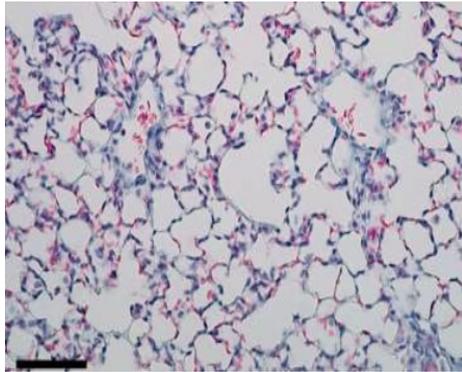
>135,000 people in US alone

World wide sales ~\$4.2B by 2020

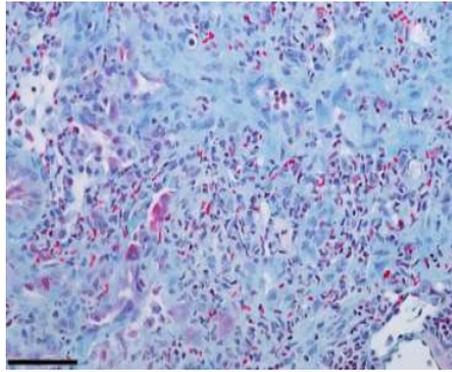
*Source: Evaluate Pharma, Orphan Drug Report 2015*

# AD-114 prevents lung fibrosis in disease models

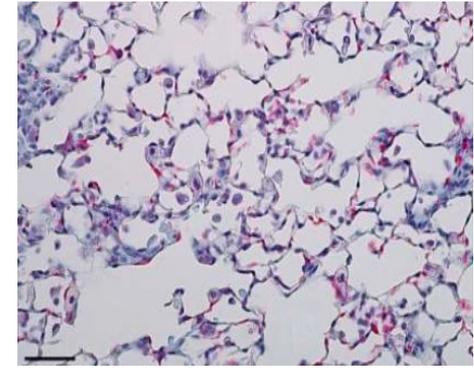
Extensive pre-clinical AD-114 studies have demonstrated positive *in vitro* (in the lab) and *in vivo* (in animals) data



**Normal  
lung tissue**



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



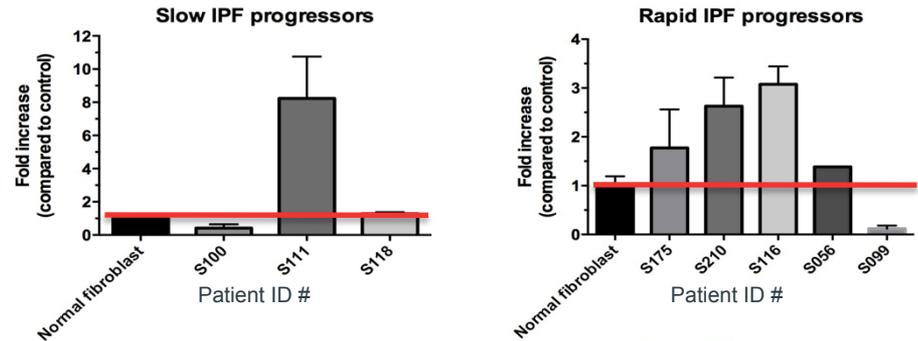
**IPF lung tissue + AD-114  
dosed for 21 days**  
(lung disease mouse model)

AD-114 reduces collagen content and inflammatory cell infiltration and demonstrates a similar architecture to that of the normal lung in the Bleomycin mouse model

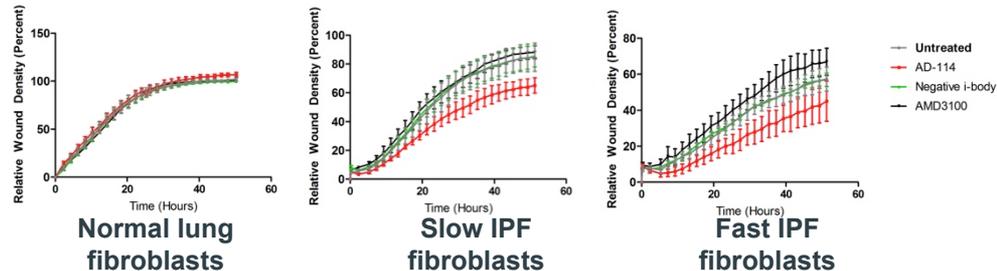
# AD-114 mechanism of action in idiopathic pulmonary fibrosis (IPF)

- ▶ AD-114 binds to the G protein-coupled receptor, CXCR4 (a chemokine receptor)
- ▶ CXCR4 has been demonstrated to play a central role in the development of fibrosis and is a novel disease pathway target in IPF
- ▶ Patients with rapid IPF disease progression express more CXCR4 compared to slow IPF progressors
- ▶ CXCR4 +ve cells (fibrocytes) significantly elevated in stable IPF patients, have been shown to be an independent predictor of early mortality
  - 7.5 months with more than 5% fibrocytes
  - 27 months with less than 5% fibrocytes
- ▶ AdAlta has shown AD-114 binds to the active edge of fast progressor patient tissue and in an animal model inhibits fibrocyte migration to the lungs

## CXCR4 expression increased in fast progressing IPF patient tissue



## AD-114 reduces fibroblast migration in both slow and fast IPF patient tissue



# AD-114 key advantages compared to existing IPF treatments

	MIGRATION	No effect on normal fibroblasts	Inhibits slow IPF progressors	Inhibits fast IPF progressors
Migration of normal & IPF patient fibroblasts <i>in vitro</i>	i-body AD-114	✓	✓	✓
	Nintedanib (Boehringer)	X	✓	✓
	Pirfenidone (Roche)	✓	X	X
	Other CXCR4 drug (Sanofi)	✓	X	X

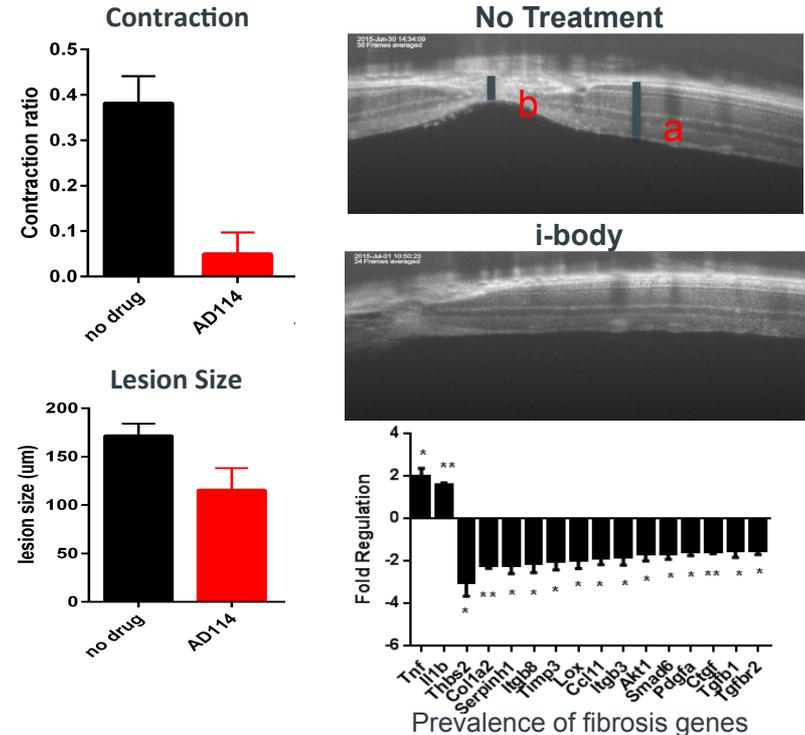
- ▶ Greater *in vitro* efficacy compared to the only approved therapies Nintedanib and Pirfenidone for IPF treatment (as detailed above)
  - Existing IPF treatments have limited efficacy; either no effect or slow down disease progression i.e. no cure
- ▶ Novel mechanism of action compared to other drugs targeting CXCR4
- ▶ Very specific for diseased tissue with effects only shown on human IPF tissue and no effects displayed on normal tissue nor any evidence of off target effects
- ▶ *In vitro* and *in vivo* pre-clinical data demonstrate that the AD-114 has both anti-fibrotic and anti-inflammatory effects

Novel mechanism of action for fibrosis treatment enabling a “first in class” therapy

# AD-114 prevents eye fibrosis and has potential for broad application

- ▶ AdAlta has shown that AD-114 has anti-fibrotic effects in treating fibrosis of the:
  - Lung; this is the **initial indication**
  - Eye; pursuing this as an additional indication (with NHMRC grant support)
- ▶ AdAlta aims to broaden the application of AD-114 to other fibrosis indications, including demonstrating therapeutic application of fibrosis diseases of the liver, skin, kidney and heart

## AD-114 reduces contraction and lesion size in eye fibrosis mouse model



# Antibody market



Source: *mAbs* (2016), 8:2, 197-204 and *mAbs* (2015), 7:1, 9-14

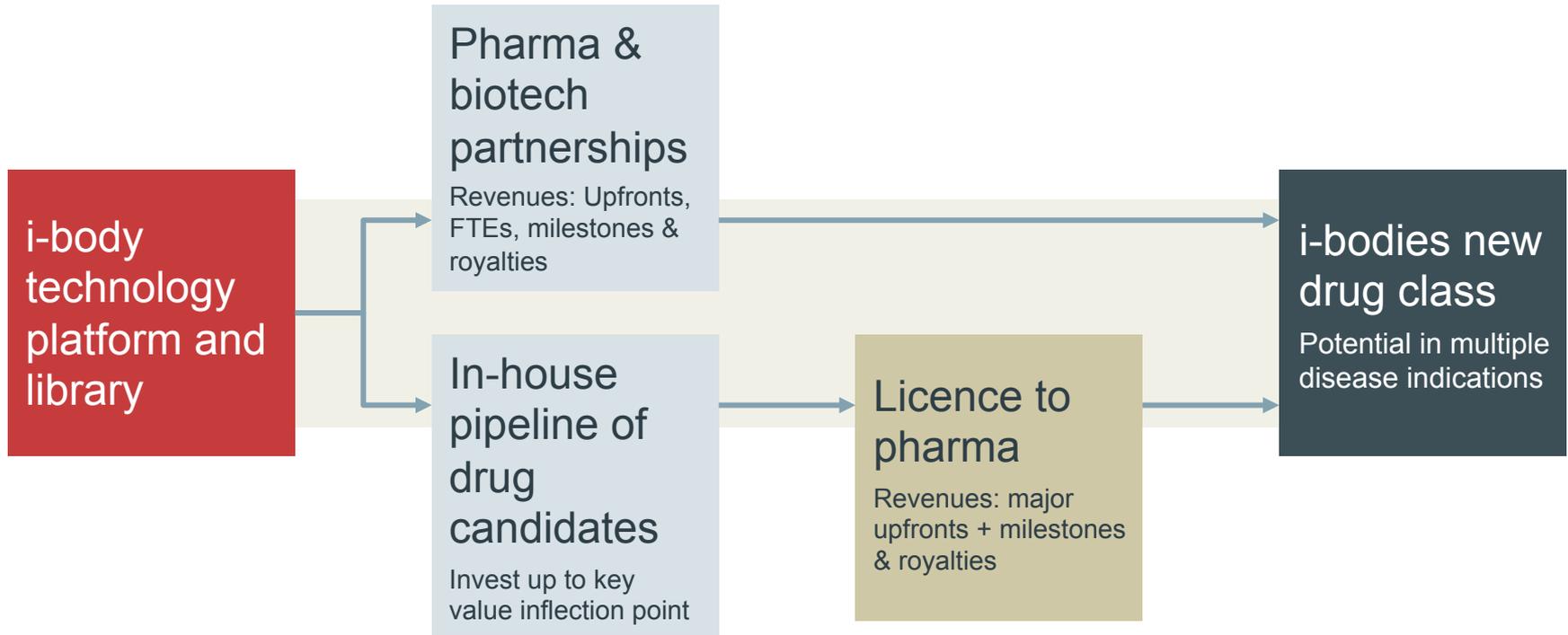
# Global market interest in fibrosis treatments

Recent transactions confirm that big pharma are actively acquiring fibrosis assets 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)

# AdAlta business model – strategy to create value



# Market benchmarks

## Fibrosis lead AD-114



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



PRM-151 exclusive license  
Aug-15 by BMS  
\$150m + \$1.25b milestones  
phase IIa asset

**Galecto Biotech AB**

Option to acquire Nov-14 by  
BMS \$444m milestones  
phase I asset

## Next gen antibodies



IPO Jul-14 on Euronext  
€40m raised  
phase Ib assets



Licence Dec-13 with Roche  
CHF55m + CHF1b milestones  
DARP-in platform



Licence deal Sep-13 with  
Abbvie  
\$175m + \$665m+ milestones  
phase IIa asset

## GPCRs



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



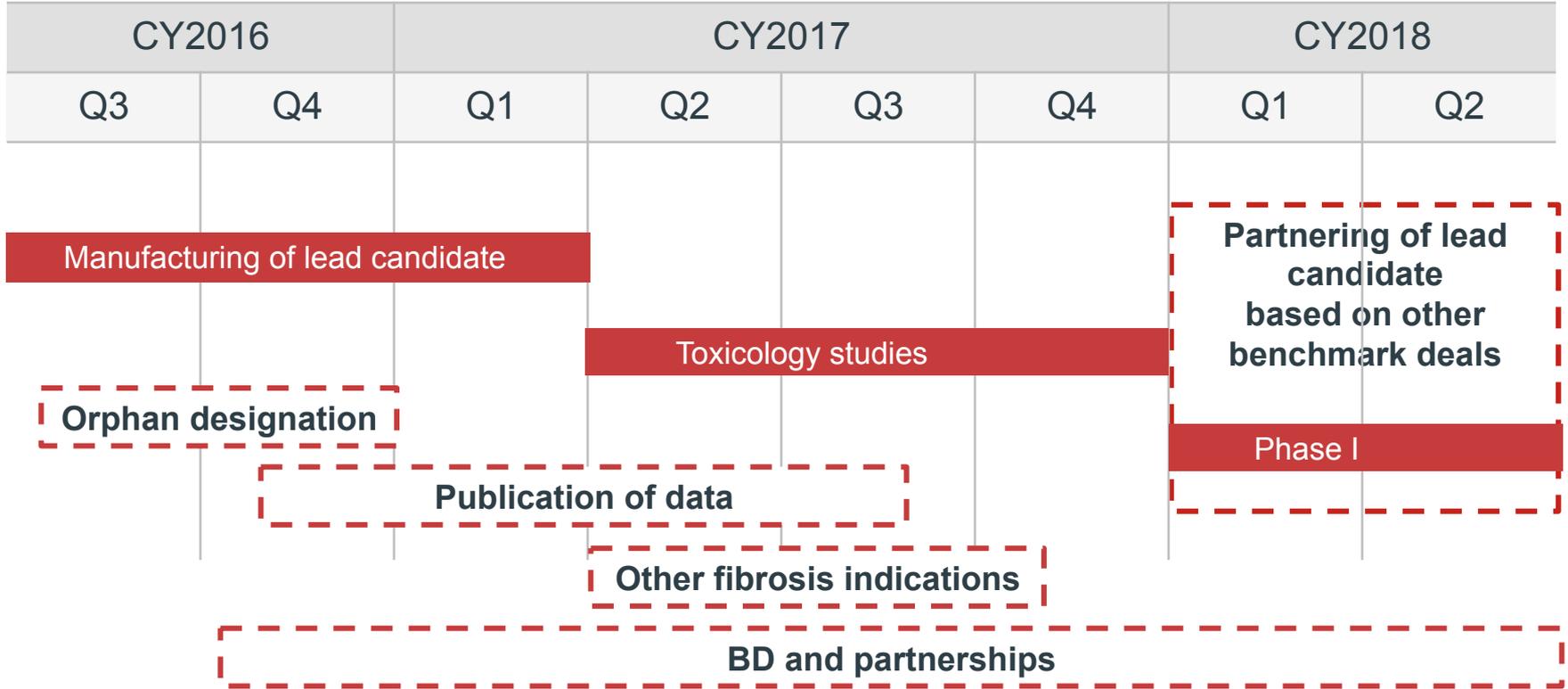
Acquired by Celgene July-15  
\$8b Ph III, Ph II and GPCR  
platform

# Strong intellectual property protection

- ▶ AdAlta has a strong portfolio of worldwide granted patents and applications that protect both the i-body technology platform and its i-body drug candidates
- ▶ **Platform protection**
  - AdAlta's granted patents specifically cover a method of modifying a number of human proteins called I-SET domains to include features of shark single domain antibodies; this modified protein is called an i-body
  - This patent family is granted worldwide: US, Europe, Japan, Canada and Australia
- ▶ **Product protection**
  - AdAlta's lead drug candidate AD-114 is covered by a patent application that covers the novel composition of matter
  - Industry standard practice for each new i-body product



# AD-114 development: key milestones



# Expected newsflow next 18 months

- Q3 2016
  - ▶ Orphan Drug Designation (US FDA)
  - ▶ Commence manufacturing of material for toxicology testing
  - ▶ Presentation at Discovery on Target, Boston
- Q4 2016
  - ▶ Additional AD-114 IPF fibrosis data
  - ▶ Hypertrophic scarring animal results for AD-114
  - ▶ Completion of evaluation of AD-114 with IPF clinicians Alfred Hospital
- H1 2017
  - ▶ Presentation at Biotech Showcase, San Francisco
  - ▶ Data available from AD-114 NASH animal studies
  - ▶ Manufactured material for toxicology testing available
- H2 2017
  - ▶ Eye fibrosis additional data, funded by NHMRC development grant
  - ▶ Completion of other pre-clinical study animal models of AD-114
  - ▶ Initial Kidney/Heart data available for AD-114
  - ▶ AD-114 toxicology results

# 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



## **Dr Mick Foley: Founding CSO**

Expert in phage display

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



## **Liddy McCall & Dr James Williams: Yuuwa Capital Directors**

Founders and investment Directors of Yuuwa Capital

Founders of iCeutica Inc (acquired 2011) and Dimerix Limited



## **Dr Paul MacLeman: Chairman**

Managing Director of a ASX listed IDT Australia Ltd

Founded biologics companies, experienced ASX listed executive



Directors of several Australian biotech and Agritech companies

Multiple FDA, CE Mark and TGA approvals

# Scientific Advisory Board

Internationally recognised with proven track record of drug development



## **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



## **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

# AdAlta investment summary

- ▶ Powerful proprietary technology platform to develop a pipeline of i-bodies for the treatment of a wide range of human diseases
- ▶ Initial focus on treating Idiopathic Pulmonary Fibrosis and other fibrotic diseases - high unmet clinical need
- ▶ Advanced lead candidate with significant pre-clinical validation of AD-114 demonstrating anti-fibrotic and anti-inflammatory effects
- ▶ Early commercialisation opportunity
- ▶ Experienced Management and Board to drive AD-114 development and secure technology platform partnerships and product licensing deals
- ▶ IPO August 2016 raised \$10M to meet major milestones: clinical trials of AD-114 in fibrosis and development of i-body pipeline