AdAlta
next generation protein therapeutics

ASX Release

AdAlta investor and analyst briefing presentation material

MELBOURNE Australia 2 February 2018: AdAlta Limited (ASX: 1AD), the biotechnology company advancing AD-114 to the clinic is pleased to release the material that will be presented in Melbourne today at a special briefing for investors and analysts on the i-body platform.

Speakers and topics on the agenda at the symposium include:

- Dr Bianca Odgen, Portfolio Manager, Platinum Asset Management
    - *Drug discovery, next generation antibodies: the landscape, the problems and the solutions*
- Professor Carol Pollock, Professor of Medicine University of Sydney
    - *Ion Channels: what is an ion channel and the drug discovery opportunity for the treatment of fibrosis*
- Associate Professor Mick Foley, Chief Scientific Officer AdAlta
    - *GPCRs: unique pharmacology of the i-body and what this means therapeutically*
- A closing panel chaired by Anthony Brown, WG Partners, including Dr Brian Richardson, Dr John Westwick and Dr Robert Peach
    - *Development of drugs that target GPCRs and ion channels: the commercial opportunity and therapeutic potential*
    - *Panel Discussion: clinical development of a drug and the need for novel drug discovery tools*
- Sam Cobb, CEO of AdAlta will provide an update on company activities
    - *Investor briefing AD-114 towards the clinic*

Highlights from the symposium will be made available during the coming week.

To find out more about AdAlta, contact Sam Cobb, CEO, Tel: (03) 9479 5159 or email enquiries@adalta.com.au.

Notes to editors

AdAlta Limited (ASX:1AD) is an Australian based drug development company headquartered in Melbourne.

The Company is focused on using its proprietary technology platform to generate i-bodies, a new class of protein therapeutics, with applications as therapeutic drugs to treat diseases.

AdAlta is developing its lead i-body candidate, AD-114, for the treatment of idiopathic pulmonary fibrosis (IPF) and other human fibrotic diseases, for which current therapies are sub-optimal and there is a high-unmet medical need. AD-114 has strong pre-clinical results for IPF, demonstrating both anti-fibrotic and anti-inflammatory activity in human lung tissue and indicating greater efficacy than existing approved IPF drugs.

The i-body is a human analogue of the antigen binding domain of the shark antibody, which combines the advantages of monoclonal antibodies (high target specificity and affinity) with the beneficial stability features of small molecules. In addition to stability, the i-body has a long binding loop that is a feature of shark antibodies not present in either human or next generation antibodies. This feature enables the i-body to recognise and bind to a diverse range of different therapeutically-relevant drug targets, including those that are difficult/intractable to access by current antibody therapies. These include clinically important targets such as G-protein coupled receptors (GPCRs) and ion channels.

AdAlta

next generation protein therapeutics

Analyst and investor briefing

i-body: a new class of protein therapeutics to treat human disease

ASX: 1AD

February 2018

AdAlta analyst & investor briefing 2018

- AdAlta's investor and analyst briefing aims to educate analysts and investors on our R&D technology platform, the i-body, as it relates to the science and the commercial opportunity to deliver value to shareholders
- AD-114 for idiopathic pulmonary fibrosis remains a core priority for the business
- AdAlta's focus is the completion of Phase I clinical studies and securing a global licensing deal for our lead i–body candidate
- Additional applications for the i-body platform and how it can be applied to undruggable targets such as GPCRs and Ion Channels will be discussed

AdAlta analyst & investor briefing 2018

- The advancement of our understanding around drug targets, and how they influence disease pathology, requires new technologies. Investor Dr Bianca Ogden will discuss the drug discovery landscape, the problems and the solutions.
- A number of diseases remain difficult to treat due to the complexity of the disease pathology. Some of the complex proteins thought to contribute to various diseases include G protein-coupled receptors (GPCR's) and Ion Channels, both representing large classes for potential therapeutic intervention. Expert researchers Prof. Carol Pollock and A/Prof. Mick Foley will discussion these potential drug targets and the opportunity for new treatments in fibrosis in further detail.
- AdAlta's world class SAB Dr John Westwick and Dr Brian Richardson and AdAlta's non-executive Director Dr Robert Peach will be available to answer specific questions and to discuss what it takes to get a drug to the clinic and a deal, chaired by analyst and IR expert Dr Anthony Brown.
- Sam Cobb, CEO of AdAlta will provide an investment update.

Agenda

	Bianca Ogden	Drug discovery, next generation antibodies: the landscape, the problems and the solutions Bianca will provide an overview of drug discovery and next generation antibodies, setting the scene in terms of the landscape, the problems and solutions.
	Carol Pollock	Ion Channels: what is an ion channel and the drug discovery opportunity for the treatment of fibrosis Carol will provide an overview of what an Ion Channel is and a number of Ion Channel target opportunities for the treatment of kidney fibrosis.
	Mick Foley	GPCRs: unique pharmacology of the i-body and what this means therapeutically Mick will provide a an overview of GPCR targets and provide details of the i-body platform and how it has been applied to the GPCR target CXCR4.

Agenda





Anthony Brown	**Development of drugs that target GPCRs and ion channels: the commercial opportunity and therapeutic potential** Anthony will discuss the commercial opportunity to selectively modulate intractable drug targets where standard antibody and small molecule approaches have failed.
PANEL DISCUSSION: Brian Richardson John Westwick Robert Peach	**Panel Discussion: clinical development of a drug and the need for novel drug discovery tools** The panel includes a number of drug development experts who have significant experience taking a drug from the research bench, through the clinic and providing to patients. The panel will discuss drug development including the current drug discovery landscape and where the opportunity lies in drugging the undruggable.
Sam Cobb	**AdAlta Investor Update** Sam will provide investors an update on AdAlta's lead candidate AD-114 and upcoming milestones

Dr Bianca Ogden

- Molecular biology was Bianca's first love before she discovered the joys and challenges of investing. After spending some time at Swiss pharmaceuticals company Novartis, researching new HIV drugs (one of which has been approved and in use today), Bianca went on to complete a PhD at UCL, investigating Kaposi's sarcoma-associated herpesvirus. She then migrated to Australia and joined Johnson & Johnson as a molecular biologist researching new drug targets in oncology.
- Bianca embarked on a career change in 2003 joining Platinum as an investment analyst. Her rich knowledge base in molecular biology, and first-hand insights into the pharmaceutical and biotech industries, give her a unique ability to delve deeply into the fundamentals of healthcare companies and identify those with a solid foundation in scientific research. Bianca has been the portfolio manager of the Platinum International Health Care Fund since 2007 and leads the healthcare sector team.

What comes after antibodies?

Paul Ehrlich (1854-1915)

Seitenkettentheorie

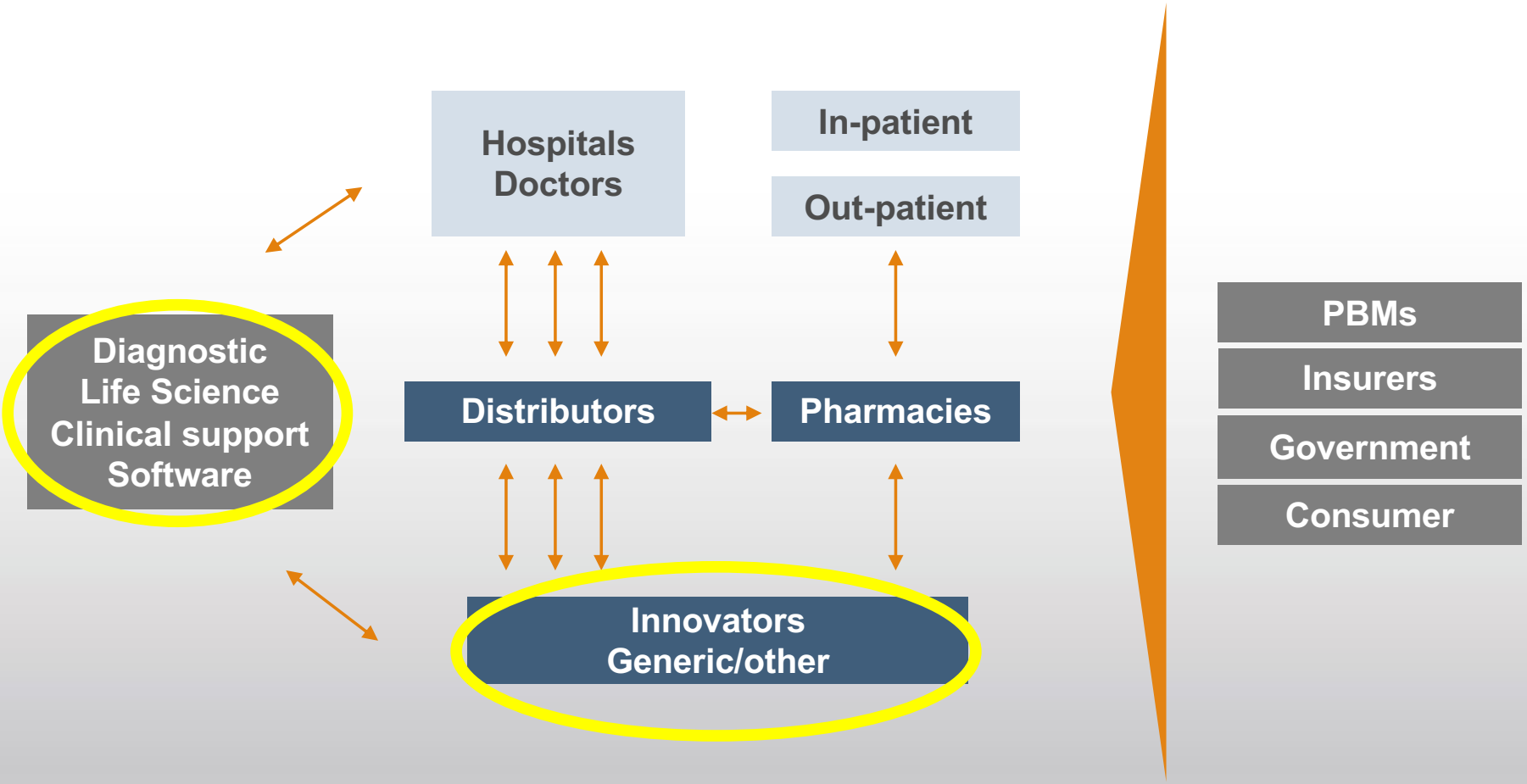
Cells have side-chains on their surface

Upon attack they grow more side chains

Side chains also break off and catch the toxins

Side chains that target toxins are “magic bullets”

Healthcare ecosystem we live in

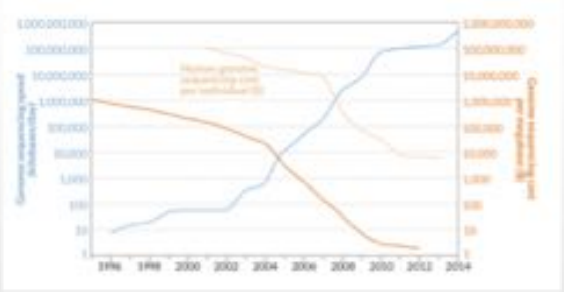


Platinum ASSET MANAGEMENT

Innovations

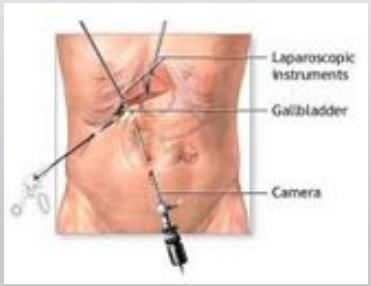
Antibodies as therapeutic modality

Targeted Therapy



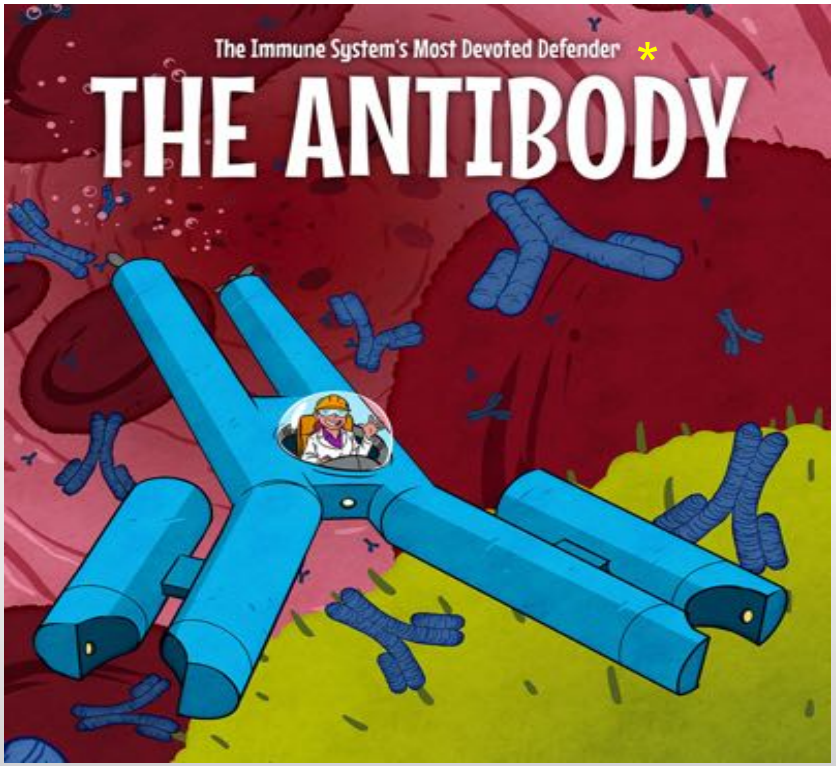
Sequencing of the genome

HIV combination therapy
HCV combination therapy



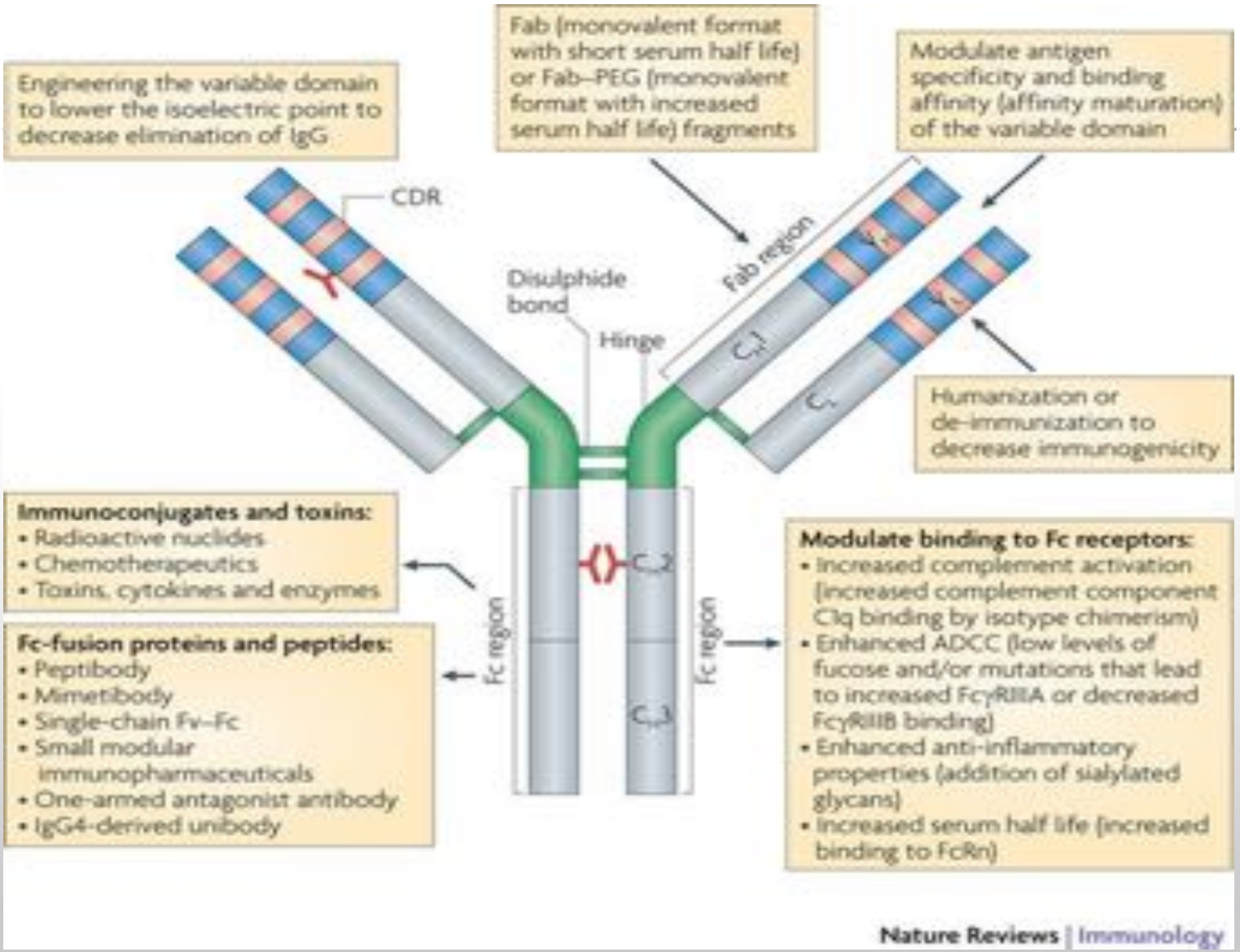
Minimally invasive surgery

The Antibody

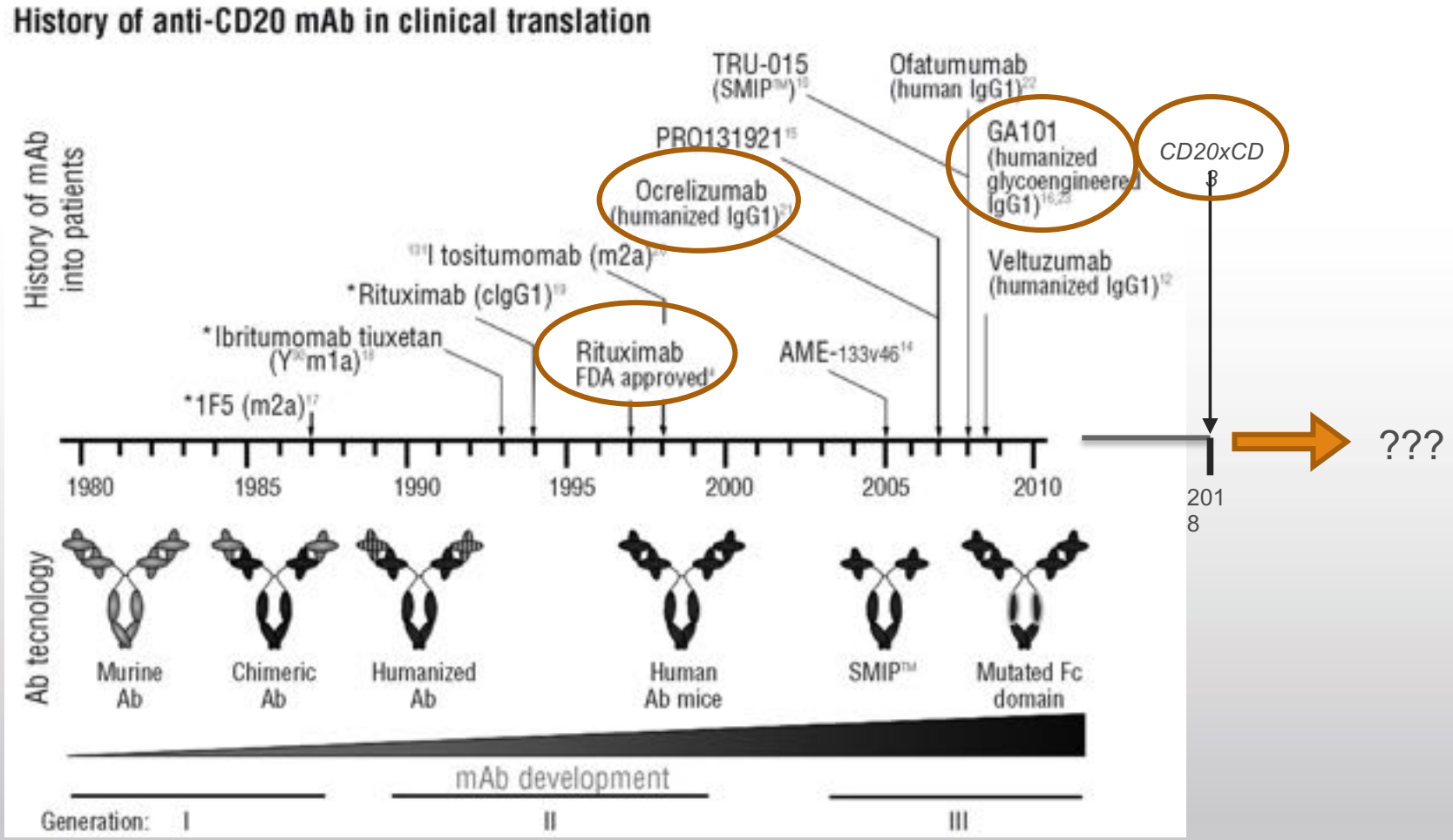


*The most devoted therapeutic modality

On average 2-3 antibodies have been approved each year over the past 25 years



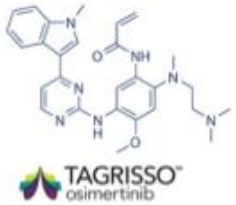
Anti-CD20



Platinum ASSET MANAGEMENT

Past, current and future innovations

Chemicals



Antibodies

Gene Therapy

RNAi

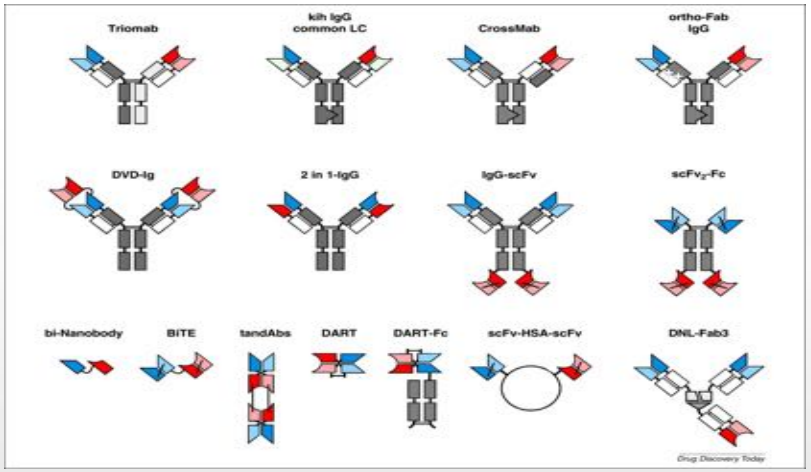
CRISPR/Cas

Modified T cells

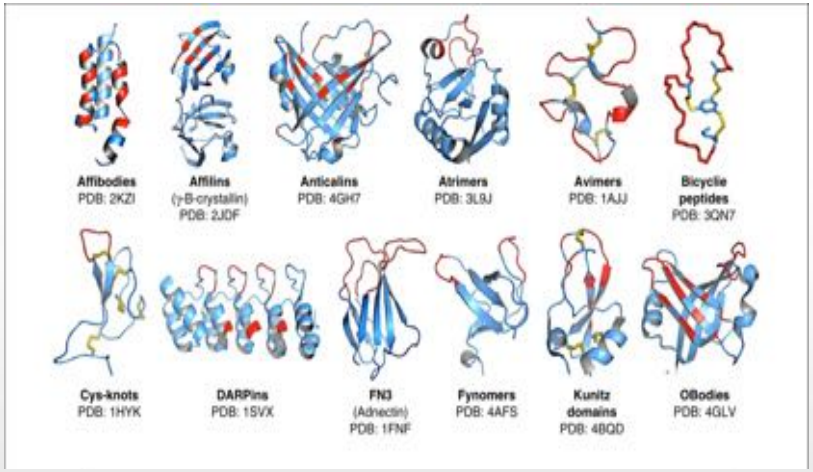
Platinum ASSET MANAGEMENT

Novel engineered “structures”

Ig-related

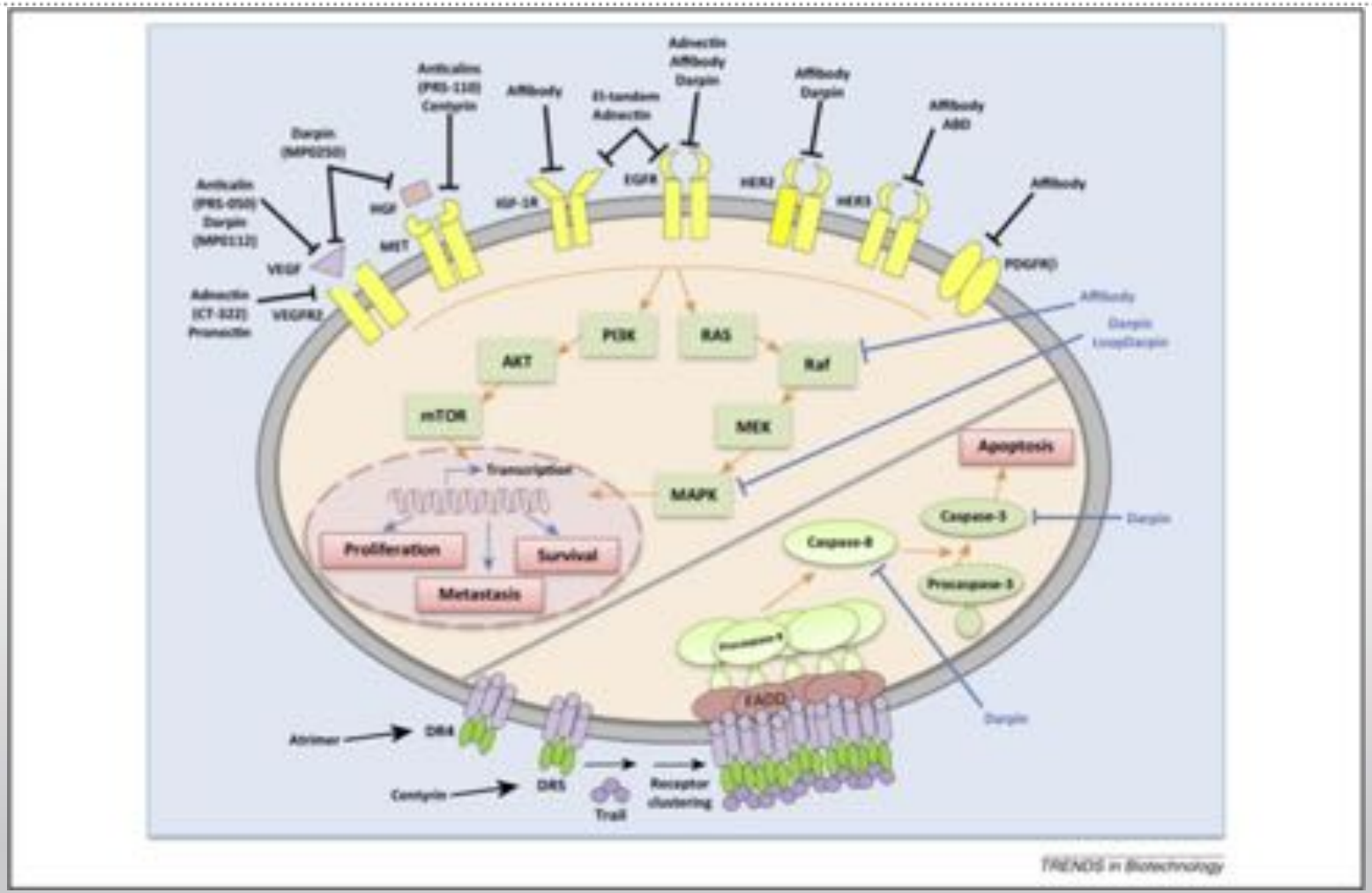


Non-Ig scaffolds



A Smorgasbord of choice

Target, data, strategy



Platinum
ASSET MANAGEMENT

Example Morphosys (E2.4b)

Celgene CD38 alliance
E70.8Mio upfront
E46.2Mio equity investment

GSK GM-CSF licensing deal
E22.5Mio upfront

Celgene CD38 alliance ends
Quiet 2 years with equity raising

Tremfya approval coming into focus
MOR208 (CD19) in DLBCL emerging
AD antibodies progressing

Platinum ASSET MANAGEMENT

Example Pieris ($342Mio)

AstraZeneca respiratory alliance (Il-4 Ra)
E57.5Mio upfront

Platinum ASSET MANAGEMENT

Ablynx (€3.9b)

Caplacizumab phase 3 data

M&A

Platinum ASSET MANAGEMENT

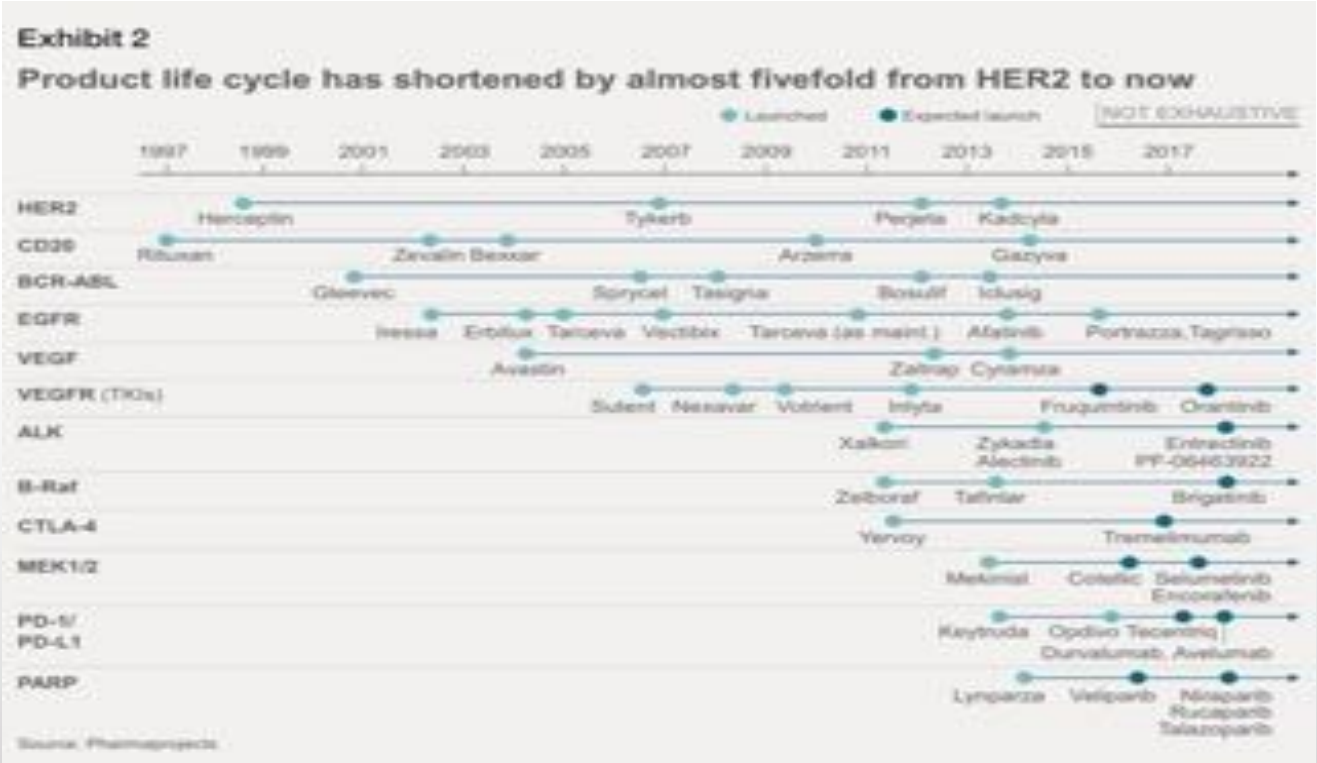
Partnerships are essential to the industry

February 1990; Roche and Genentech alliance

September 2003; Aventis (Sanofi) and Regeneron alliance (Sanofi holds 22.6%)

December 2016; Incyte and Merus alliance (Incyte holds 16.5%)

Desire for innovation is immense



….particularly as everyone is aiming at the same targets

Professor Carol Pollock

- Carol Pollock is an academic nephrologist with over 300 publications in basic research and clinical medicine.
- She is an inaugural Fellow of the Australian Academy of Health and Medical Sciences (2015),was conferred a Vice Chancellors Award for Excellence in Research Supervision (2012) and recognised as a ‘Distinguished Professor’ by the University of Sydney (2012). She was the 2014 recipient of the Ministerial Award for Excellence in Cardiovascular Research. She was Scientific Chairman of the 2013 World Congress of Nephrology. She is Chair of the NSW Cardiovascular Research Network and Chairs the Research Advisory Committee of the Australian and New Zealand Society of Nephrology.
- Health leadership roles include inaugural Chair of the NSW Agency for Clinical Innovation, immediate past Chair of the Clinical Excellence Commission, remaining as a director of both organisations till April 2016. She was Chair of the Northern Sydney Local Health District Board since its inception in 2011 till Dec 2016, was appointed to the Board of the Bureau of Health Information in April 2016 and assumed Chairmanship of the Bureau in November 2016.
- She is the Chair of Kidney Health Australia and Deputy Chair of the Board of the Australian Organ, Tissue and Transplant Authority.

THE UNIVERSITY OF SYDNEY

KOLLING Institute of Medical Research

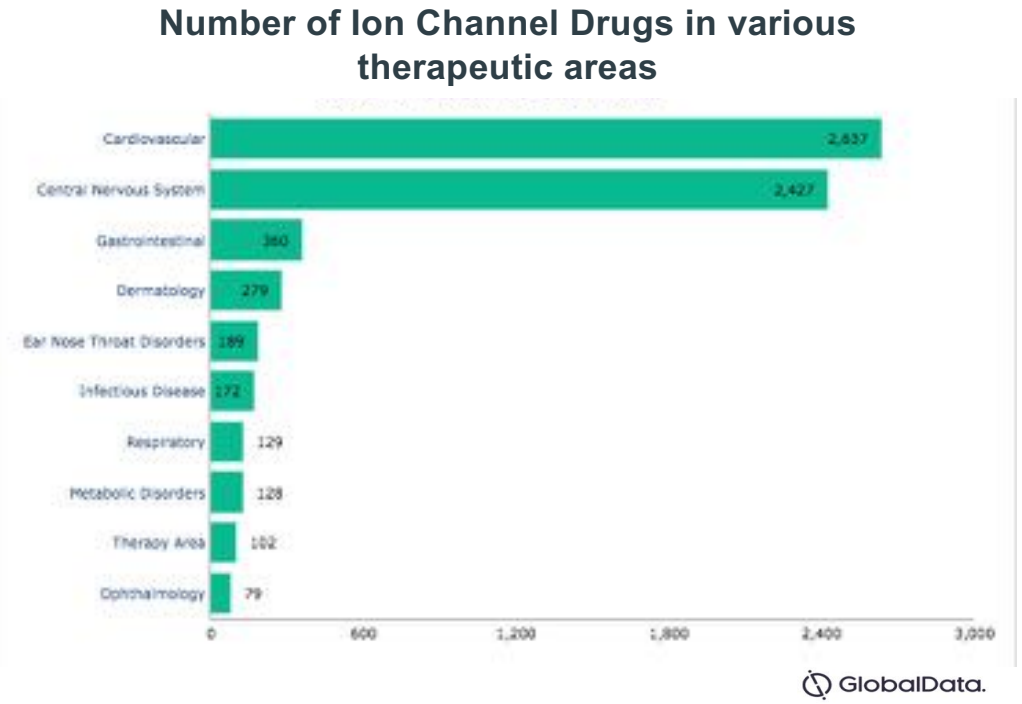
Ion Channels: what is an ion channel and the drug discovery opportunity for the treatment of fibrosis

Professor Carol Pollock

Royal North Shore Hospital,
Kolling Institute and University of Sydney Australia

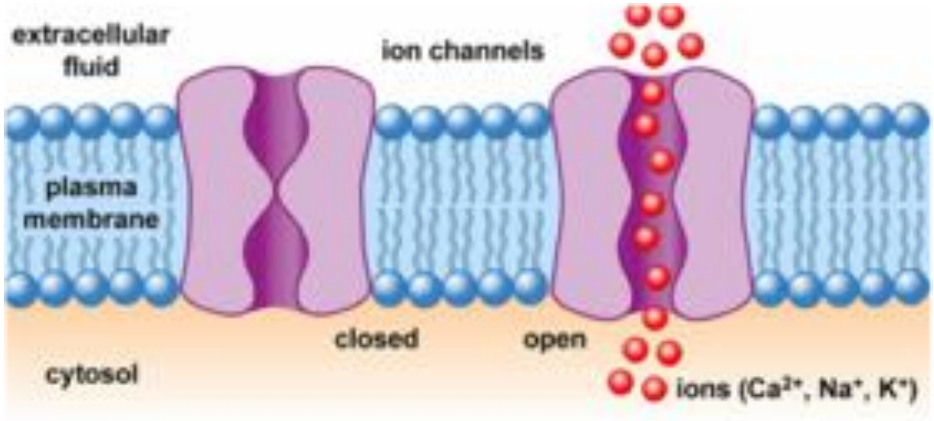
Ion Channels

- **Ion channels** are membrane proteins that allow ions to pass through the channel pore.
- The ion channel family is involved in almost all aspects of physiology and plays a critical role in diverse processes such as nerve and muscle relaxation, cognition, sensory transduction, regulation of blood pressure, and cell proliferation.
- Modulation of ion channels has been linked to a wide range of diseases including cardiac disorders, neurological indications, kidney failure and the perception of pain.



What is an Ion Channel?

- **Ion Channels** are transmembrane proteins that control the flow of ions between the intracellular and the extracellular environments.
- Ion Channels can be opened and shut in response to an electrical stimulus (voltage-gated) or binding of a drug compound (ligand-gated).
- Ion Channels are expressed by virtually all living cells and create a pathway for charged ions from dissolved salts including sodium, potassium, calcium, and chloride ions.

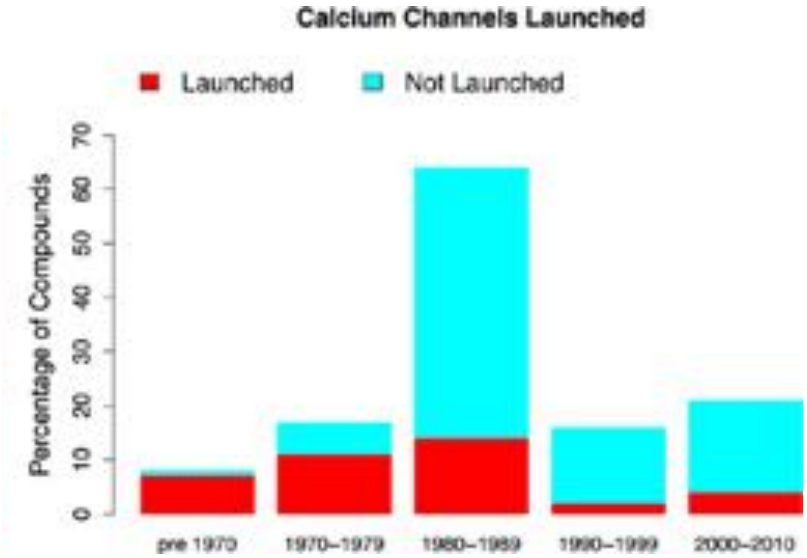


Translation to drugs difficult

- Most Ion Channel drugs came about by serendipity without an understanding around the mode of action or the precise target!
- Given a lack of understanding behind the early drugs it is not surprising that significant side effects emerged following approval, with approximately 10% of approved Ion Channel drugs being subsequently withdrawn from the market.

Withdrawn Ion Channel Drugs

Drug	Class	Date Approved	Date Withdrawn
Terodiline	Uninary Incontinence		1991
Posicor	Pain	1997	1998
Terfenadine	Antihistamine	1985	1998
Astemizole	Antihistamine		1999
Grepafloxacin	Antibiotic	1997	1999
Cisapride	treatment of gastroesophageal reflux		2000
Sparfloxacin	Antibiotic	1997	2000
Levomethadyl	treatment of Opiod dependence	1993	2003

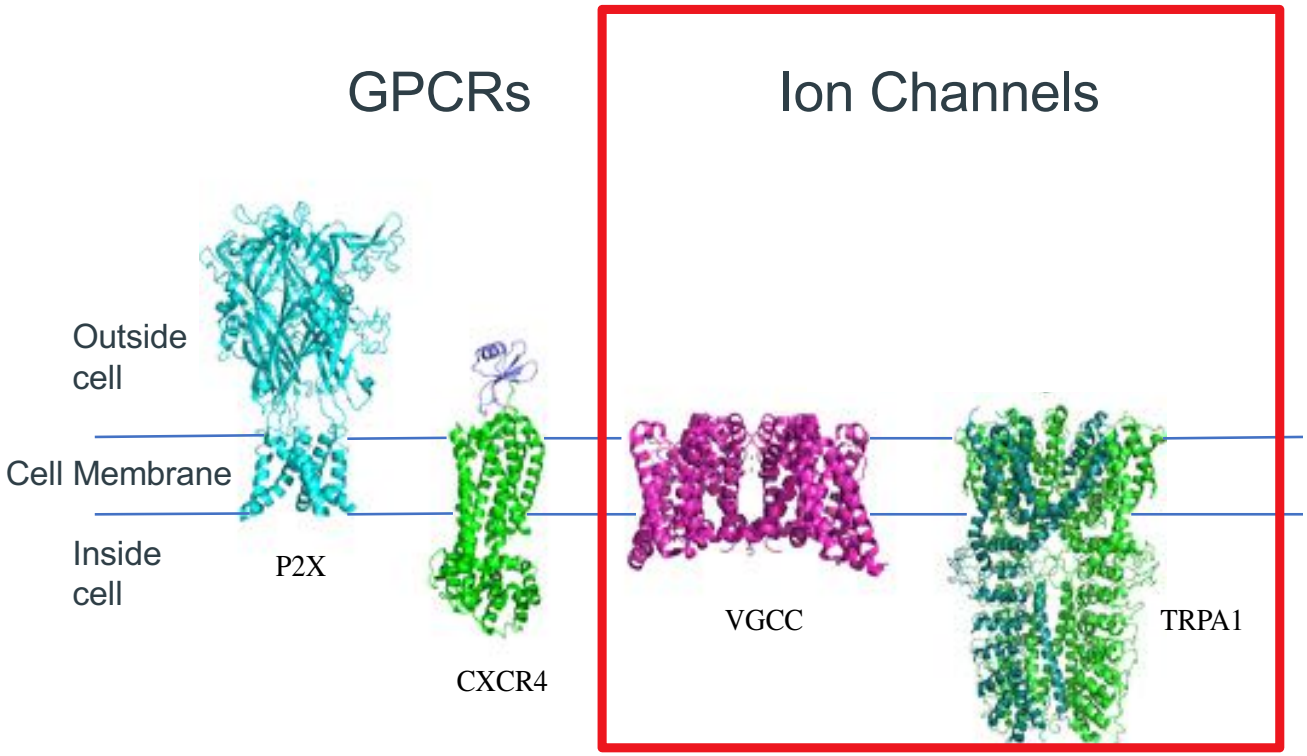


J. Med. Chem.2013, 56, 593−624

AdAlta

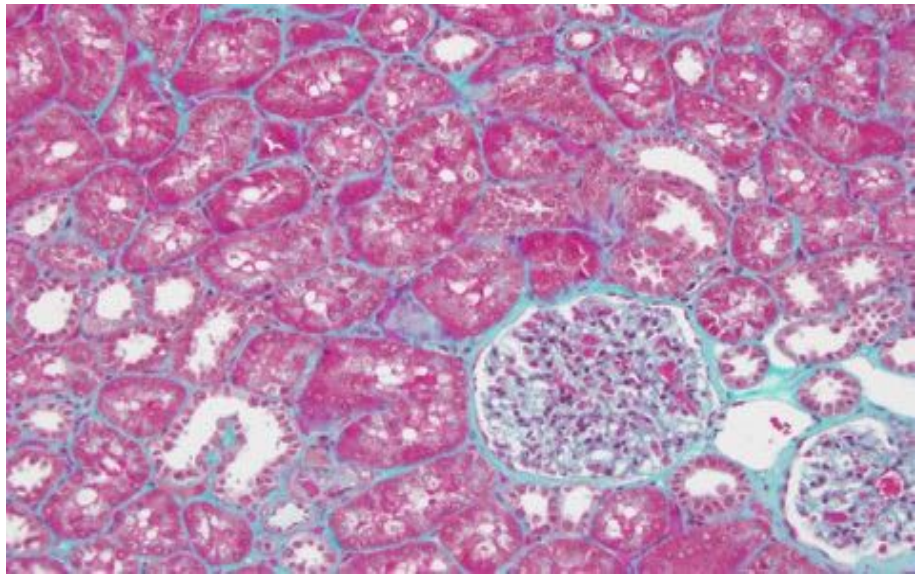
Why are Ion Channels difficult to drug?

- 40% of ion channels have no known ligands making drug discovery difficult.
- Reduced exposure of ion channel receptors on the cell surface makes it difficult for traditional antibodies to bind to them.
- Similarity between ion channel family members increases the risk of off target effects due to low selectivity of peptide/small molecule drugs.

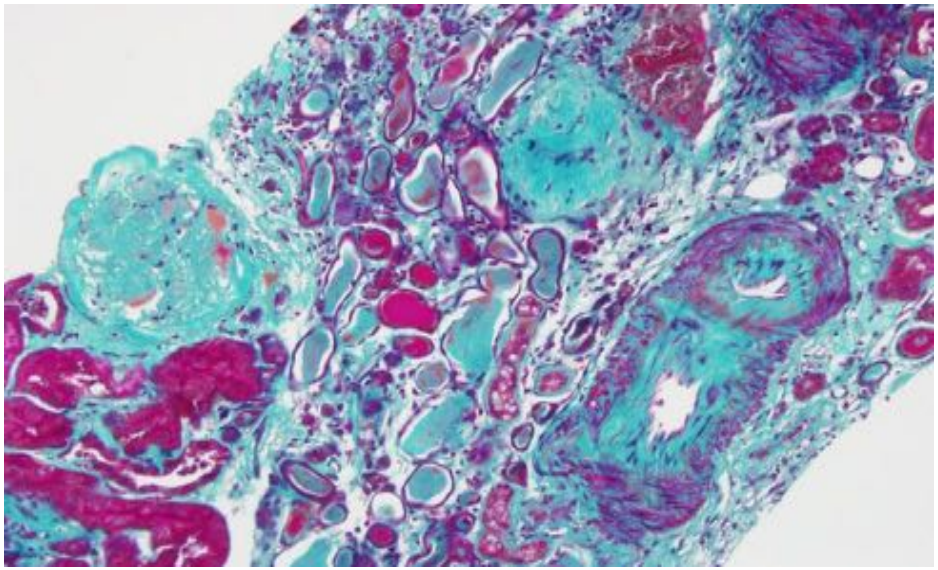


Kidney Fibrosis

Kidney fibrosis is seen in virtually all progressive kidney diseases including diabetic nephropathy, allograft nephropathy or aging

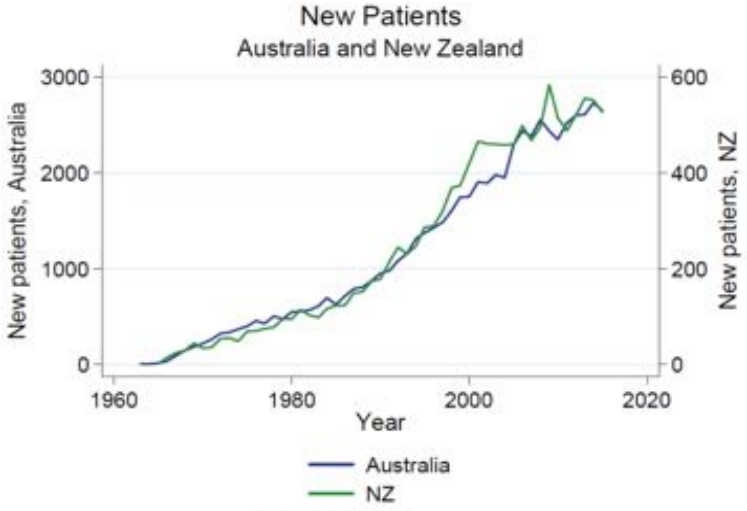


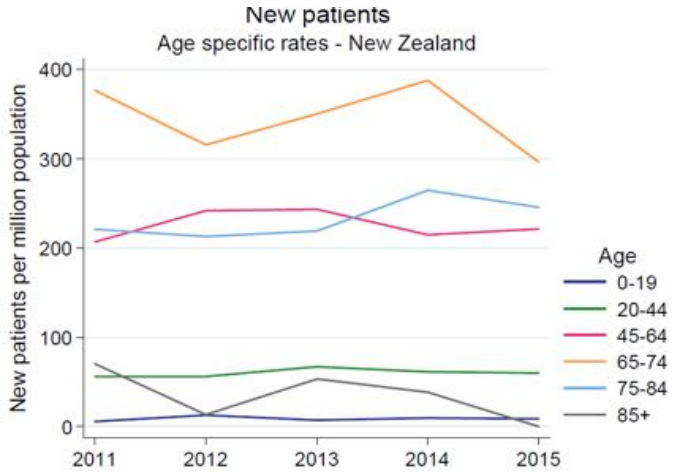
Normal Kidney

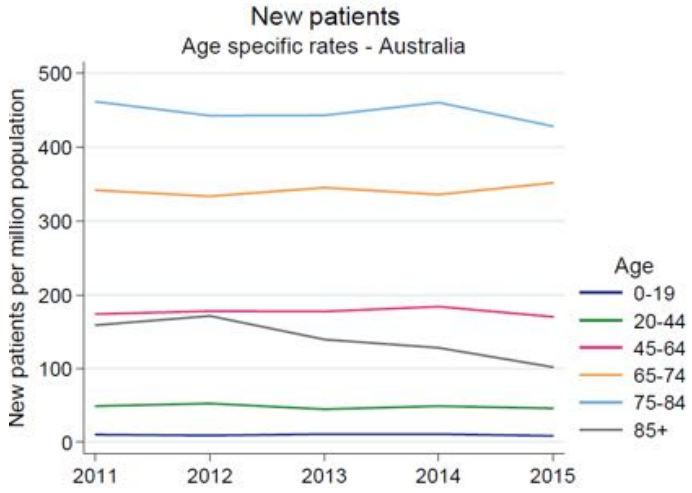


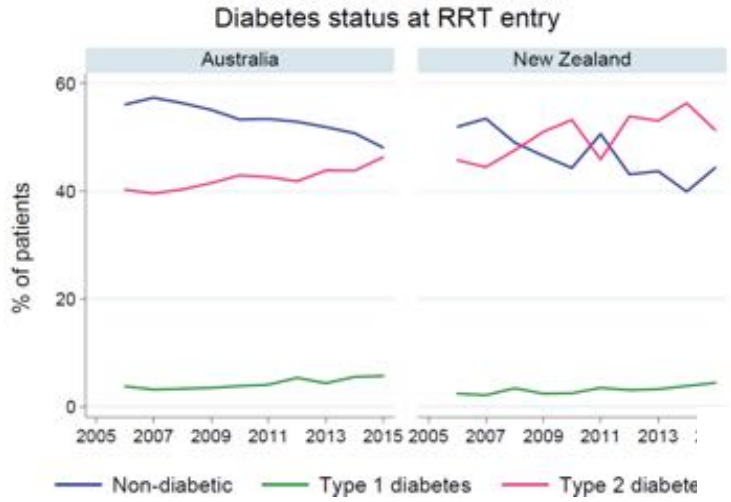
CKD

Trends in End Stage Kidney Disease in Australia and New Zealand









AdAlta

Estimated burden of diabetes in 2015

Table 3.1 *IDF Diabetes Atlas* global estimates, 2015 and 2040

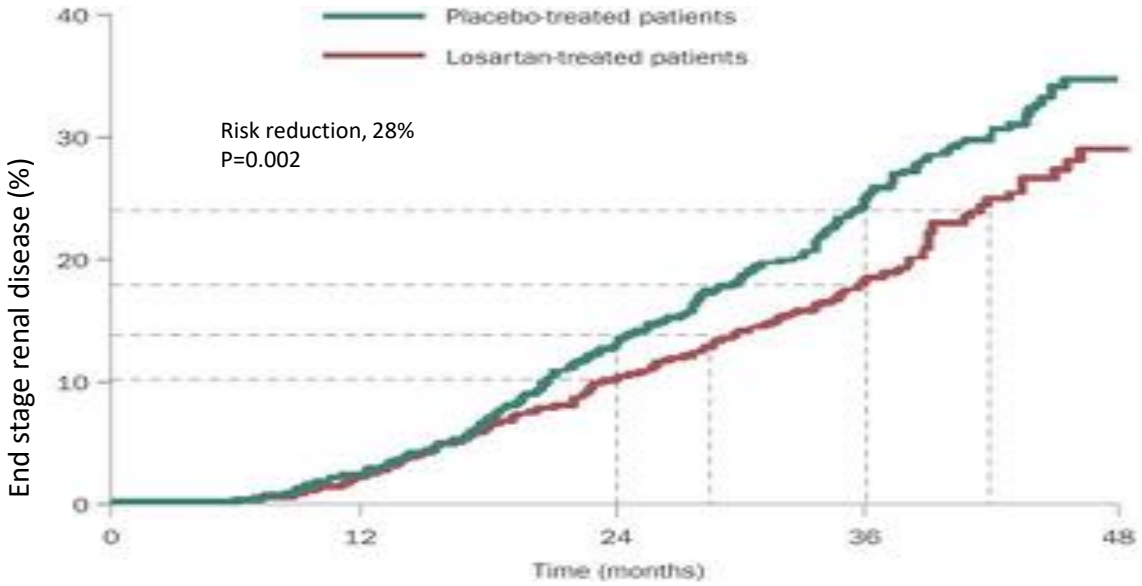
	2015	2040
Total world population	7.3 billion	9.0 billion
Adult population (20-79 years)	4.72 billion	6.16 billion
Child population (0-14 years)	1.92 billion	-
Diabetes (20-79 years)		
Global prevalence	8.8% (7.2-11.4%)	10.4% (8.5-13.5%)
Number of people with diabetes	415 million (340-536 million)	642 million (521-829 million)
Number of deaths due to diabetes	5.0 million	-
Health expenditure due to diabetes (20-79 years)		
Total health expenditure, PPP* 2015 USD	673 billion	802 billion
Hyperglycaemia in pregnancy (20-49 years)		
Proportion of live births affected	16.2%	-
Number of live births affected	20.9 million	-

IDF Diabetes Atlas · Seventh Edition

AdAlta

Requirement for novel therapies

- Existing therapies only mildly reduce end stage renal disease.
- A number of novel drugs and targets are in the clinic, but many have failed.
- Current high unmet therapeutic need with a growing burden due to the aging population and increasing incidence of diabetes.



Brenner B, et al. N Engl J Med 2001
Vilayur et al.Nat Rev Nephrol (2009)

Potassium channels and kidney fibrosis KCa3.1

- KCa3.1 is voltage-independent potassium channel which is activated by intracellular calcium.
- KCa3.1 regulates membrane potential and calcium signalling in various types of cells.
- KCa3.1-mediated Ca2+ influx is associated with inflammation, atherogenesis, and proliferation of
  - endothelial cells resulting in plaque instability
  - T lymphocytes
  - macrophages
  - fibroblasts

KCa3.1 and kidney fibrosis

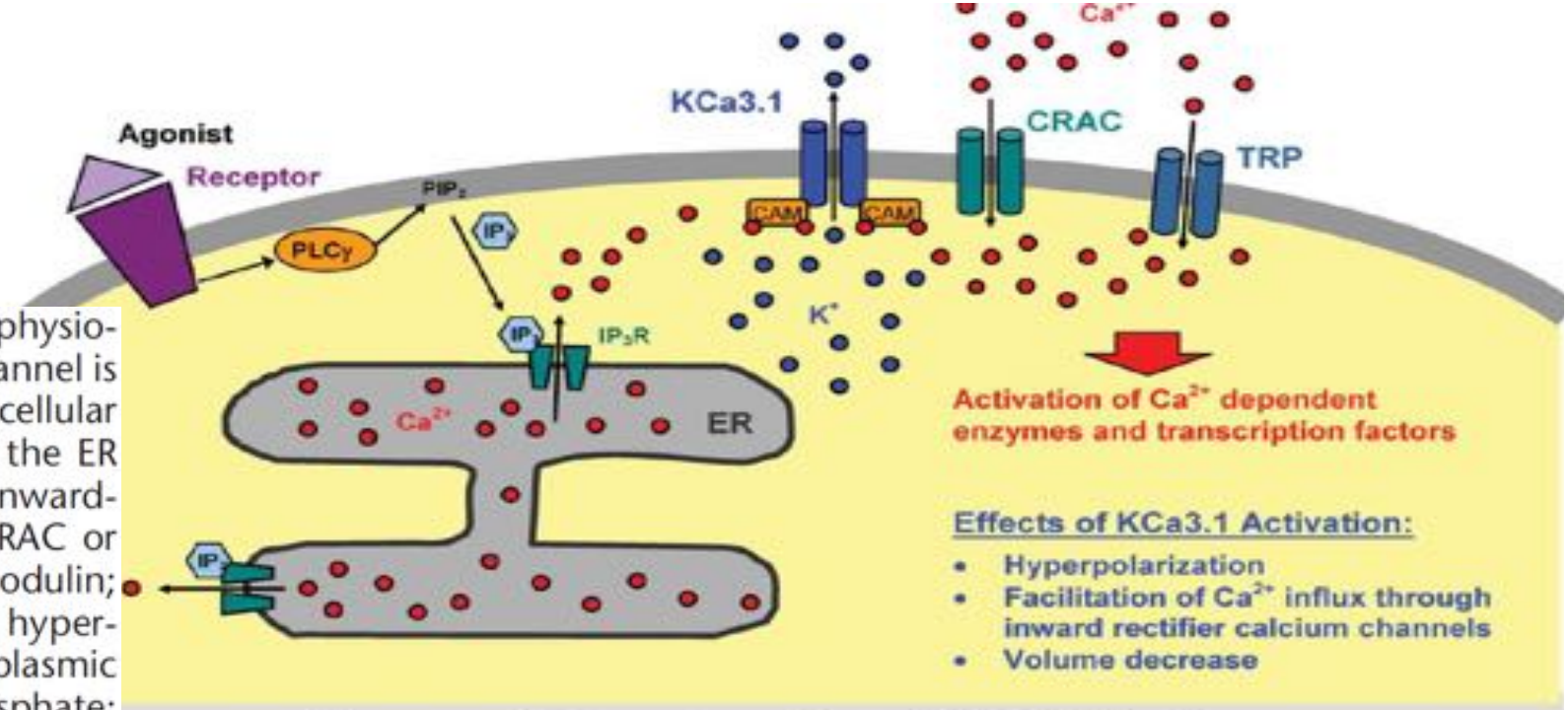


FIGURE 1. Cartoon of the physiological role of KCa3.1. The channel is activated by increases in intracellular Ca^{2+} after Ca^{2+} release from the ER and/or Ca^{2+} influx through inward-rectifier Ca^{2+} channels like CRAC or TRP channels. CAM, calmodulin; EDHF, endothelium derived hyperpolarizing factor; ER, endoplasmic reticulum; IP_3, inositol triphosphate; PLC, phospholipase C.

Tissue-specific Downstream Effects of KCa3.1 Activation:

Erythrocytes:
- Volume decrease

T cells:
- Ca^{2+} influx
- NFAT translocation
- Proliferation
- Cytokine secretion

Dedifferentiated VSMC, fibroblast, cancer cell:
- Ca^{2+} influx
- Proliferation
- Migration

Macrophages/microglia:
- Migration
- Oxidative burst

Vascular Endothelium:
- Hyperpolarization resulting in vasodilation (EDHF)

Secretory Epithelia (gut/lung):
- Salt and fluid secretion

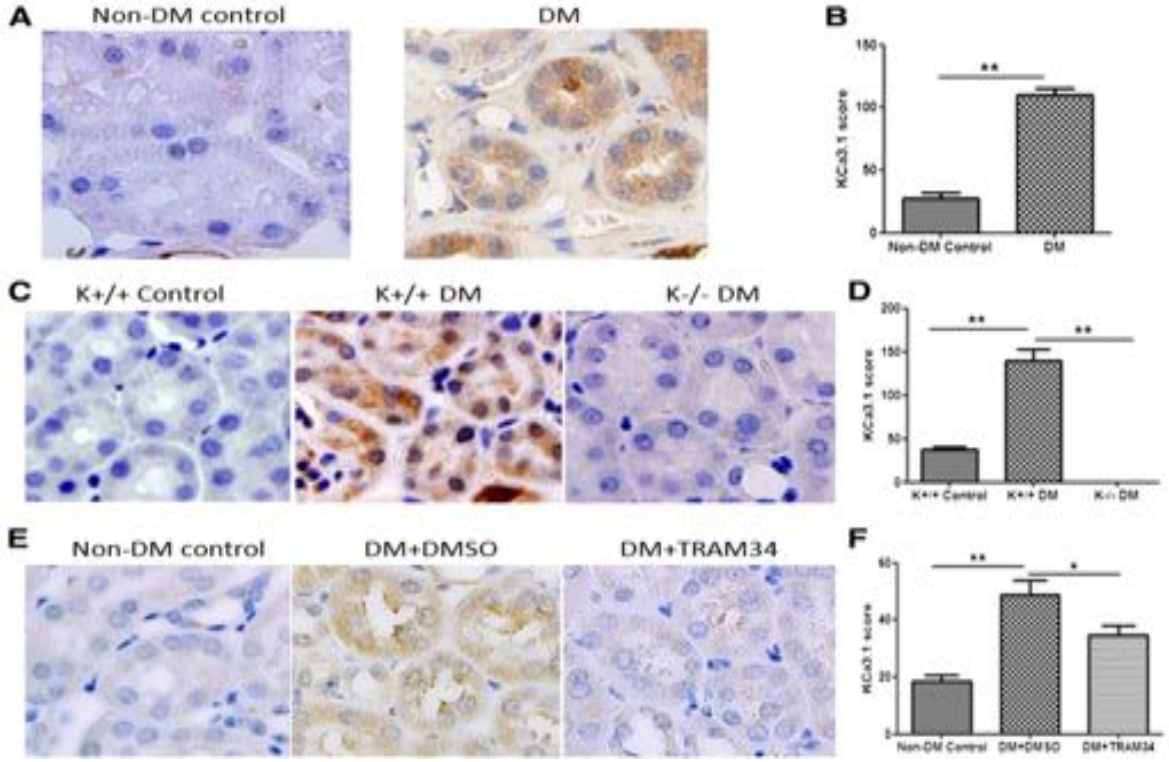
AdAlta

KCa3.1 blockade demonstrated effective in mouse model of fibrosis

Blockade of KCa3.1 Ameliorates Renal Fibrosis Through the TGF-β1/Smad Pathway in Diabetic Mice

DIABETES, VOL. 62, AUGUST 2013

Chunling Huang,[1,2] Sylvie Shen,[1] Qing Ma,[1] Jason Chen,[3] Anthony Gill,[3] Carol A. Pollock,[1] and Xin-Ming Chen[1]



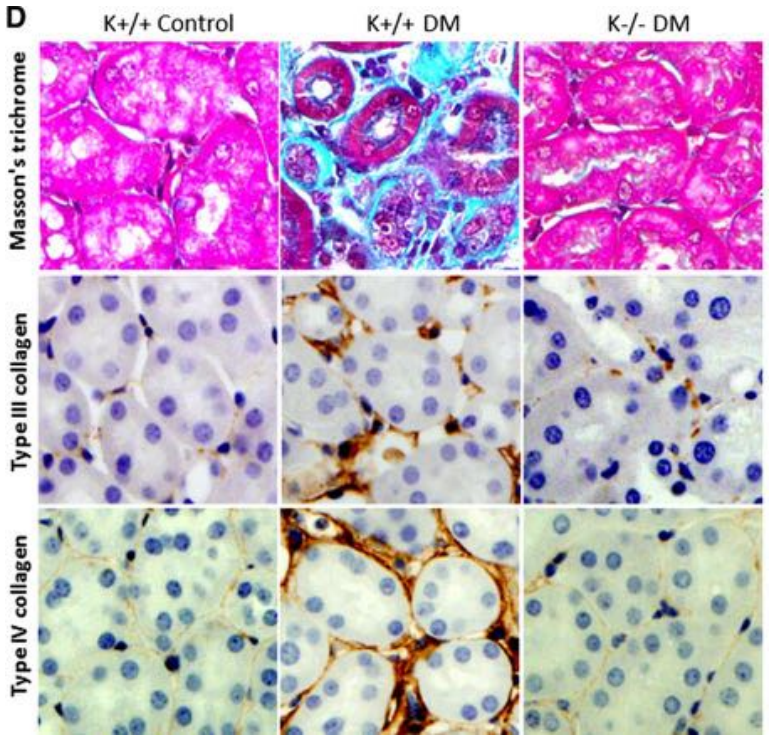
THE UNIVERSITY OF SYDNEY

AdAlta

KCa3.1 blockade demonstrated effective in mouse model of fibrosis

Blockade of KCa3.1 Ameliorates Renal Fibrosis Through the TGF-β1/Smad Pathway in Diabetic Mice

Chunling Huang,[1,2] Sylvie Shen,[1] Qing Ma,[1] Jason Chen,[3] Anthony Gill,[3] Carol A. Pollock,[1] and Xin-Ming Chen[1]



KCa 3.1 inhibition by genetic deletion or pharmacologically reduced

- Extracellular matrix expression
- Inflammation (macrophage accumulation, adhesion molecule and MCP1 secretion)
- TGF B and down stream signalling and PAI-1 expression

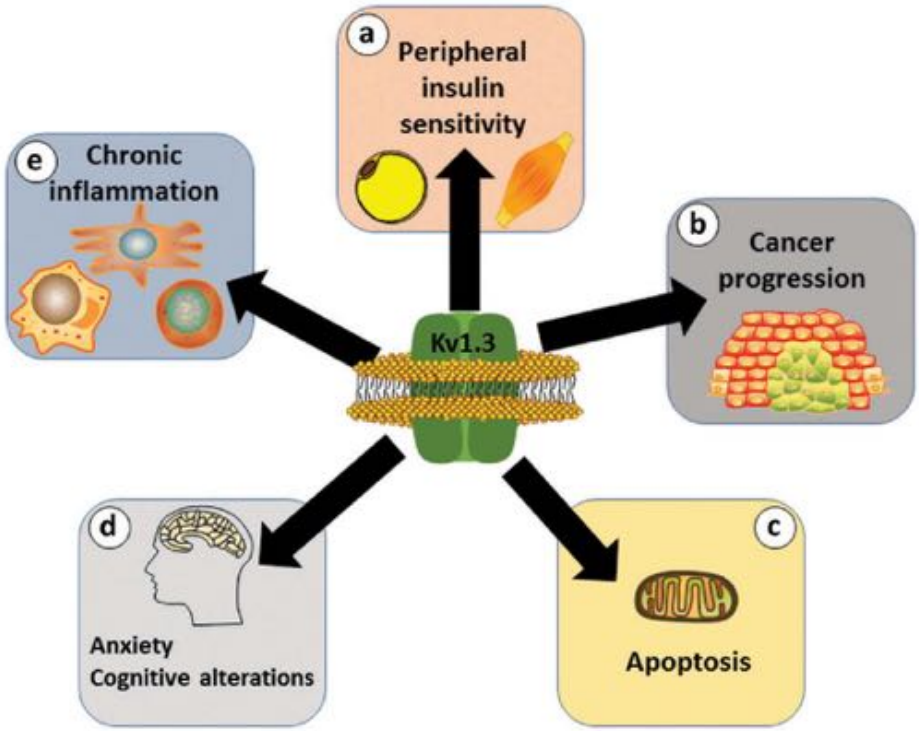
DIABETES, VOL. 62, AUGUST 2013

Potassium channels and kidney fibrosis Kv1.3

- **Kv1.3**, a voltage-gated K^+ channel is known to be involved in the regulation of energy homeostasis and body weight
- Kv1.3 inhibition has been shown to improve many adverse parameters associated with diabetes mellitus.
  - reduces weight gain and adiposity,
  - decreases hyperglycaemia,
  - improves dyslipidaemia,
  - normalises leptin
  - enhances peripheral insulin sensitivity
- Importantly, inhibiting Kv1.3 slowed the progression of renal fibrosis in model of 5/6 nephrectomy.

Multiple disease effects of Kv1.3

The potassium channel Kv1.3 is involved in multiple diseases including cancer, diabetes, inflammation, anxiety and fibrosis

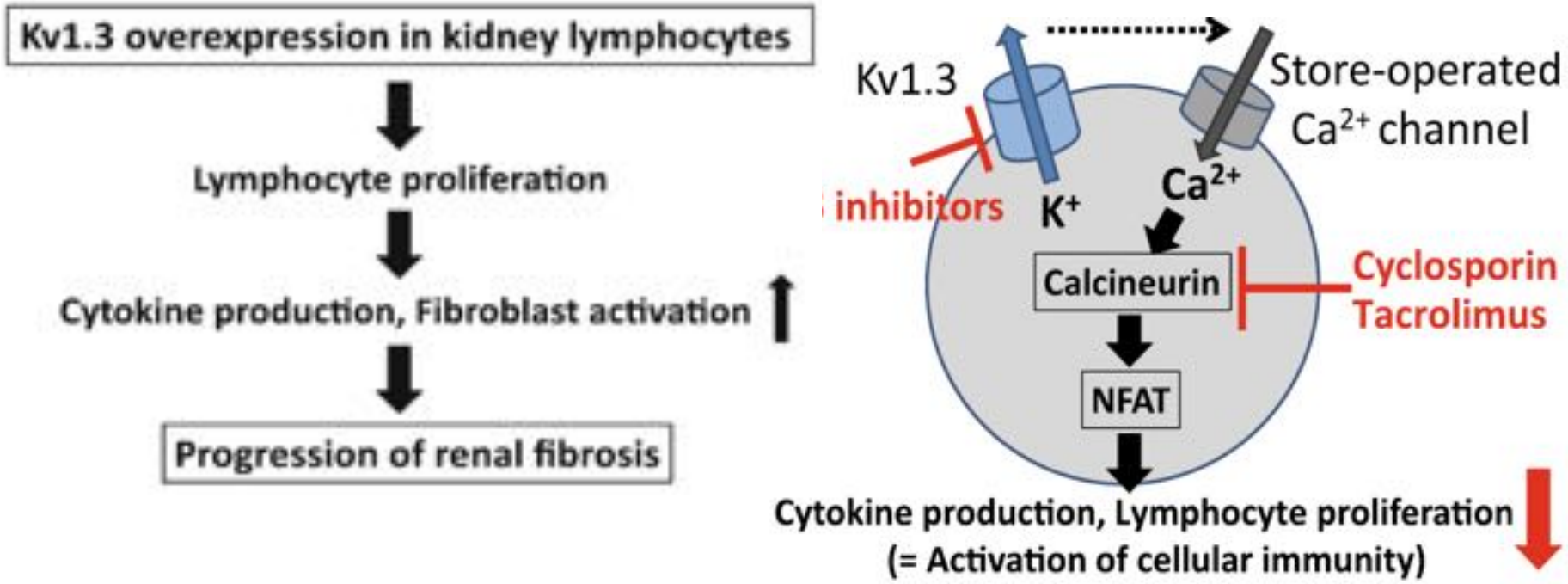


Antonio Serrano-Albarrás, Expert Opinion on Therapeutic Targets. 2018

AdAlta

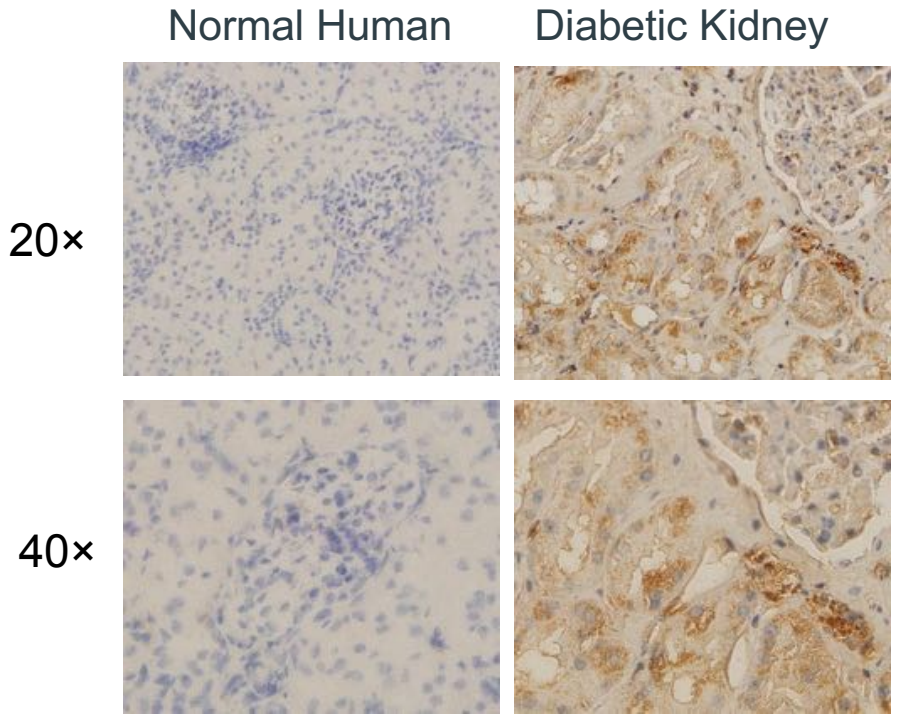
Potassium channels and kidney fibrosis

- Kv1.3 expression is increased in kidney lymphocytes
- Inhibiting Kv1.3 may therefor limit fibrosis, improving end stage kidney disease



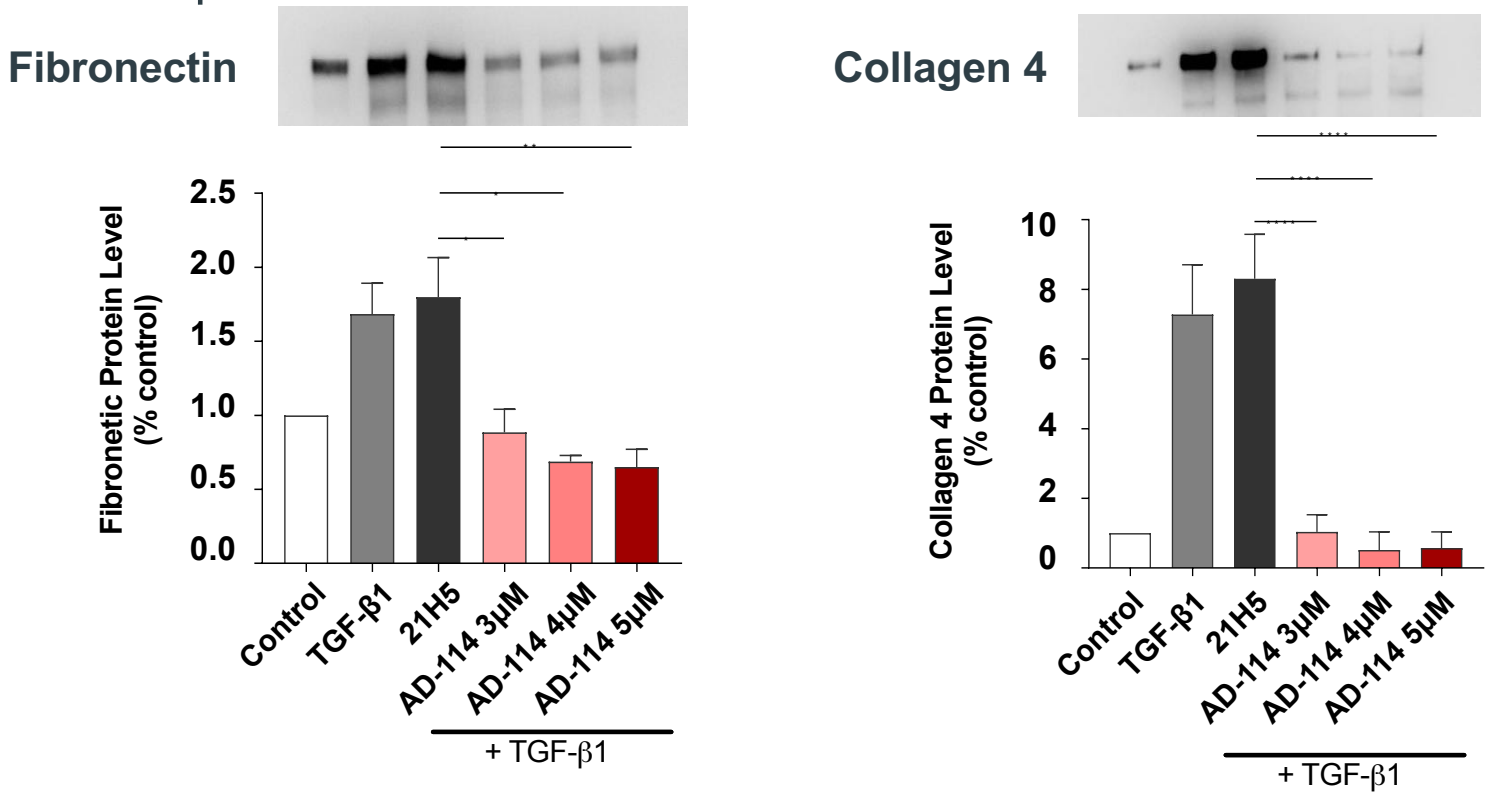
GPCR CXCR4 increased in diabetic nephropathy and renal fibrosis

- CXCR4 is significantly upregulated in fibrotic tissue from human diabetic nephropathy patients and not in normal kidney tissue
- AD-114 binds specifically to diabetic nephropathy kidney tissue and does not bind to normal kidney tissue



AD-114 reduces key proteins involved in kidney fibrosis

AD-114 reduces key fibrosis markers Fibronectin, Collagen 1 and 4 as well as Matrix Metalloproteinase 2 in human renal tubular cells

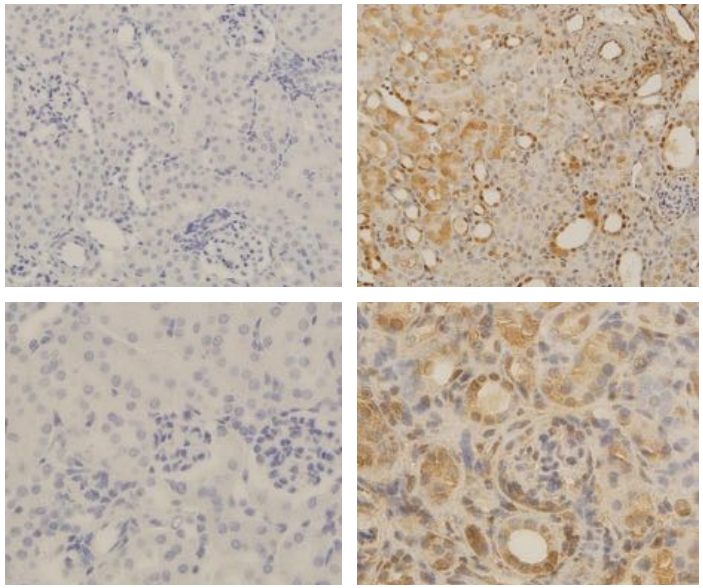


AdAlta

AD-114 and kidney fibrosis

Normal mouse kidney

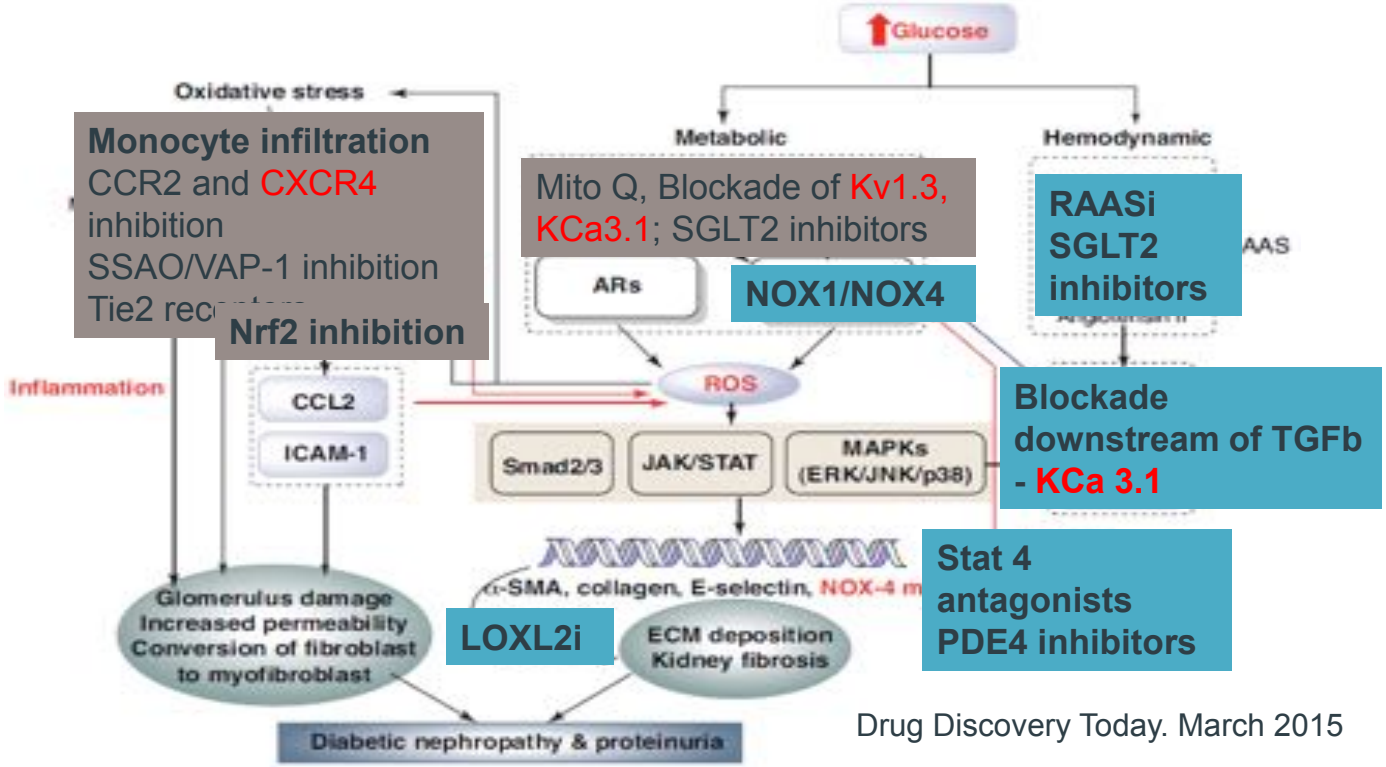
Diseased mouse kidney



- AdAlta's lead i-body candidate, AD-114 has shown broad anti-fibrotic and anti-inflammatory activity
  - Increased CXCR4 expression in diabetic nephropathy patient tissue compared to normal tissue
  - Increased CXCR4 expression in multiple models of mouse kidney disease
  - AD-114 causes reduction of fibrotic markers with human proximal tubules *in vitro*
  - Pollock laboratory awarded $768k NHMRC grant to complete *in vivo* evaluation of AD-114 in several kidney models of fibrosis

GPCRs and Ion Channels involved in renal fibrosis and chronic kidney disease

- A number of GPCRs and Ion Channels are involved in kidney fibrosis
- Pollock laboratory demonstrated the role of GPCR CXCR4 and ion channels KCa3.1 and Kv1.3 in kidney fibrosis



Drug Discovery Today. March 2015

AdAlta

Summary

- There is a significant unmet need for new therapeutic options of kidney fibrosis
- There is also a global recognition, demand and commercial opportunity to develop new therapeutics for the treatment of chronic kidney disease
- CXCR4 and Potassium Channels are promising targets for the development of new therapeutics for the treatment of kidney fibrosis
  - AdAlta's i-body technology has been screened against the GPCR target CXCR4 and demonstrated anti-fibrotic activity in various in vitro models of kidney fibrosis
  - AdAlta's long loop i-body technology has potential advantages with Ion Channel targets such as KCa3.1 and Kv1.3

THE UNIVERSITY OF SYDNEY

KOLLING Institute of Medical Research

Professor Carol Pollock

Royal North Shore Hospital,
Kolling Institute and University of Sydney
Australia

A/Prof Mick Foley

- Mick is the founding scientist of AdAlta and a key inventor of AdAlta's lead i-body candidate, AD-114.
- Upon completion of his PhD Mick was awarded a Wellcome Training Fellowship and worked at the Walter and Elisa Hall Institute. In 1995 Mick was awarded an ARC QEII Fellowship where he established the phage display of antibodies and peptide technology as a means of answering fundamental questions of immunity to infectious diseases.
- Mick is an internationally recognized leader in phage display, the technology used to screen the i-body library to identify new drug candidates. Having published over 70 scientific publications, Mick has received funding from ARC, NHMRC and NIH (US).

AdAlta

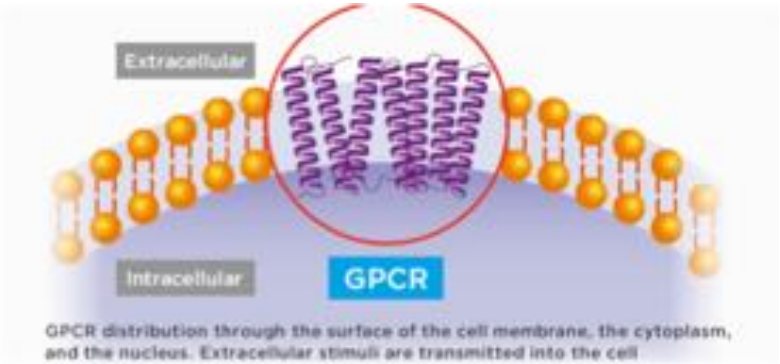
next generation protein therapeutics

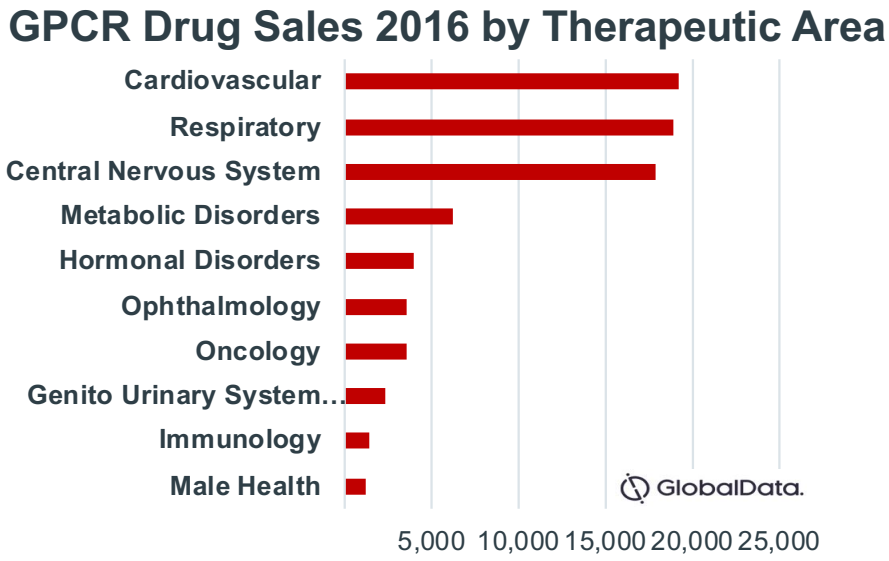
GPCRs: unique pharmacology of the i-body and what this means therapeutically

Mick Foley, AdAlta Chief Scientific Officer

G Protein Coupled Receptors (GPCRs)

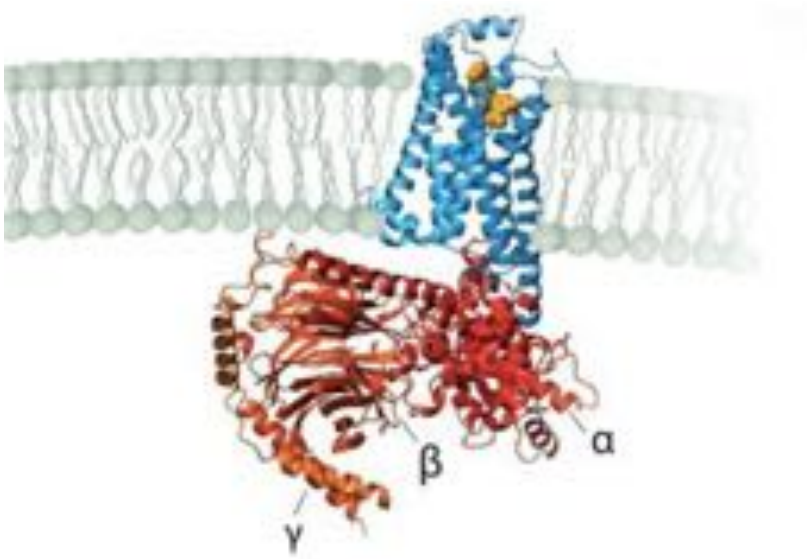
- **G-protein-coupled receptors** (GPCRs) are the largest and most diverse group of membrane receptors
- GPCRs play a number of roles in the human body and increased understanding of these receptors has greatly affected modern medicine.
- Of the top 200 selling pharmaceuticals, 25% target a GPCR with a total market of $82 billion in 2016.
- There are more than 800 different GPCR receptor targets, representing the largest class of membrane proteins in the human genome





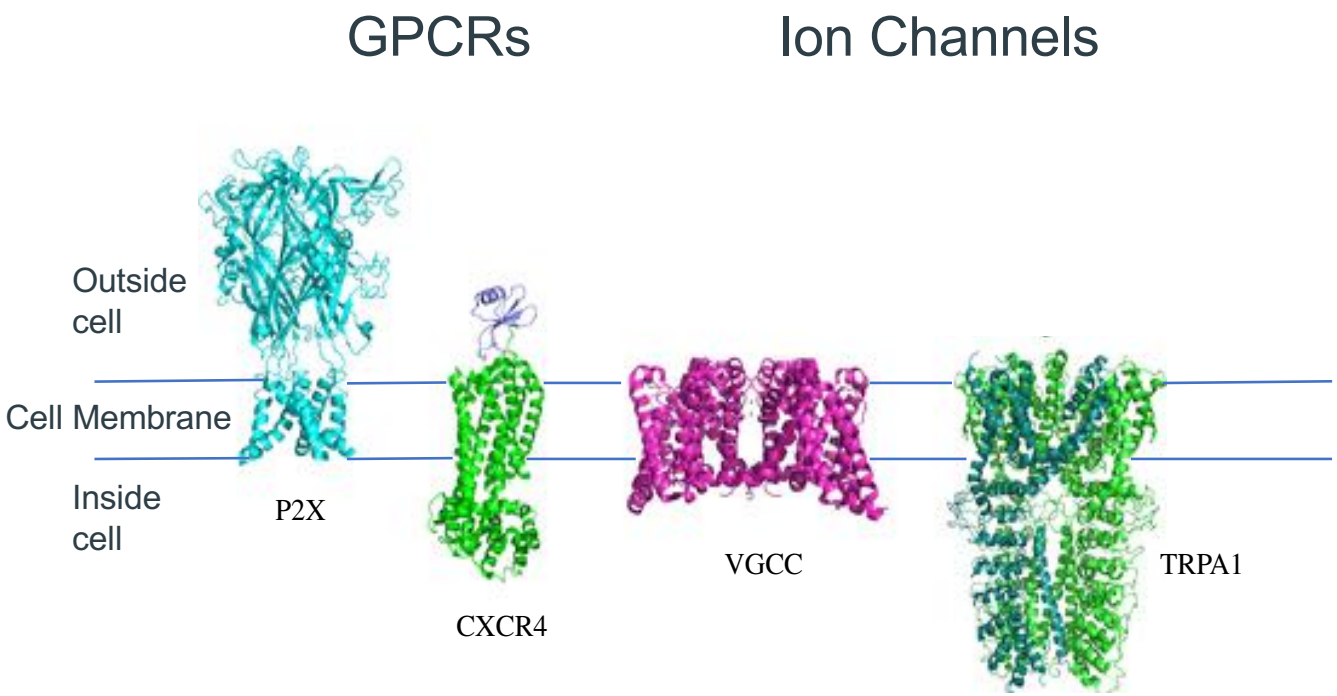
What is a GPCR?

- GPCRs are receptors within the plasma membrane.
- When an external signaling molecule binds to a GPCR, it causes a conformational change in the GPCR. This change then triggers a number of pathways internal to the cell
- Agonist v antagonist
- Biased agonism v biased antagonism
- Complex internal signaling pathways
  - Complex drug discovery process and identification of therapeutics challenging



Why are GPCRs difficult to drug?

- Limited surface exposure of G protein-coupled receptors and ion channels outside of the cell surface makes it difficult for traditional antibodies to bind to them
- Similarity between family members means off target effects



Therapeutic opportunity

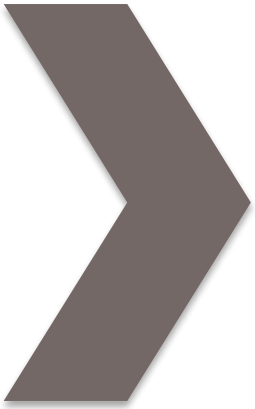
Current discovery approaches for GPCR and ion channel drugs are sub-optimal

Current compound technologies are inadequately addressing this target space

- Limited candidates identified (small molecule and toxin libraries are small)
- Lack of selectivity (small molecules, many toxins)
- Lack of developability (toxins)
- Limited potency (small molecules)
- Inadequate epitope/receptor access (biologics)

High value targets remain untapped or intractable

- First in class and superior medicines required
- New biology constantly emerging



i-bodies represent a unique solution

- Selective (vs. small molecules)
- Developable (vs. toxins)
- Target cryptic epitopes/clefts (vs. mAbs)

Revolution in drug discovery

Traditional drug development approach

Small molecule libraries of ~1m compounds screened to identify lead
Leads identified require resource intensive chemistry
Sub-optimal candidates identified that are not specific for the target
Structure helps to design new molecules however structure only available for limited number of molecules

Antibodies generated to fragments of the GPCR and not to the conformational epitopes
Specific binders identified, however are to external, incorrectly folded epitopes

AdAlta's approach

AdAlta i-body library has 20 billion different i-bodies
No need for structure of drug target
Screened in native format, GPCR unmodified
Long loop can access unique epitopes
Selective and specific binders identified to conformational epitopes

CXCR4 is involved in fibrosis and other disease states

CXCR4 is important in maintaining stem cells in bone marrow with AMD3100 (Mozobil) approved for single use only.

HIV-1 uses CXCR4 as a co-receptor for viral entry into host cells

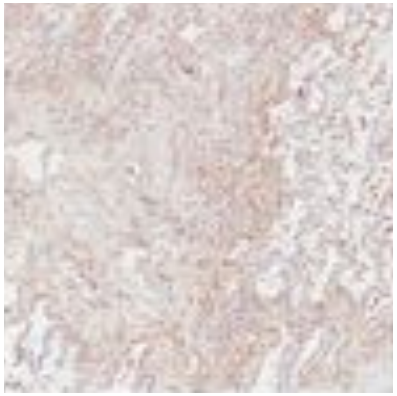
CXCR4 expression is low or absent in many healthy tissues but has been shown to be increased in more than 23 types of cancers

CXCR4 expression is increased in a number of diseases associated with fibrosis including:

- Lung: IPF
- Kidney: CKD
- Eye: wet-AMD
- Skin: SSc

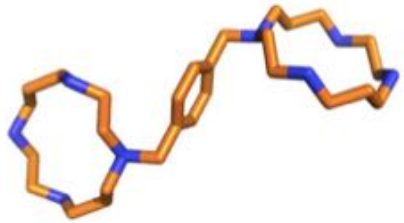
Normal human lung tissue

Diseased IPF lung tissue



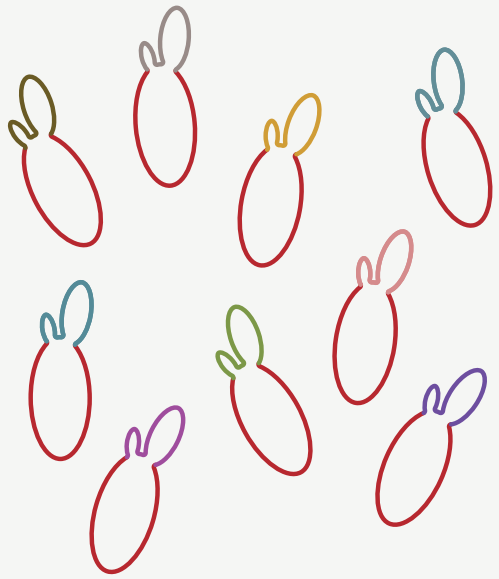
AMD3100

- AMD3100: Plerixaflor (Mozibil) is a CXCR4 antagonist that is used to mobilise stem cells for transplantation.

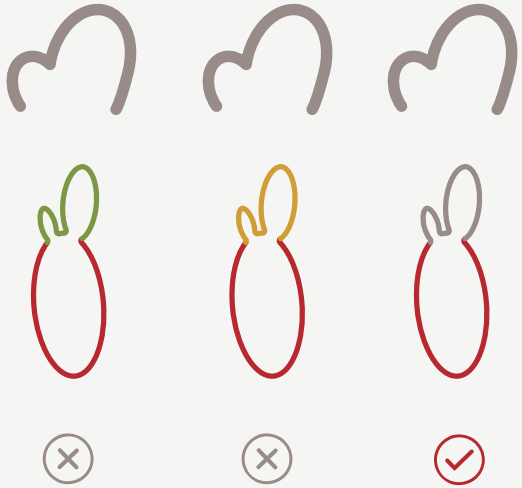


- Side effects:
  - Toxic in animals
  - Increase in stem cells/white blood cells in peripheral circulation (Leukocytosis)
  - Can cross CNS and have off-target side effects: by binding to a number of GPCRs and ion channels causing cardiac and blood pressure effects (ACEII, Dopamine2, Adrenergic receptor, Neuropeptide Y2 and Y3)
  - Plerixafor treatment caused mobilisation of tumor cells in patients with leukaemia
- Problems with existing CXCR4 therapeutics
  - The majority of current antagonists mobilise stem cells from the bone marrow into the circulation; however, this may be a severe safety issue when trying to treat chronic diseases such as HIV infection, cancer, inflammation and fibrosis.

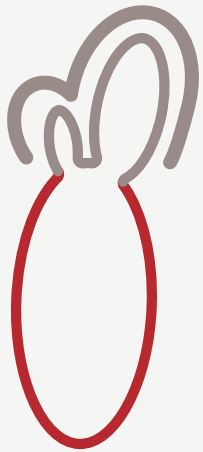
Screening the i-body library



AdAlta can **modify the i-body binding loops** to create a library of 20 billion different i-bodies.



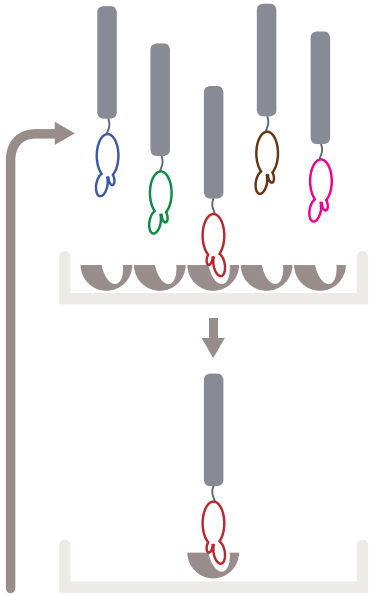
The library can be **screened** against a drug target of choice, to identify a unique i-body.



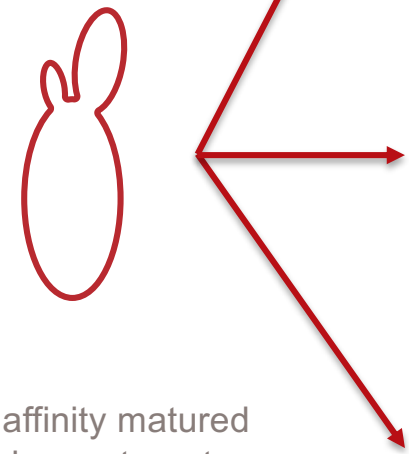
The **i-body** that **binds to the drug target** has potential therapeutic application.

AdAlta approach: i-body to CXCR4

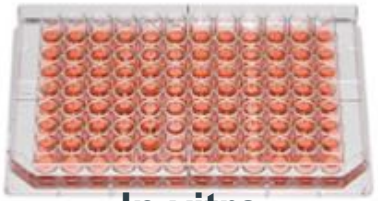
Large diverse synthetic library of 20 billion i-body protein compounds that can bind to a broad range of therapeutically relevant targets



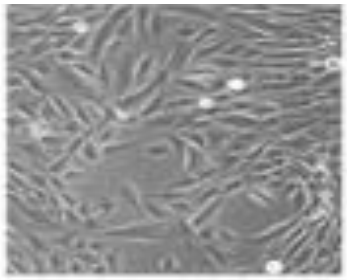
i-body identified by rapid screening on CXCR4 lipoparticles



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



In vitro



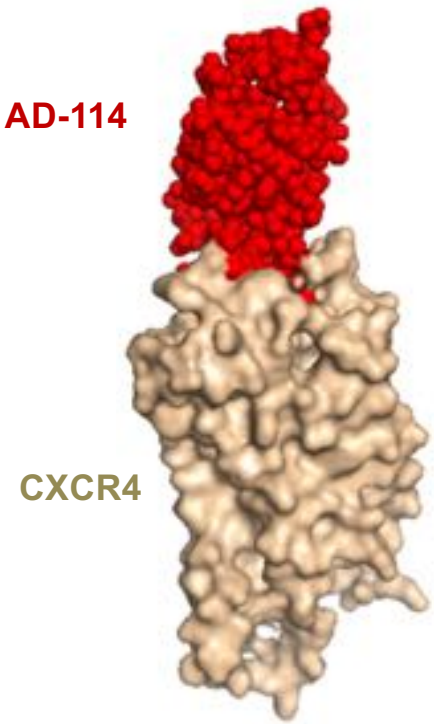
Human cells

In vivo

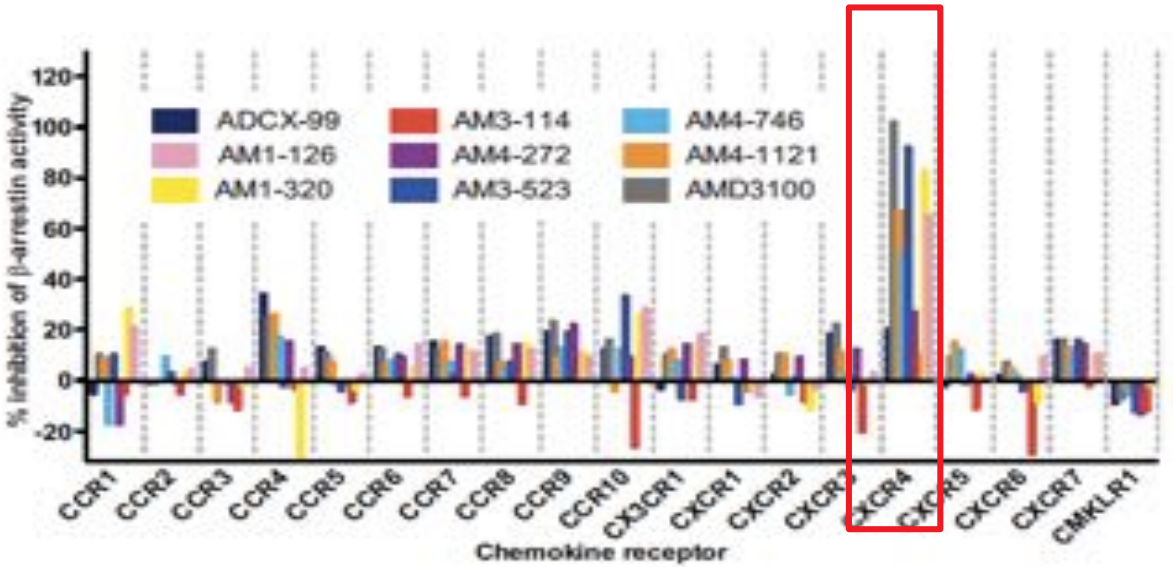
AdAlta

AD-114: high affinity and specificity

High affinity: AD-114 binds to CXCR4 at 4nM



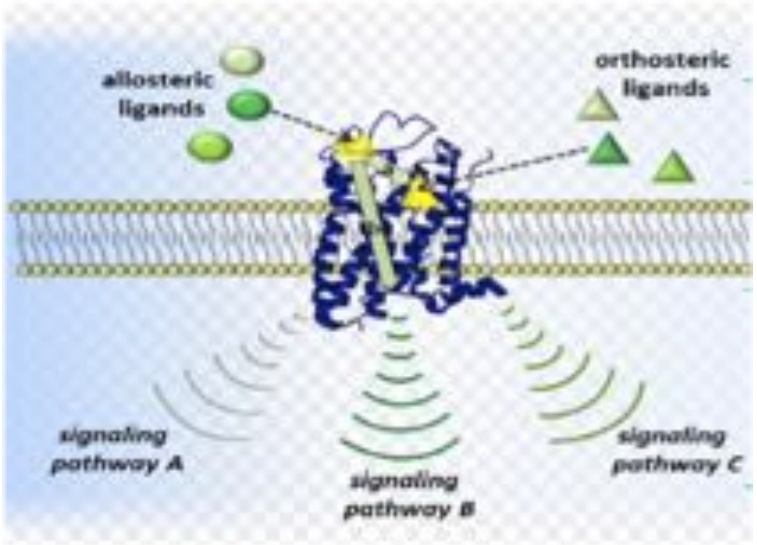
Highly specific: AD-114 tested against 167 GPCRs and shown only to antagonise CXCR4

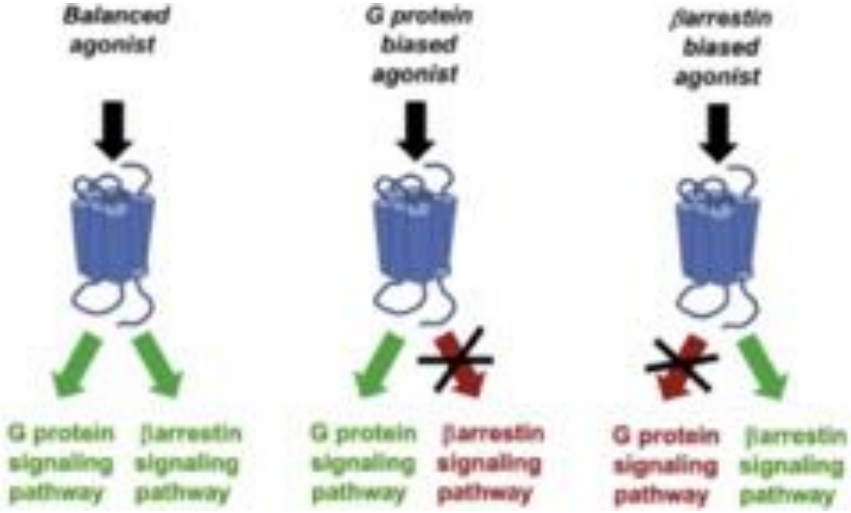


AdAlta

GPCRs: exciting potential

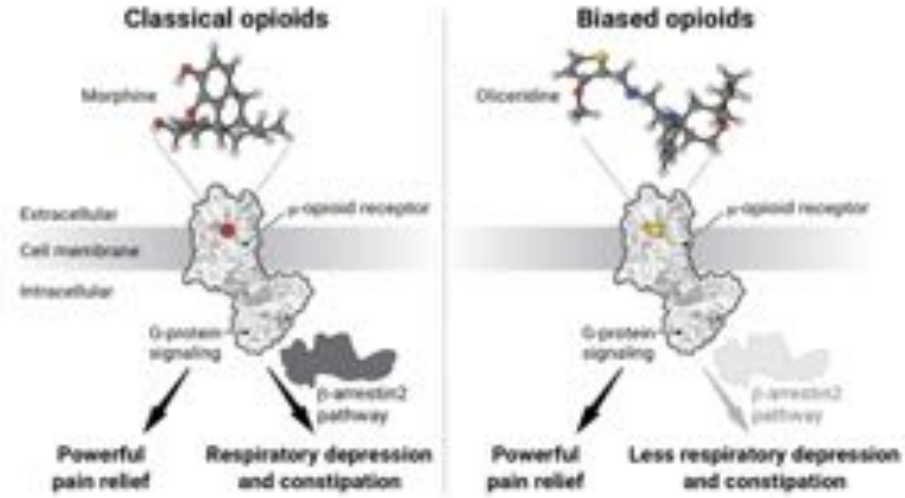
- GPCRs have ‘biased signaling’
- Many traditional drugs to GPCRs have side effects because they activate several signaling pathways, some may be beneficial others may be detrimental
- Currently intense interest in finding ’biased drugs’ to selectively activate one pathway over another





Biased signaling: The opioid example

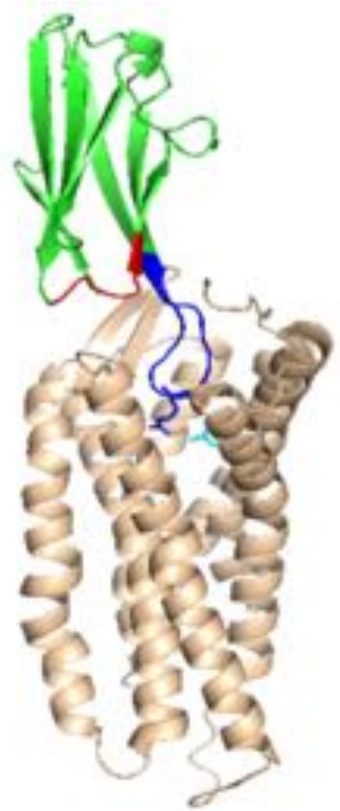
- When opioid drugs act on receptor they dull pain by activating the ‘painkilling’ pathway but they also activate respiratory suppression
- Biased drugs aim to trigger only the ‘painkilling’ pathway
- “There are many groups creating biased agonists. And one of them is going to get it right,” Bryan Roth, University of North Carolina



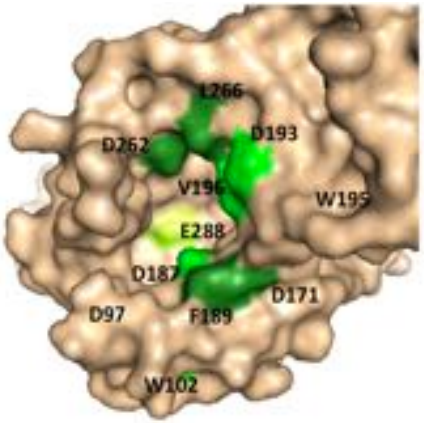
V. Altounian, Science November 2017

AD-114: exploiting biased signaling in GPCRs

- i-bodies have a long loop that can penetrate the binding pocket
- i-bodies AD-114, AD-272 and AD-523 each bind to CXCR4 with high affinity, however distinct footprints
- While binding to CXCR4 with high affinity, very few changes in each i-body resulted in affecting signaling different ways

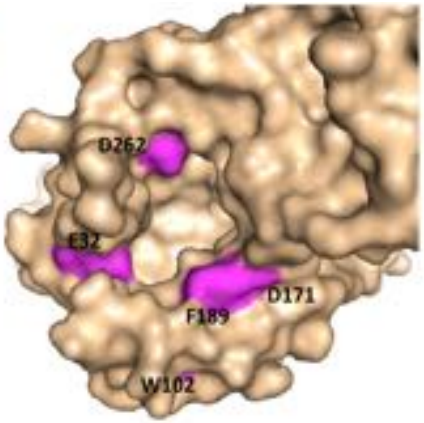


AD-114



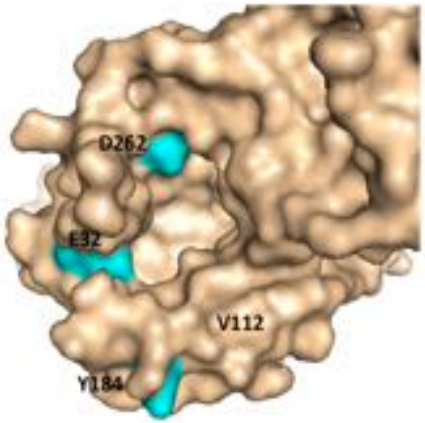
High β-arrestin
High cAMP

AD-272



Low β-arrestin
High cAMP

AD-523



Medium β-arrestin
Medium cAMP

Griffiths et al, JBC 2016

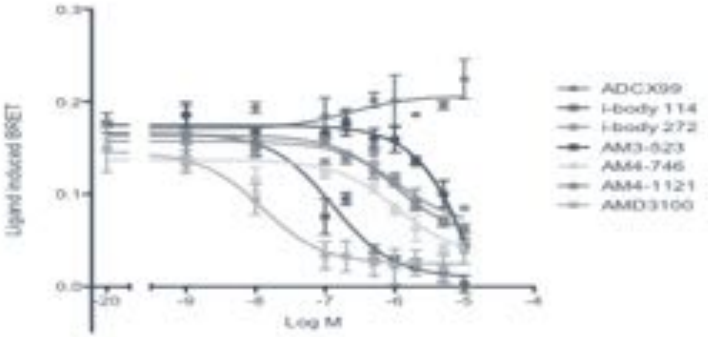
AdAlta

Panel of i-bodies: differential/biased activity

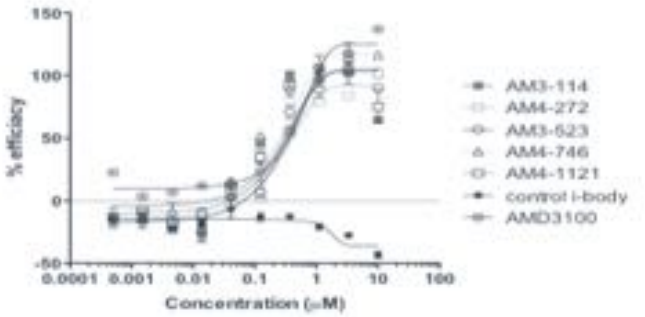
i-bodies with 1-2 amino acid changes all bind with high affinity to CXCR4.

These single point mutations resulted in affects to signaling and *in vitro* activity in different ways

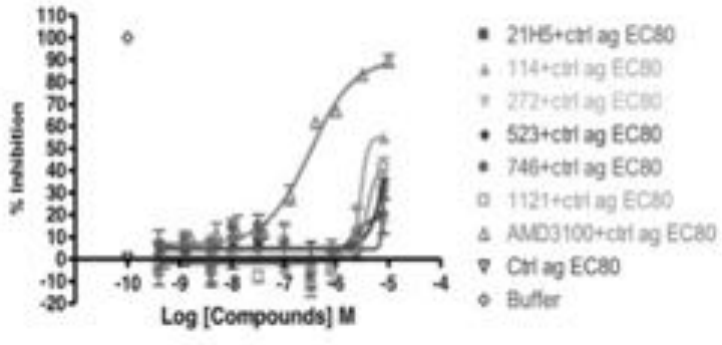
β-arrestin BRET Assay



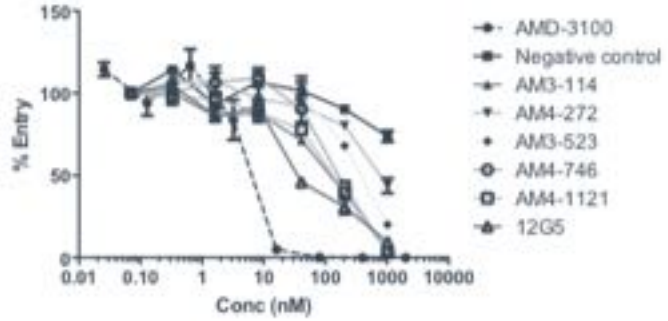
cAMP Assay



Ca^{2+} Assay

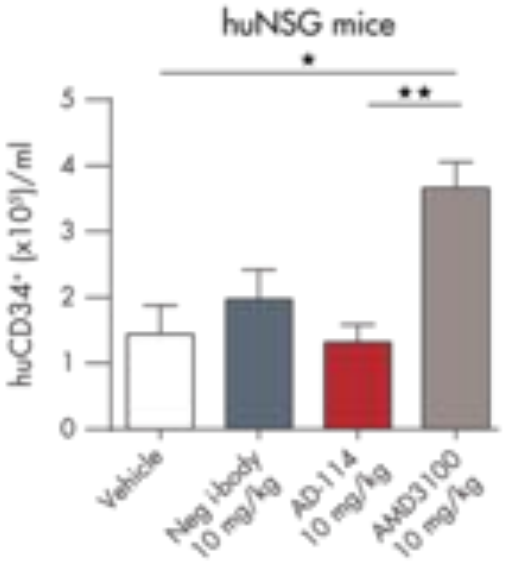


i-bodies block HIV infection



AD-114: novel *ex vivo* and *in vivo* activity

AD-114 does not mobilize stem cells in humanised mouse model or in non-human primates unlike AMD3100 (Mozobil), which mobilised stem cells

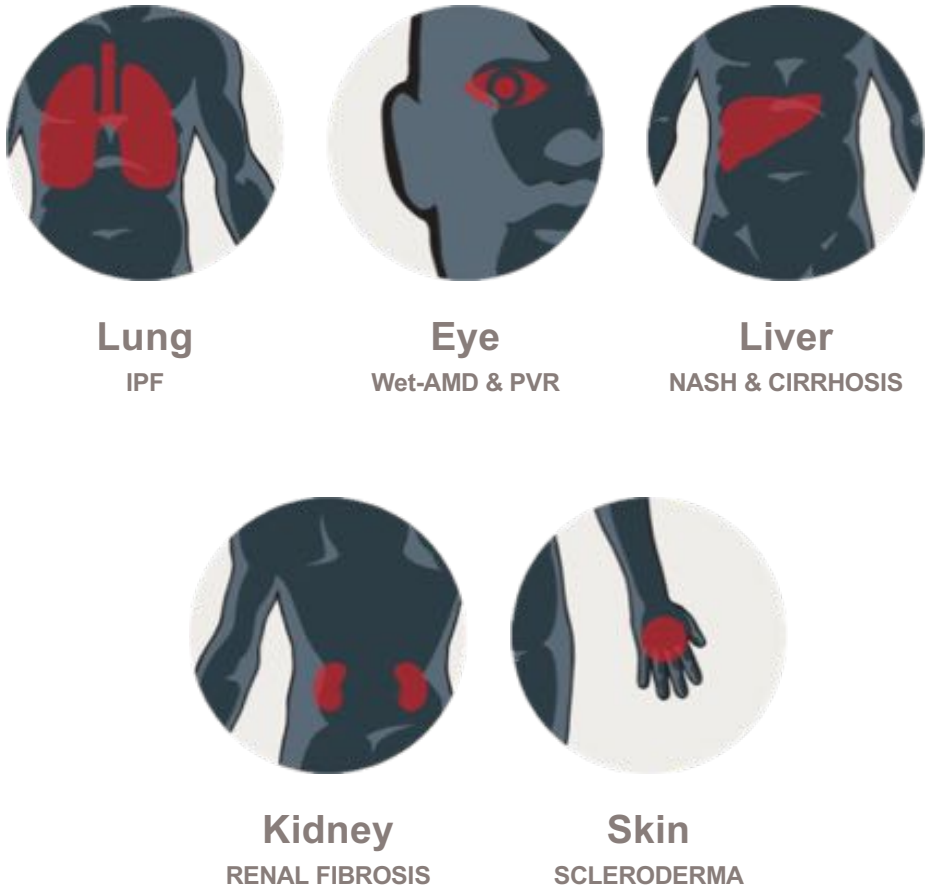


AD-114 specifically inhibited migration of diseased IPF fibroblasts but did not have any effect on normal fibroblasts unlike AMD3100, which had no activity with normal or diseased IPF fibroblasts

MIGRATION	No effect on normal fibroblasts	Inhibits IPF fibroblasts
i-body AD-114	✔	✔
Nintedanib (Boehringer)	✗	✔
Pirfenidone (Roche)	✔	✗
Other CXCR4 drug (AMD3100)	✔	✗

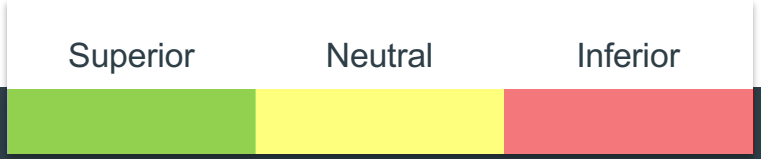
CXCR4 and fibrosis

- Broad fibrotic application with demonstration in other animal models and human tissues
  - Lung: IPF
  - Eye: wet-AMD
  - Liver: NASH
  - Kidney: CKD
  - Skin: HT Scarring
- AD-114 has demonstrated broad anti-fibrotic and anti-inflammatory effects in several animal models of disease and with human tissues
- AD-114 has demonstrated safety in non-human primate studies



AD-114 best in class treatment for IPF

	AD-114	Mozobil (Sanofi)	BL8040 (BiolineRx)	Nanobody (Ablynx)	Ulocuplumab (BMS)
Affinity for CXCR4	1-5nM	84nM	1-10nM	5nM	5nM
Specificity for CXCR4	Yes	No	?	?	?
CXCR4 binding site	Extracellular and transmembrane	Transmembrane domain	Extracellular domain	Extracellular domain	Extracellular domain
Molecule type	i-body	Small molecule	Peptide	Nanobody	Antibody
Plasma Half life	More than 24hrs*	~3-5hrs	1-3hrs	?	More than 24hrs
Indication	Fibrosis	Cancer: ??	Cancer: MM	Not being developed	Cancer: RCC and HCC
Anti-fibrotic activity	In animals and fibrotic human tissue	In animals but not fibrotic human tissue	?	?	?
Stem cell mobilisation & ability to treat acute diseases	No	Yes	Yes	Yes	Yes



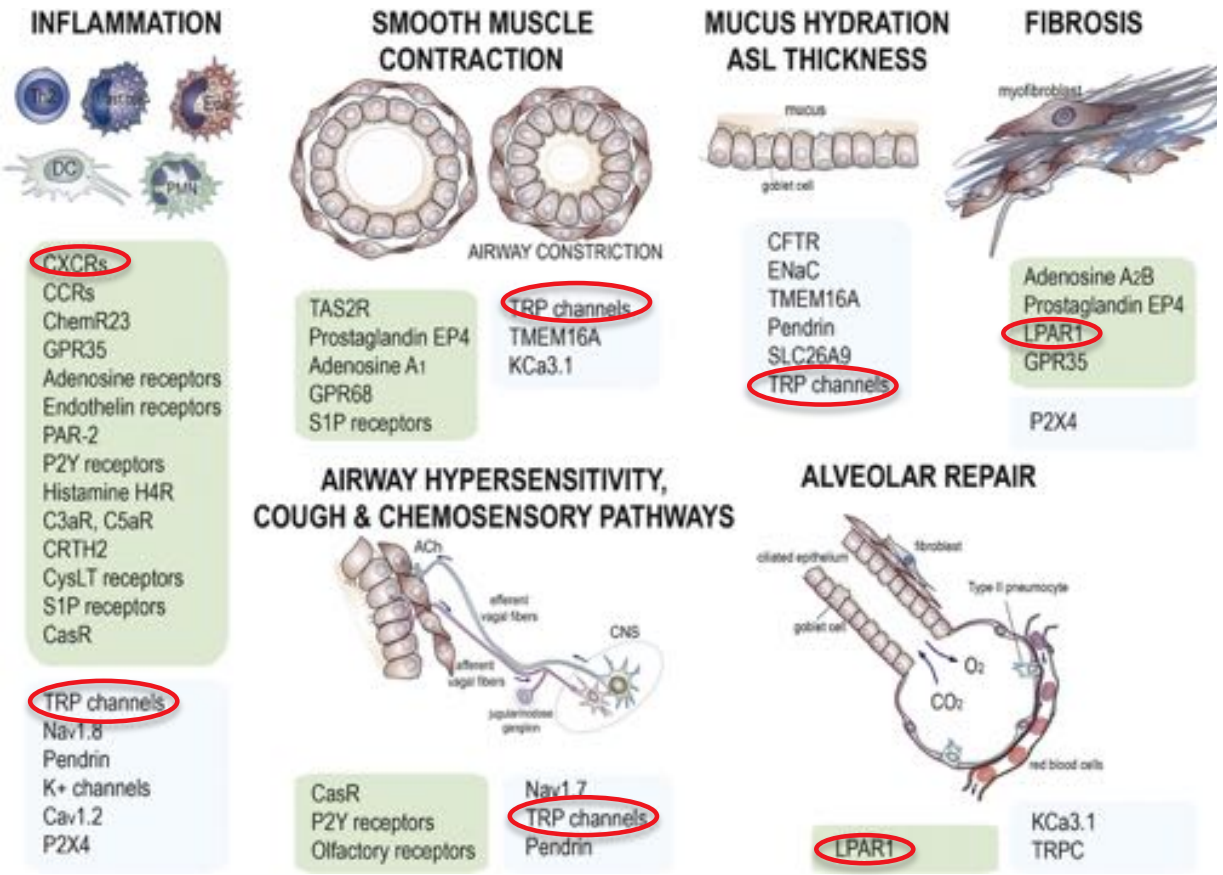
** Based on non-human primate data*

AdAlta

AD-114: selective modulation

- As far as GPCRs are concerned, there is an opportunity to find i-bodies that modulate these targets in ways that small molecules cannot.
- AD-114 inhibits CXCR4 in a very selective way, blocking agonist induced cAMP generation, beta-arrestin recruitment and receptor internalisation whilst leaving calcium influx unaffected.
- Searching for these biased agonists or biased antagonists, has not been approached in a systematic prospective manner, rather the concept has been used retrospectively to explain different effects of agonists on the same receptor.
- With the clever use of assays it should be possible to identify i-bodies that are capable of biased antagonism or biased agonism.
- It might also be possible to identify i-bodies that activate or inhibit GPCRs in a tissue selective manner using i-body technology.

GPCRs and ion channels involved in respiratory disease and fibrosis



- AdAlta has identified i-bodies that bind to a number of GPCR and ion channel targets and demonstrated unique *in vitro* and *in vivo* activity
- A number of these drug targets have been linked to respiratory disease and fibrosis

J.A. Douthwaite et al. / Pharmacology & Therapeutics 169 (2017) 113–123

AdAlta

Summary

- GPCRs are an important class of high value drug targets whose potential remains untapped or intractable
- i-bodies provide a novel drug discovery engine with unique pharmacology
- AdAlta has identified a number of i-bodies to both GPCRs and ion channels
- AD-114 binds to the drug target CXCR4 and has unique activity for treatment of fibrosis unlike other CXCR4 drugs
  - AD-114 modulates GPCRs in a way that small molecules can not: using its long loop and binding with high affinity and selectivity
- The i-body platform provides significant pipeline and partnering opportunity to target GPCR and ion channel targets

AdAlta

next generation protein therapeutics

Mick Foley, CSO

AdAlta Limited (ASX:1AD)

m.foley@adalta.com.au

www.adalta.com.au

Dr Anthony Brown

- Anthony entered the financial services sector on the buy-side at Royal Sun Alliance investment management after completing a Ph.D at the Institute of Cancer Research in London.
- RSAIM became part of F&C via two mergers and during this time Anthony won the Thomson Extel Award as best-buy side Biotech analyst of 2005.
- In 2007 Anthony joined the Abu Dhabi Investment Authority, one of the world's largest sovereign wealth funds, in London. In 2011 Anthony left financial services to join AstraZeneca working directly for the CFO Simon Lowth before joining the Investor Relations department in 2013.
- Anthony emigrated to Australia in December 2014 and joined WG Partners in early 2015.

WG Partners

Development of drugs that target GPCRs and ion channels: the commercial opportunity and therapeutic potential

February 2018

WG partners

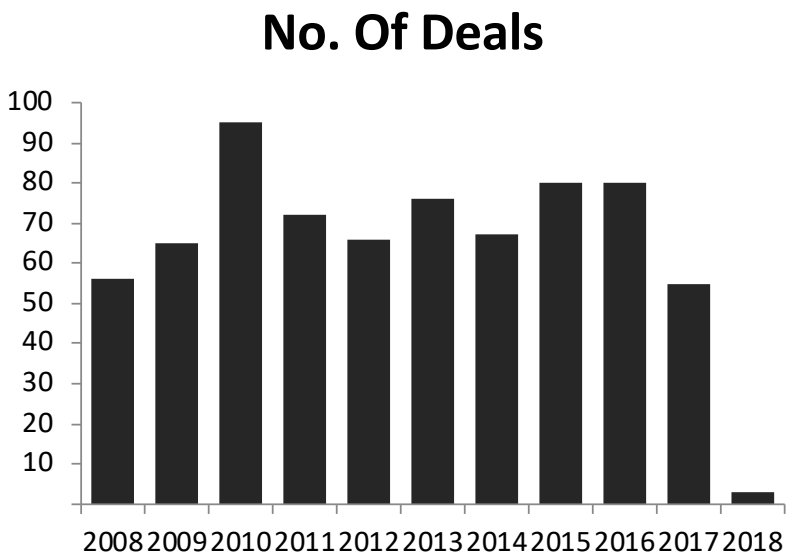
GPCR drugs have a strong pedigree

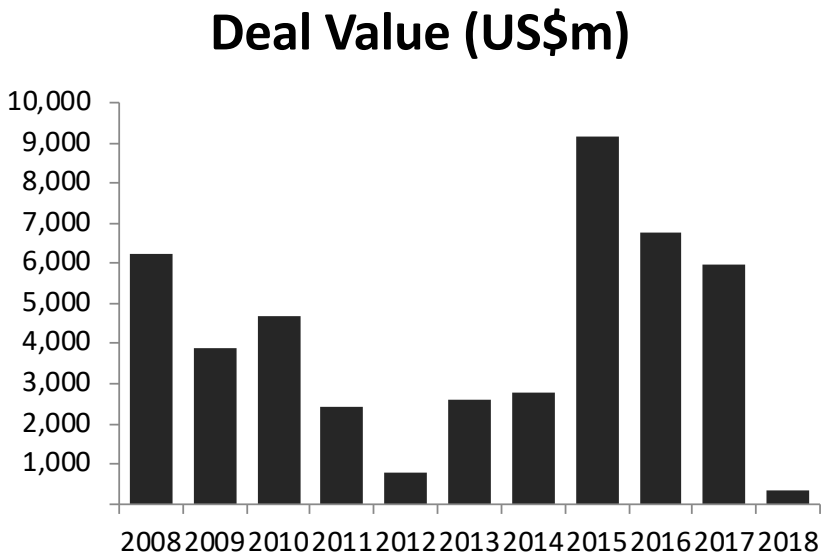
Drugs targeting G-protein coupled receptors are estimated to account for 25-35% of all drugs and include 6 of the top 20 highest selling drugs of all time

Drug	Generic name	Indication	Year of peak sales
Plavix	clopidogrel	Anti platelet	2011
Abilify	arpiprazole	Schizophrenia/Bi-polar	2011
Seroquel	quetiapine	Schizophrenia/Bi-polar	2011
Diovan	valsartan	Blood pressure	2010
Singulair	montelukast	Asthma	2011
Zyprexa	olanzapine	Schizophrenia/Bi-polar	2010

These drugs were all discovered around the same time and represent the low hanging fruit of this target class which could be identified with simple high throughput screens

GPCR drugs continue to be important





- The number of licensing deals involving GPCR targets fairly steady
- Values increase as big pharma looks to restock pipeline following period of under investment in early stage research
- 2012 value anomaly at least partly due to lack of disclosure in that year's deals

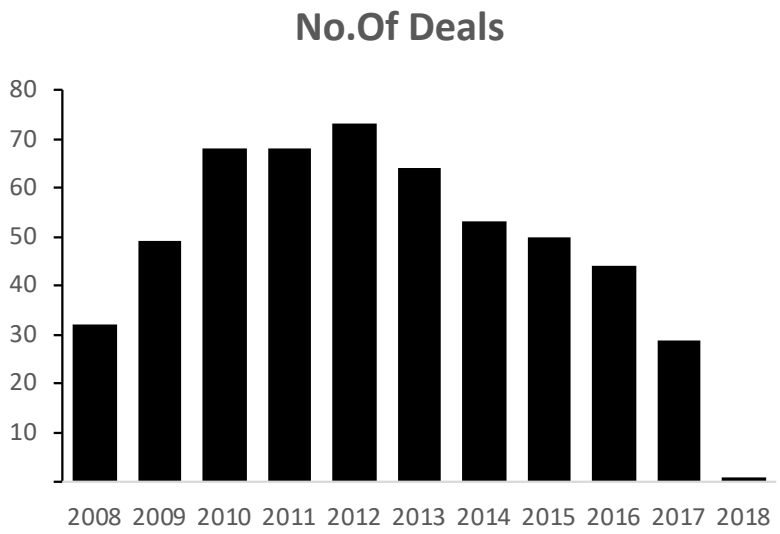
Source: Global Data (Deals database)

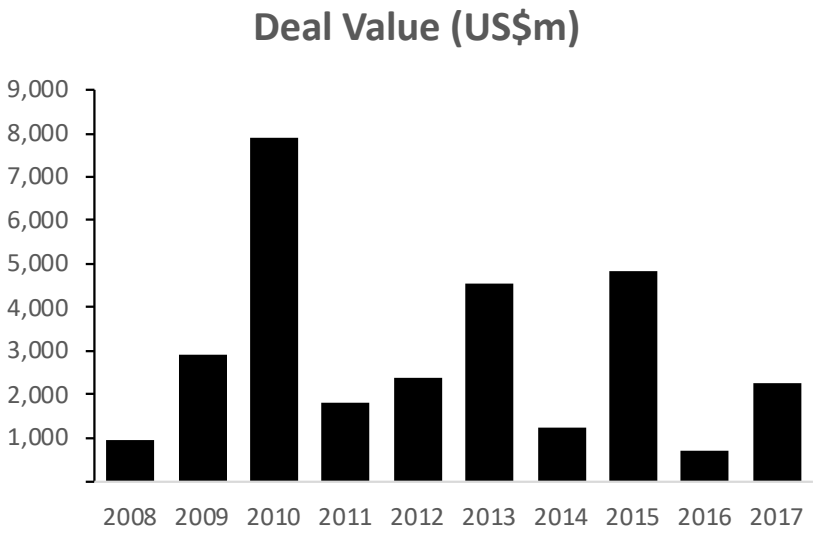
Ion channel drugs

- Low hanging fruit with most drugs discovered a decade ago with most possessing low selectivity
- The number of successfully drugged ion channels is low
- Very few drugs approved in the last decade

drug	target channel	disease target	year of first clinical usage
verapamil	L-type Ca_v	hypertension	1982
diltiazem	L-type Ca_v	hypertension	1982
amlodipine	L-type Ca_v	hypertension	1990
nifedipine	L-type Ca_v	hypertension	1977
gabapentin	Ca_v ($\alpha 2\delta$)	pain	1994
pregabalin	Ca_v ($\alpha 2\delta$)	pain	2004
sotalol	hERG	arrhythmia	1992
flecainide	$Na_v1.5$	arrhythmia	1982
ziconotide	$Ca_v2.2$	severe pain	2004
lidocaine	Na_v	local anesthetic	1949
bupivacaine	Na_v	local anesthetic	1987
lamotrigine	Na_v	epilepsy, bipolar	1994
riluzole	Na_v	amyotrophic lateral sclerosis	1995
phenytoin	Na_v	epilepsy	1953
lacosamide	Na_v	seizures and pain	2008
carbamazepine	Na_v	epilepsy	1963
varenicline	nAChR	smoking cessation	2006
flupirtine	KCNQ2/3	epilepsy	1984
retigabine	KCNQ2/3	epilepsy	2011
diazepam	$GABA_A$	depression	1963

Ion channel drugs continue to be important





- The number of licensing deals involving ion channel targets also fairly steady
- Value variable, however very few drugs approved in the last decade

Source: Global Data (Deals database)

What are pharma companies looking for?

In licensing

- Good strategic fit
- Validated target
- Clinical proof of concept
- Strong IP
- Strong pre-clinical package with the right tox studies and target engagement
- Validated GMP manufacturing

Acquisitions

- Unencumbered pipeline (multiple assets)
- Platform technology
- Confidence in the lead program (avoid paying royalties)
- Risk appetite
- CEO involvement
- Pre existing partnerships (buying a known entity)

Ablynx 0-US$4.8bn: a case study

Ablynx

Rapid growth since its foundation in 2001

2001
Foundation

2002
Technology platform

- €5M seed financing
- No products
- No partnerships
- 10 employees

2007
R&D – early stage

- €70M private equity
- €85M IPO (Euronext)
- 11 R&D projects
- 1 Nanobody in the clinic
- 3 partners
- 144 employees

Today
R&D – late stage

- > €370M in equity and debt
- > €400M cash from partners
- > 45 R&D projects
- > 1,500 patients treated
- 8 Nanobodies in the clinic
- 1st Nanobody expected to be launched in 2018
- 8 partners
- ~ 400 employees
- €235M in cash at 31st Dec 2016

Evolving into a commercial stage biotech company

Ablynx: a case study

Ablynx: GPCR deals

- **Boehringer Ingleheim**
  - €8m payment for Ph1 GPCR nanobody to CX3CR1 + €125m milestones & royalties
  - This novel Nanobody blocks the function of the G-protein coupled receptor (GPCR), CX3CR1, a protein that has proven to be difficult to address with conventional antibodies. By blocking the function of CX3CR1, the activity of inflammatory immune cells, which play a major role in chronic kidney disease, may be inhibited.

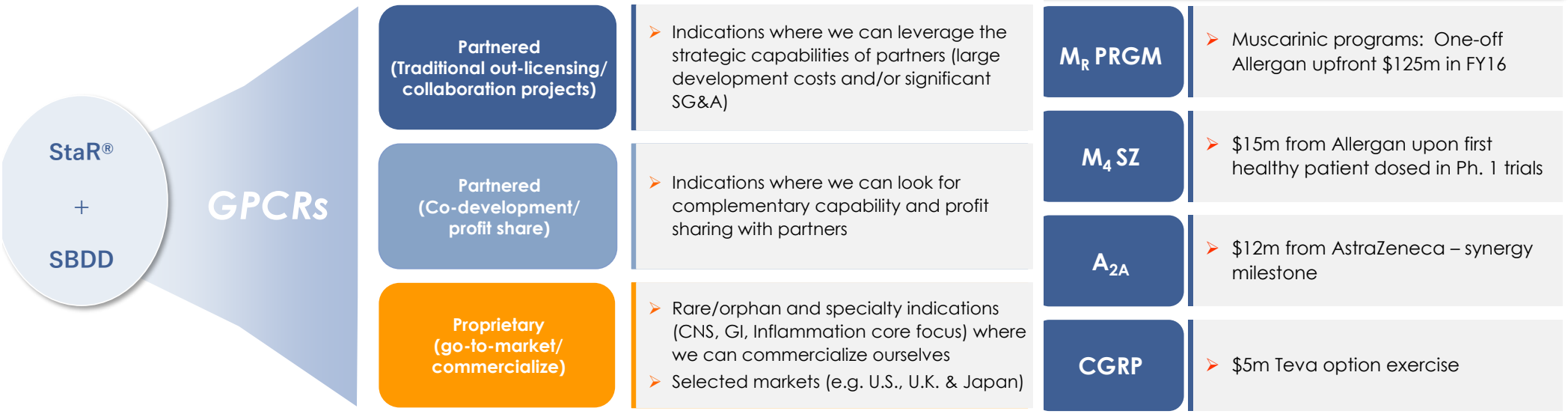
- **Novartis**
  - CXCR2 € 1m received, terminated

Ablynx: Ion Channel deal

- **Merck**
  - In October 2012, Ablynx and a subsidiary of Merck & Co, Inc. entered into a collaboration to develop and commercialise Nanobody candidates directed towards a voltage gated ion channel, with the option to develop and commercialise a Nanobody to a second target.
  - Under the terms of the agreement, Merck gains exclusive global rights to Nanobodies against the selected target, with an option for similar rights to a second target.
  - Upon signing, Merck paid Ablynx a €6.5 million upfront payment. In addition, Ablynx is eligible to receive research funding (extended now twice) and up to €448 million in research, regulatory and commercial milestone payments associated with the progress of multiple candidates, as well as tiered royalties on any products derived from the collaboration.
  - In March 2015, the company announced a first extension of the research term to September 2016 triggering a €1 million milestone payment to Ablynx.

Heptares: a case study

- Acquired by Sosei in Feb-2015 for US$400m: at the time had 1 product phase 1b and 7 pre-clinical leads
- Heptares use Structure Based Drug Design (SBDD) ie have to know structure of GPCR before can design drug
- Multiple development milestones received (Allergan M4, Teva CGRP, AstraZeneca A2A)



Heptares: case study

- Allergan M4: US$3.3b deal (US$125m upfront and US$665m in milestone payments for three targets)
- Teva CGRP: US$10m upfront and US$400m in milestone payments + royalties
  - US$5m payment for selection of candidate
- AstraZeneca A2A: US$10m upfront and US$500m in milestone payments + double digit royalties
  - Pre-clinical program US$12m milestone payment (for new A2A candidates)
  - Phase I US$10m milestone payment
- Daichi (undisclosed GPCR)
  - US$4m upfront and $8m research funding

Conclusions

- Pharma is hungrier than ever for innovative approaches to difficult to drug targets.
- GPCR (and ion channel) drugs will continue to be important but may need new approaches as low hanging fruit has gone.
- Pharma acquires companies with:
  - Validated platforms (clinical data)
  - Unencumbered pipelines
- Validating platforms and building pipelines takes both time and money

PANEL

Clinical development of a drug and the need for novel drug discovery tools

WG partners

The panel

Brian Richardson PhD

Brian was most recently a member of The Leadership Team and The Global Head of The Musculoskeletal Disease Therapeutic Area at The Novartis Institutes for Biomedical Research having previously held several other senior positions during a 42 year career in the pharmaceutical industry. Those positions included Deputy Head of Drug Safety, Head of Pathology and Experimental Toxicology, Head of Immunology, Inflammation and Respiratory Research as well as Senior Project Manager for the worldwide development of new therapies for metabolic, cardiovascular and respiratory diseases for Sandoz Pharma. Subsequently Brian was appointed Head of Pre-Clinical Research in Switzerland and UK and played a key role in the merger of the Sandoz and Ciba Research organisations that ultimately resulted in the creation of The Novartis Institutes for Biomedical Research. Research conducted in Brian's laboratories has led to the discovery, development and introduction of several new therapies.

He has published more than 60 original peer-reviewed research papers and contributed many book chapters in the fields of pathophysiology, endocrinology and receptor pharmacology.

John Westwick PhD

John has extensive experience in drug discovery in the Pharmaceutical Industry and as a Professor of Pharmacology. With over 14 years at Novartis Institutes for Biomedical Research, John was responsible for the build-up and leadership of all aspects of drug discovery and early development from target validation to the completion of proof of concepts in the respiratory area, which included severe asthma, Chronic Obstructive Pulmonary Disease (COPD), cystic fibrosis, pulmonary arterial hypertension, and pulmonary fibrosis. During his period of leadership at Novartis Respiratory, John was responsible for five global launches (Xolair, Podhaler, Onbrez, Seebri, and Ultibro). In addition he had 13 positive proof of concepts in respiratory, which include a number of compounds and monoclonal antibodies which are now in phase III clinical trials.

John is currently visiting Professor at the NHLI, St Mary's Campus, Imperial College London, working with Professor Peter Openshaw. In addition he works with pharmaceutical and biotechnology companies in Europe as well as not-for-profit organisations such as Bill and Melinda Gates Foundation (Seattle), Drugs for Neglected Diseases Initiative (DNDi) Geneva, and Drug Discovery and Development Centre (H3-D), Capetown.

Robert Peach PhD

NON-EXECUTIVE DIRECTOR

Dr Peach has over 25 years of drug discovery and development experience in the Pharmaceutical and Biotechnology industry. In 2009 he co-founded Receptos, becoming Chief Scientific Officer and raising $59M in venture capital and $800M in an IPO and three subsequent follow-on offerings. In August 2015 Receptos was acquired by Celgene for $7.8B. Robert held senior executive and scientific positions in other companies including Apoptos, Biogen Idec, IDEC and Bristol-Myers Squibb, supporting in-licensing, acquisition and venture investments. His extensive drug discovery and development experience in autoimmune and inflammatory diseases, and cancer has resulted in multiple drugs entering clinical trials and 3 registered drugs. He currently serves on the Board of Directors of Innate Immunotherapeutics and Avalia Immunotherapies and is a consultant for several other biotechnology companies. Robert is the co-author of 70 scientific publications and book chapters, and 17 patents. He was educated at the University of Canterbury and the University of Otago, New Zealand.

Sam Cobb

- Sam is the founding CEO of AdAlta and has over fifteen years' experience in business development and commercialisation of early stage scientific technologies.
- Prior to AdAlta, Sam was the Business Development Director at the Co-operative Research Centre for Diagnostics. Sam has also worked for the biotech start up companies Sensologix Inc and Nephrogenix Pty Ltd and at the University of Queensland's technology commercialisation companies, Uniquest Pty Ltd and IMBcom Pty Ltd.
- Sam has a Bachelor of Science, a Masters of Intellectual Property Law and has completed the Australian Institute of Company Directors course.

AdAlta

next generation protein therapeutics

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

Analyst Briefing, February 2018

Sam Cobb, CEO and Managing Director

AdAlta Limited (ASX:1AD)

s.cobb@adalta.com.au

Disclaimer

Investment in AdAlta is subject to investment risk, including possible loss of income and capital invested. AdAlta does not guarantee any particular rate of return or performance, nor do they guarantee the repayment of capital.

This presentation is not an offer or invitation for subscription or purchase of or a recommendation of securities. It does not take into account the investment objectives, financial situation and particular needs of the investor. Before making any investment in AdAlta, the investor or prospective investor should consider whether such an investment is appropriate to their particular investment needs, objectives and financial circumstances and consult an investment advisor if necessary.

This presentation may contain forward-looking statements regarding the potential of the Company's projects and interests and the development and therapeutic potential of the company's research and development. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercialising drugs that are safe and effective for use as human therapeutics and the financing of such activities. There is no guarantee that the Company's research and development projects and interests (where applicable) will receive regulatory approvals or prove to be commercially successful in the future. Actual results of further research could differ from those projected or detailed in this presentation. As a result, you are cautioned not to rely on forward-looking statements. Consideration should be given to these and other risks concerning research and development programs referred to in this presentation.

Corporate and investment summary

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.

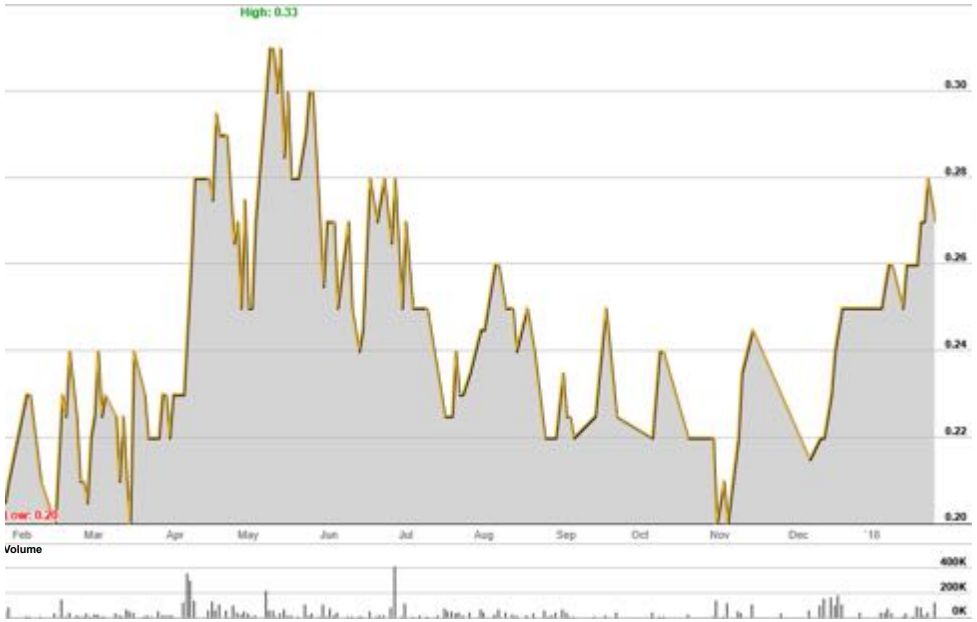
Investment highlights

- Initial focus on treating fibrosis – high unmet medical need
- Advanced lead fibrosis drug candidate AD-114 with significant pre-clinical validation
- Fully funded for phase 1 development of lead fibrosis drug and i-body pipeline
- Orphan drug designation granted by US FDA for AD-114
- Early commercialisation potential
- Experienced team with strong track record of drug development and ability to deliver

Financial position

Key Financial Details	
ASX code	1AD
Share price (31st January 2017)	AU$0.295
Market capitalisation	AU$30.4m
Shares on issue*	101,845,845
Escrowed shares (August 2018)	24,000,000
Options on issue	3,690,866
Current cash (30 December 17)	AU$5.26m
Trading range (12 months)	AU$0.325 to $0.20
Average daily volume	72,993

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%



AdAlta

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

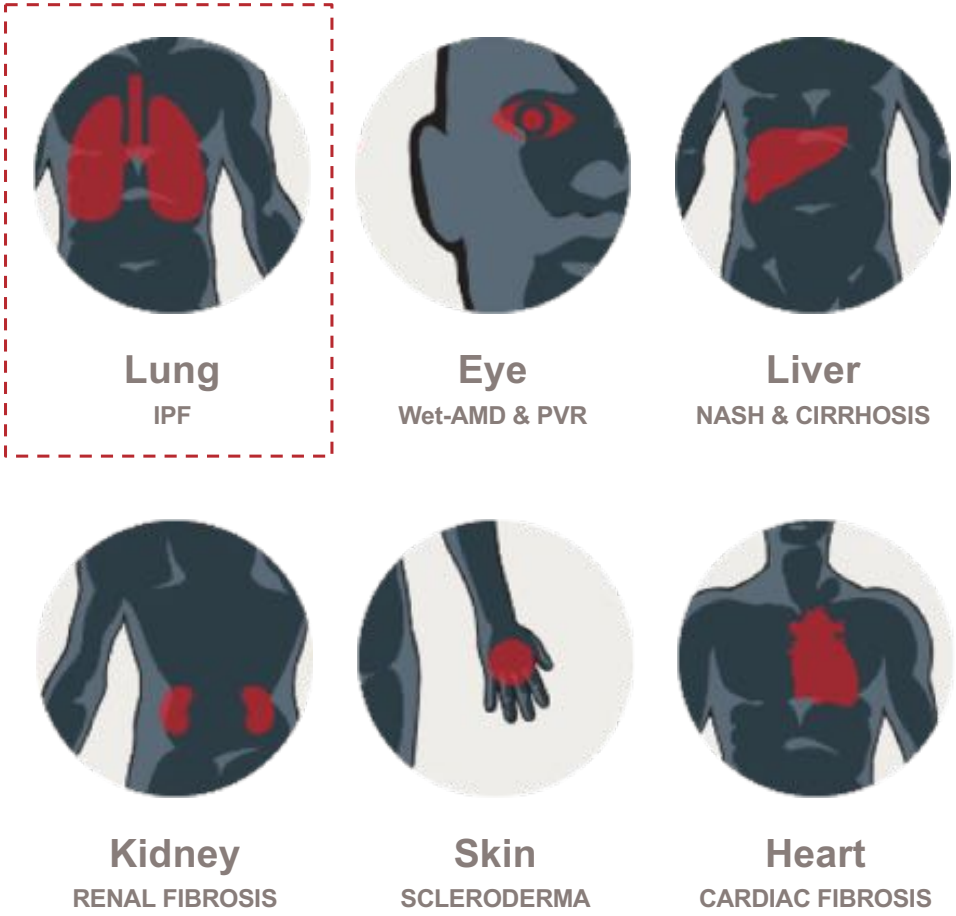
i-body human protein scaffold

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

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



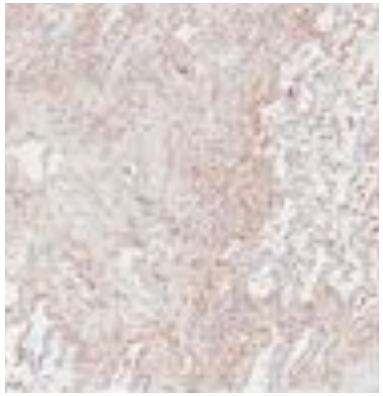
CXCR4 increased in disease

- IPF diseased lung tissue has increased CXCR4 expression compared with normal lung tissues
- Significant CXCR4 expression is present in fibrotic regions of the lung including hyperplastic epithelium of honeycomb cysts, within mucus plugs, and immediately adjacent to fibroblastic foci of IPF diseased lung tissue. CXCR4 can also be seen lining thickened interstitium and within fibrotic interstitial tissue.

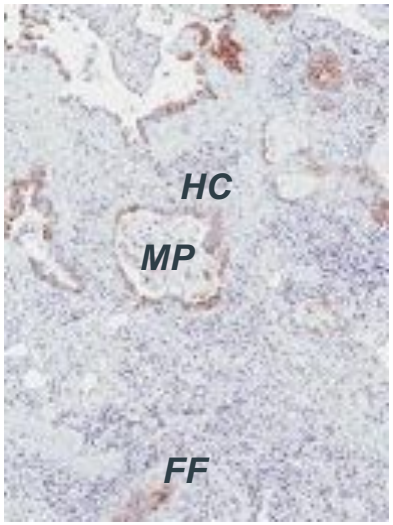
CXCR4 is shown to be increased in diseased IPF tissue and not present in normal lung tissue

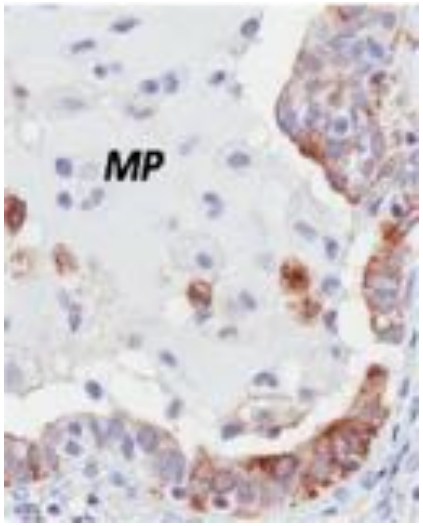
Normal human lung tissue

Diseased IPF lung tissue



Diseased IPF lung tissue

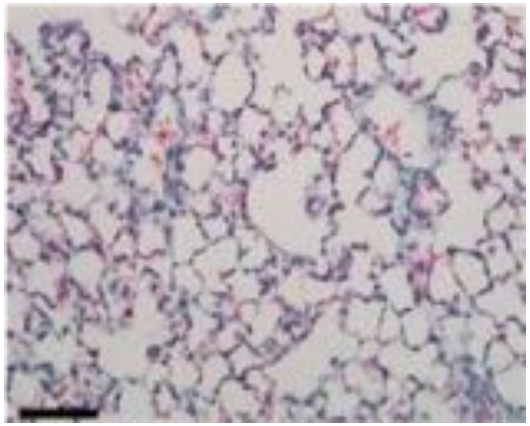




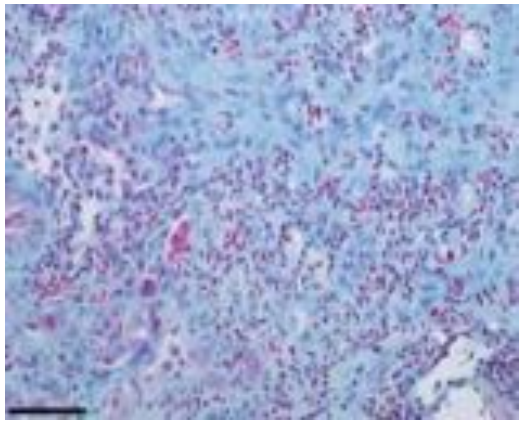
AdAlta

AD-114 prevents lung fibrosis in Bleomycin mouse model

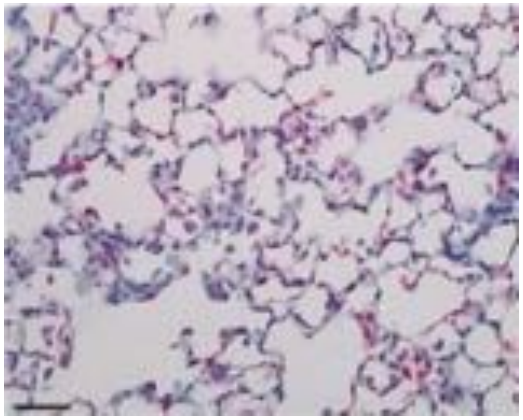
Extensive pre-clinical AD-114 studies have demonstrated positive *in vitro* (in the lab) and *in vivo* (in animals) data



Normal lung tissue



IPF lung tissue
(lung disease mouse model)

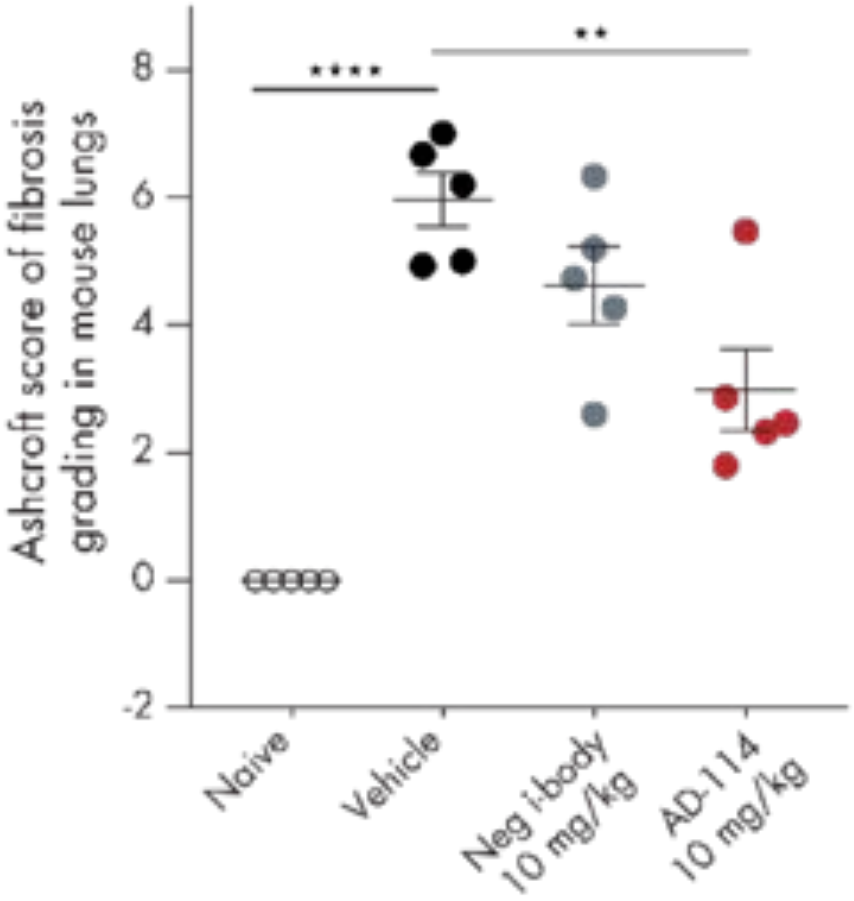


IPF lung tissue + AD-114 dosed for 21 days
(lung disease mouse model)

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 prevents fibrosis in Bleomycin mouse model

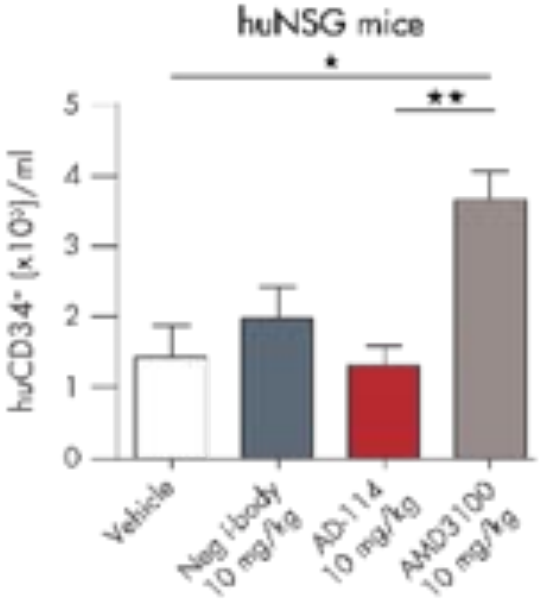
- AD-114 significantly reduced the Ashcroft score compared to the Bleomycin treated mice
- The negative i-body at the same dose as AD-114 had no significant effect on preventing fibrosis



AdAlta

AD-114: novel *in vitro* and *in vivo* activity

- AD-114 does not mobilize stem cells in humanised mouse model or in non-human primates unlike AMD3100 (Mozobil), which mobilised stem cells

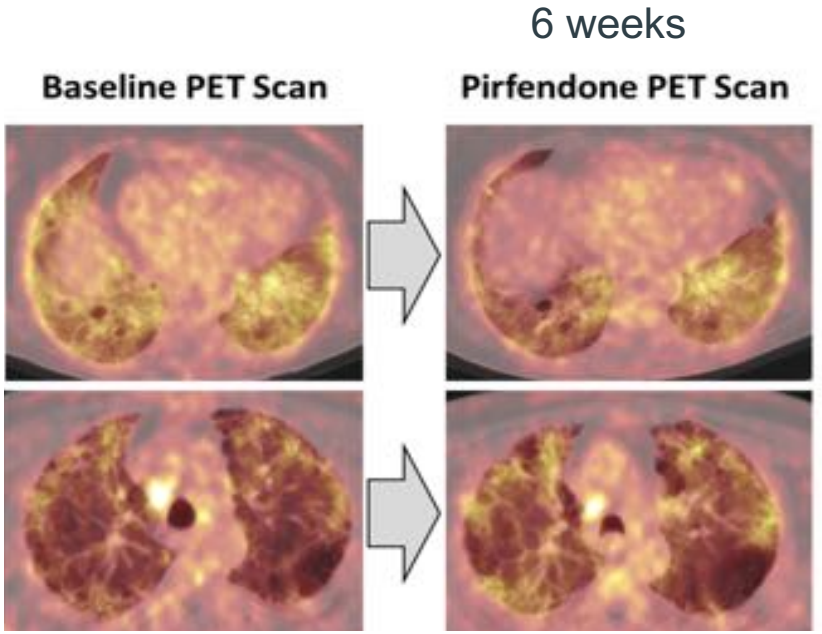


- AD-114 specifically inhibits migration of diseased IPF fibroblasts but does not have any effect on normal fibroblasts unlike AMD3100, which had no activity with normal or diseased IPF fibroblasts

MIGRATION	No effect on normal fibroblasts	Inhibits IPF fibroblasts
i-body AD-114	✔	✔
Nintedanib (Boehringer)	✗	✔
Pirfenidone (Roche)	✔	✗
Other CXCR4 drug (AMD3100)	✔	✗

CXCR4 as a biomarker in IPF

- Strong CXCR4 expression from PET imaging agent, correlated with areas of honeycombing (associated with IPF) and with clinical parameters known to be predictive of outcome in IPF
  - Patient A (top panels) had lower expression of CXCR4 at 6 weeks and responded to Pirfenidone treatment with lung function improvement
  - Patient B (bottom panels) had a high expression of CXCR4 at 6 weeks and did not respond to Pirfenidone treatment, with no lung function improvement



REF: Prasse A, et al. American Journal of Respiratory and Critical Care Medicine 2017;195:A7678

CXCR4 imaging may have a role in monitoring disease progression and may predict response to treatment with Pirfenidone

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 $1.4billion 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

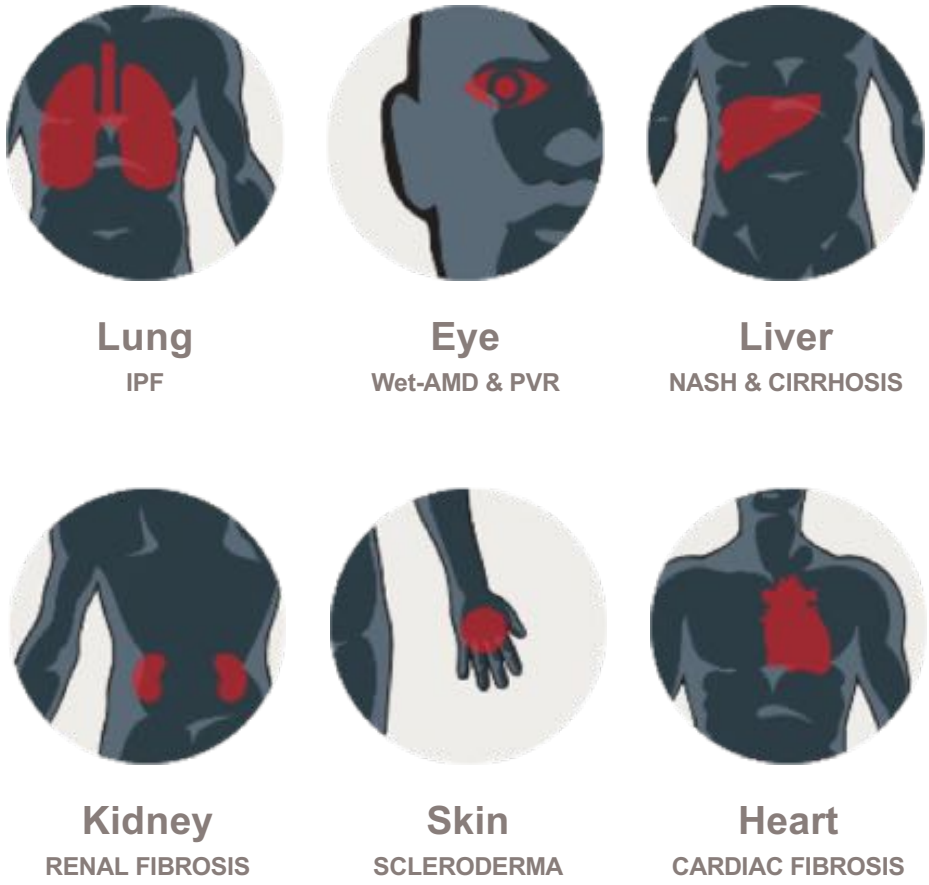
AD-114 has broad application in treating fibrosis

AdAlta data shows that AD-114 can improve fibrosis across a range of fibrotic diseases

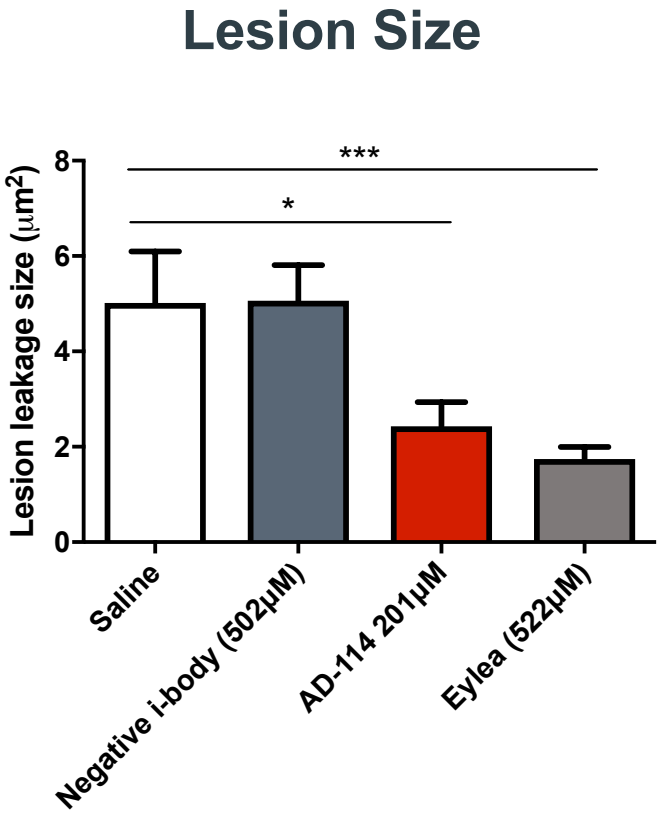
- **LUNG:** Idiopathic Pulmonary Fibrosis
- **EYE:** Wet Age Related Macular Degeneration
- **LIVER:** NASH
- **SKIN:** Hypertrophic scar
- **KIDNEY:** Chronic Kidney Disease

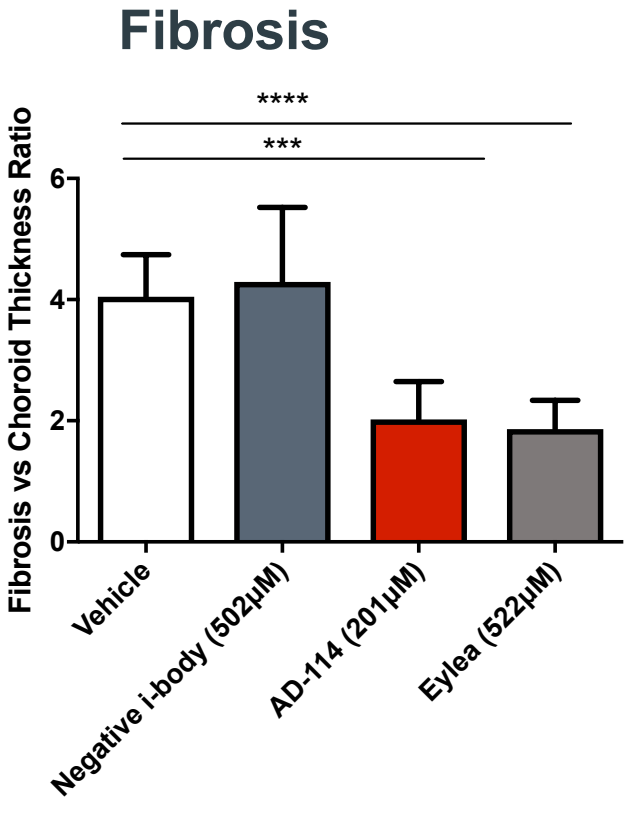
AD-114 has demonstrated broad anti-fibrotic and anti-inflammatory effects in several animal models of disease and with human tissues

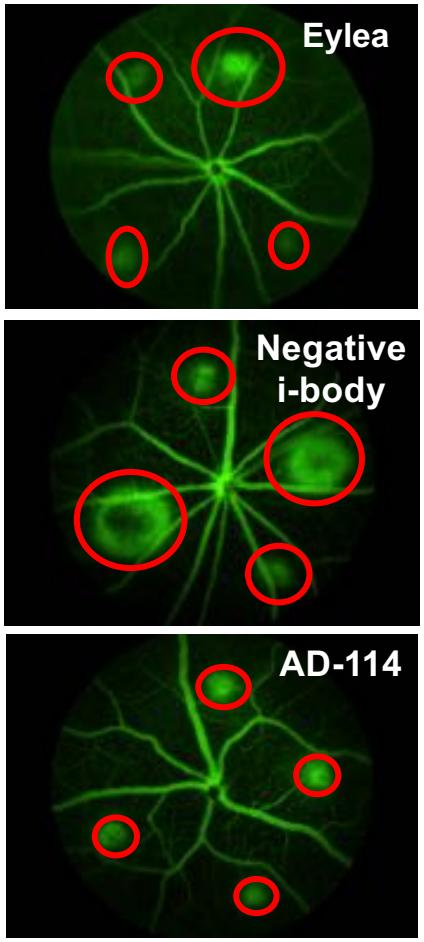
AD-114 has demonstrated safety in non-human primate studies



AD-114 reduces fibrosis in mouse wet-AMD eye model





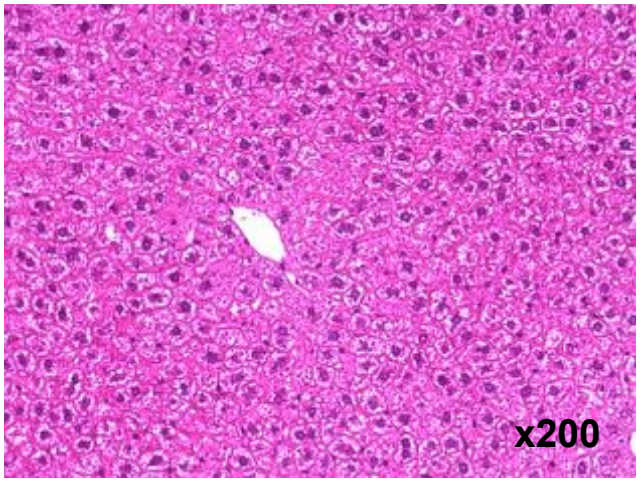


AdAlta

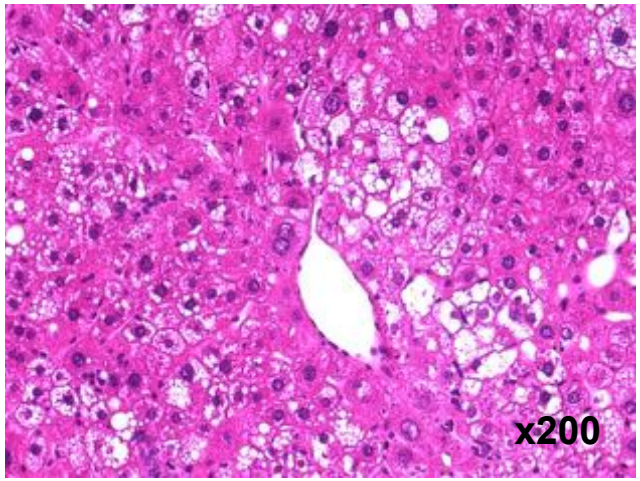
AD-114 prevents fibrosis in a mouse model of liver fibrosis

Therapeutic setting

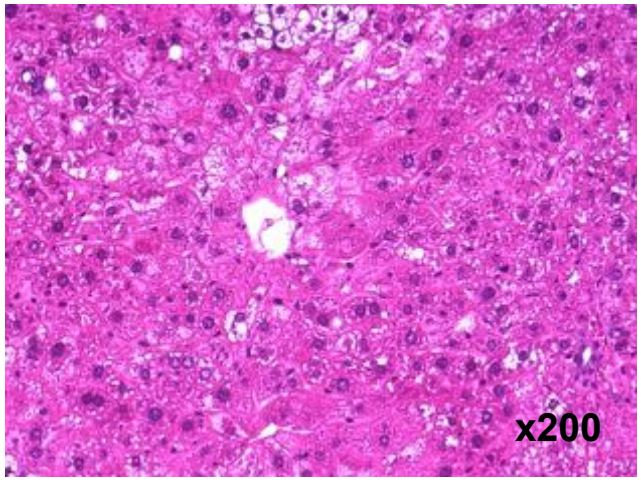
Stelic Institute & Co., Inc.



Normal liver tissue



NASH liver tissue
(liver disease mouse model)

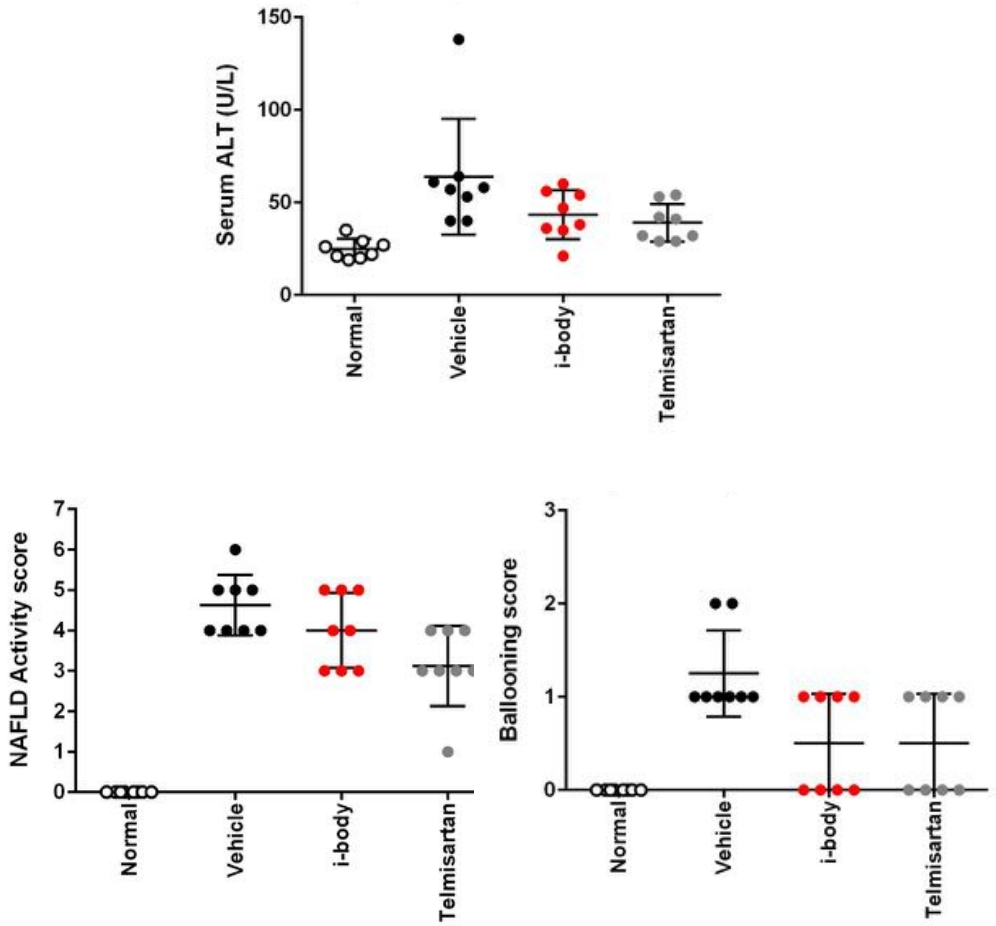


NASH liver tissue + AD-114 dosed for 21 days
(liver disease mouse model)

AD-114 significantly reduces hepatocellular ballooning, a key feature required for the diagnosis of NASH

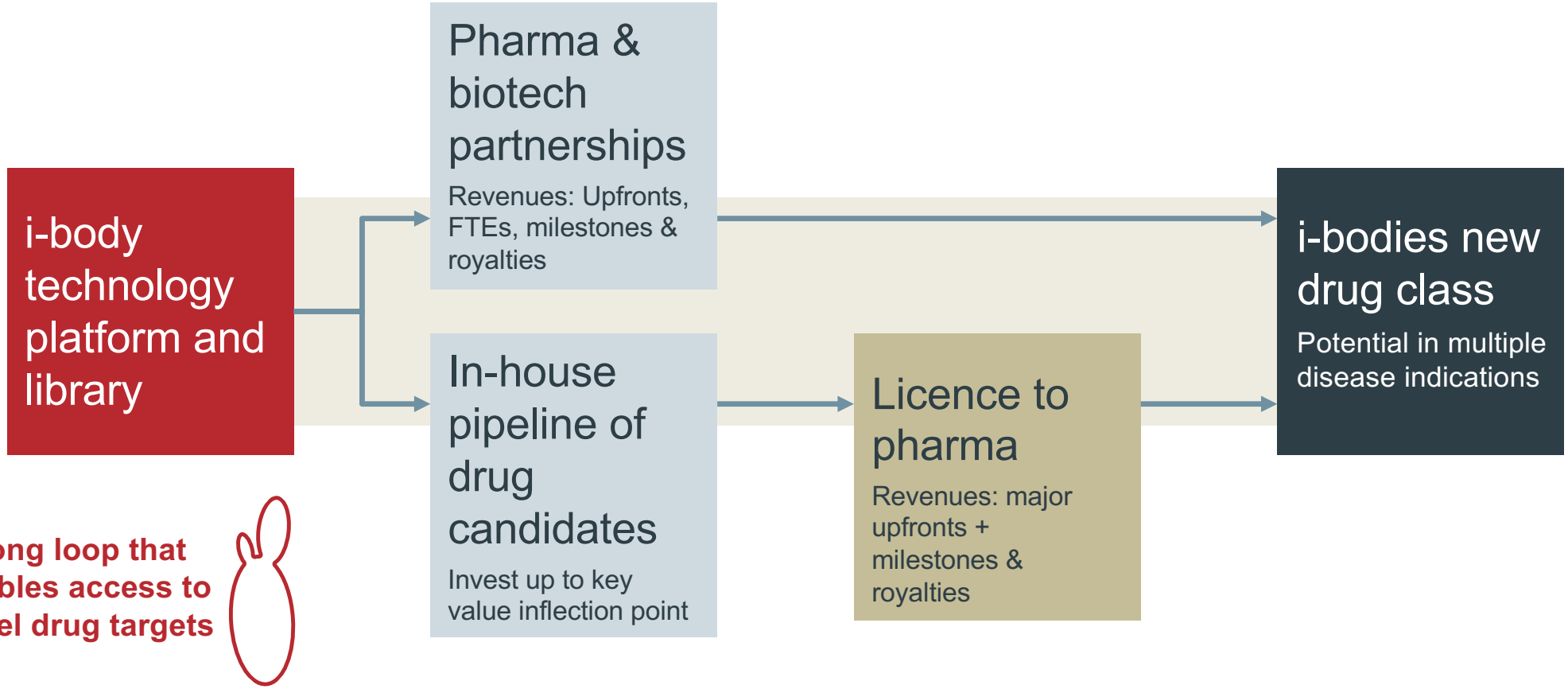
AD-114 prevents fibrosis in a mouse model of liver fibrosis

- AD-114 decreased serum ALT levels and non-alcoholic fatty liver disease (NAFLD) score compared with the vehicle or disease model group
- The improvement in serum ALT levels suggests that i-body ameliorated hepatocellular injury and inflammation preventing progression of disease
- Hepatocyte ballooning was significantly decreased compared with the vehicle or diseased group
- AD-114 possess hepatoprotective and anti-NASH effects



AdAlta

AdAlta business model – strategy to create value



Market benchmarks

Fibrosis lead AD-114	adheron THERAPEUTICS Sep-15 acquired by Roche $105m + $475m milestones phase I asset	Promedior 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	arGEN-X April-16 with Abbvie $40m upfront + $645m milestones & royalties	pieris May -17 with AZ $58m upfront + $2.1b milestones & royalties	Ablynx July-17 with Sanofi €31m upfront + €2.4b milestones & royalties
GPCRs	HEPTARES therapeutics Acquired Feb-15 by Sosei $400m Phase Ib asset + 7 pre-clinical leads	receptos Acquired by Celgene July-15 $8b Ph III, Ph II and GPCR platform	Ablynx April-16 with Boehringer €8m payment for Ph1 GPCR nanobody + €125m milestones & royalties

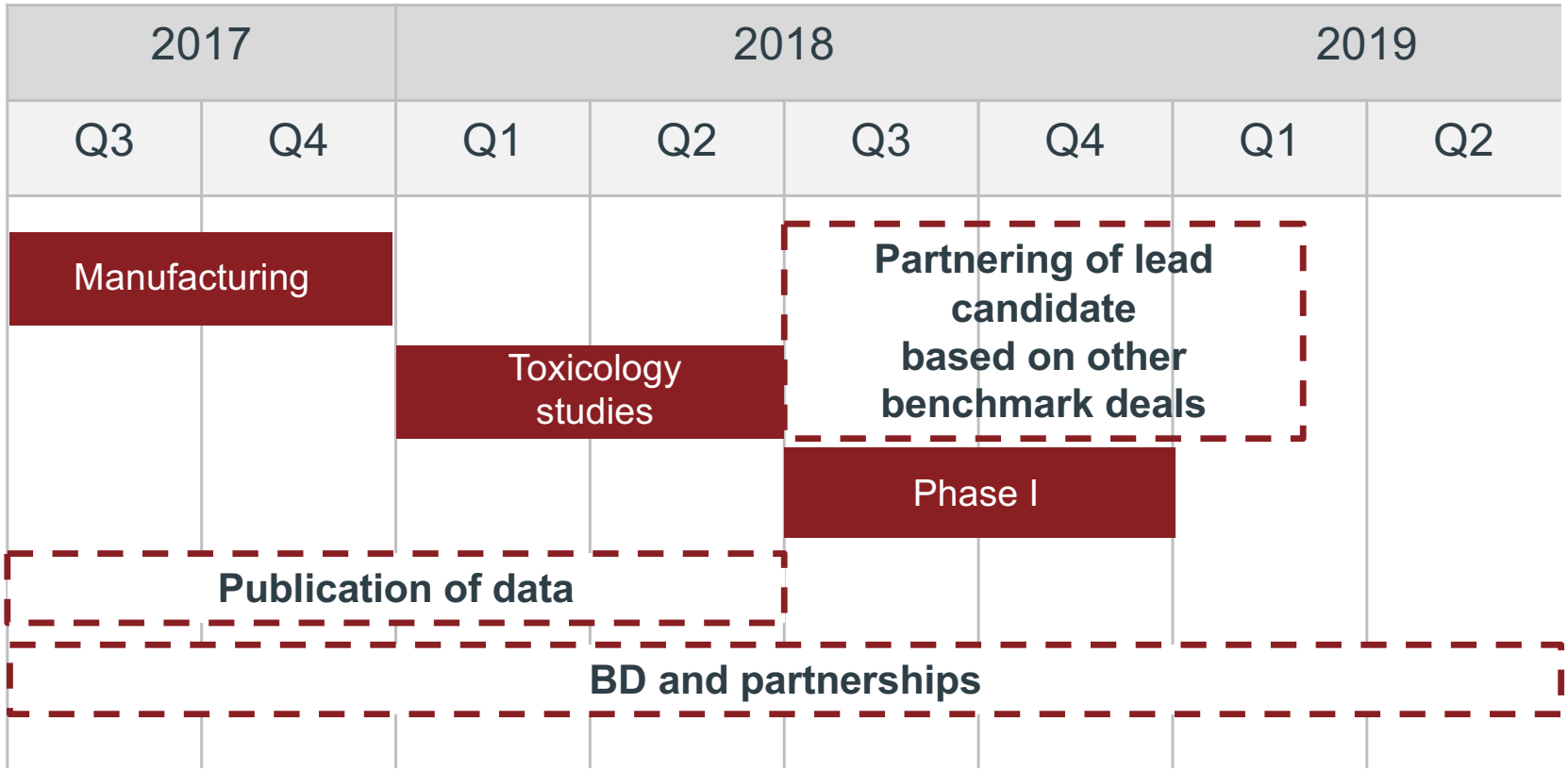
2017 Highlights

- Manufacturing agreement of AD-114 kicked off with Fuji
- Innovation Connection Grant with Alfred Health; a collaboration with local IPF clinicians to evaluate AD-114 as a biomarker
- Presented at a number of international conferences including Discovery on Target, Bio Europe, Biotech Showcase (JPMorgan), ARVO, Bioshares, IPF Summit
- Strengthened Board and SAB
- Orphan Drug Designation IPF USA FDA
- XL protein collaboration for half life extension technology for AD-114
- Crossbeta license deal of shark antibody for Alzheimer's treatment
- SIEF Grant for i-body pipeline development
- Fibrosis Symposium February 2017 bringing clinicians and investors together

Increasing global recognition and engagement

- Interest in AD-114 led to AdAlta's CEO Sam Cobb being invited to present at the inaugural IPF Summit in the US, alongside big pharma in August 2017
- This activity was followed by CSO, A/Prof Mick Foley speaking at the Anti-Fibrotic Drug Development Summit in Boston in November 2017
- To continue to drive interest in AdAlta's programs and interest in IPF, integrated campaigns were run across AdAlta's own media channels in 2017 throwing a spotlight on IPF and the unmet medical need that exists around the disease

AD-114 development: key milestones



Expected news flow next 12 months

H1 2017	✓	Orphan Drug Designation (US FDA)
	✓	Data available from AD-114 NASH animal studies
	✓	Manufactured material for toxicology testing available
H2 2017	✓	Additional grants to support pre-clinical development of AD-114 including NHMRC Development Grant with Melbourne University, Innovation Connection Grant with Alfred Health and NHMRC Project grant with University of Sydney
	✓	Completion of additional pre-clinical animal models in diseased of the lung, kidney, skin; strengthening broad anti-fibrotic data package of AD-114
	✓	AD-114 pharmacokinetics (half life) and toxicology results in 3 non-human primate studies
	✓	Presentation of AD-114 data at multiple fibrosis conferences
H1 2018	▶	Update on manufacturing
	▶	4 week NHP toxicology study
	▶	Publication of lung data
H2 2018	▶	Phase I study with AD-114

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 Paul MacLeman: Chairman

Director of CMAX Clinical Research Pty Ltd and Protec Groupe

Founded biologics companies, experienced ASX listed executive

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

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)

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

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

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

Steve Felstead: clinical advisor

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

Developed Zithromax, Vfend, Celsentri, Viagra

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.

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

AdAlta summary

- 2018 major milestones: phase I clinical trials of AD-114 in lung fibrosis and development of i-body pipeline
- Initial focus on treating Idiopathic Pulmonary Fibrosis (IPF) and other fibrotic diseases - high unmet clinical need
- AD-114 has significant pre-clinical validation demonstrating broad anti-fibrotic and anti-inflammatory effects as well as safety
- AD-114 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-114 development and secure technology platform partnerships / product licensing deals

AdAlta

next generation protein therapeutics

Sam Cobb, CEO

AdAlta Limited (ASX:1AD)

Email: s.cobb@adalta.com.au

Web: **www.adalta.com.au**

Twitter: **@AdAltaCEO**

Linkedin: **AdAlta Ltd**