AdAlta
next generation protein therapeutics

Next generation protein and cell therapies: solutions to debilitating diseases

Tim Oldham PhD, CEO and Managing Director, AdAlta (ASX:1AD)

Overview for investors, 26 October 2023

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AdAlta (ASX:1AD) business and focus

Purpose: i-body® targeting for next generation therapeutics

Going where antibodies can't to produce high-value, next generation protein and cell therapies for debilitating diseases

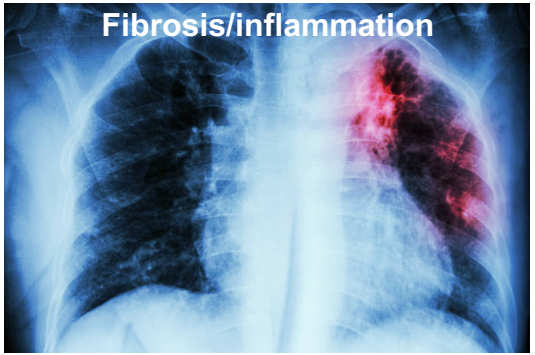
Discovery business

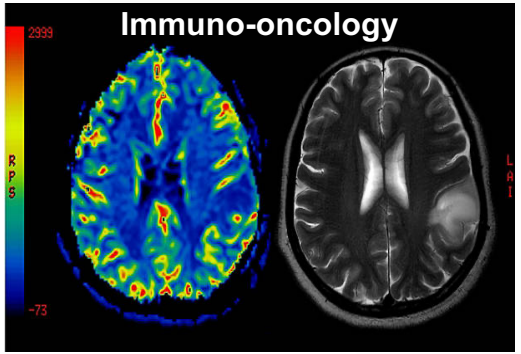
i-body® "inventory" of high value product candidates for development or licensing

i-body® platform + in-house discovery team

Product development business

Product candidates progressing through value-adding development milestones for out-licensing or co-development

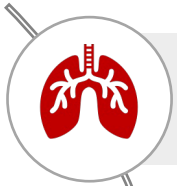




Experienced leaders, in-house protein engineering + cost effective Australian location

Progressing multiple transaction opportunities

AdAlta's portfolio: high value therapeutics and a platform to help other companies address challenging diseases in fibrosis and immuno-oncology



Fibrosis: degenerative, progressive, fatal

AdAlta's AD-214 could meet a desperate need for new approaches for debilitating diseases of the lung (US$4.3b), kidney (US$10b) and eye (US$15b)

Comparator licensing transactions: >$45m up front; >$320m milestones

CAR-T cell therapy providing new hope… for blood cancer patients so far

AdAlta and Carina's i-CAR-T cells could offer the same hope for solid tumour patients (US$20b by end of decade)

Comparator licensing transactions: >$10m up front; >$300m milestones

Immuno-oncology drugs revolutionising cancer treatment… for some

AdAlta and GE Healthcare's GZMB i-PET imaging agent could identify responders early (US$6b)

Comparator product revenue potential: >$400m pa

Traditional antibodies can't do everything!

AdAlta's i-bodies® are a differentiated drug discovery platform partners can leverage for difficult diseases

AD-214: new hope for fibrotic disease patients

The need: better outcomes for Idiopathic Pulmonary Fibrosis (IPF) and other fibrotic diseases

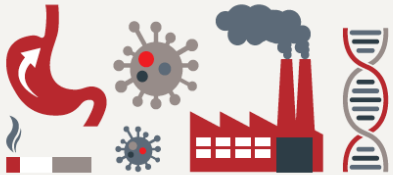
IPF prevalence

>490,000 worldwide

50% of sufferers die within 3-5 years following diagnosis

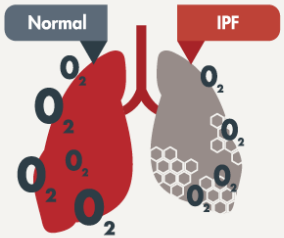
>100,000 pa

Causes



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

Pathology



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

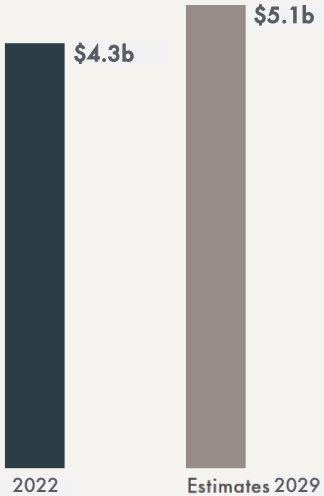
Current IPF treatments

Pirfenidone **Nintedanib**

Roche Boehringer Ingelheim

Slow, but do not halt progression. Serious side effects limit compliance, tolerability

IPF Therapy Sales (US$)



Source: GlobalData,[2] company financial reports, AdAlta analysis

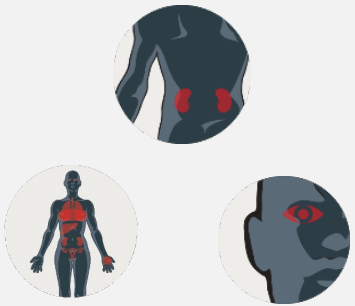
45% of developed world deaths have a chronic fibrosis component

Every organ vulnerable:

- Lung (**US$4b**)
- Kidney (**US$10b**)
- Eye (**US$15b**)
- Cancer (**US$1b** each)[3]

New drivers of incidence

- "Long COVID"[1]
- Re-emergence of silicosis



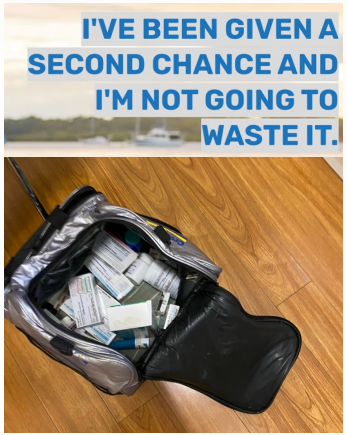
[1] PM George, et al, "Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy", Lancet published online May 15, 2020.
[2] GlobalData, Idiopathic Pulmonary Fibrosis: Competitive Landscape, April 2023
[3] GlobaData, disease analysis reports

Bill van Nierop: IPF survivor on the challenge of living with IPF

"… sadly I am one of a few who can actually relate to the lived experience with and without PF …"

"***You see our symptoms are basically an ongoing internal struggle to breathe freely*** … and it's invisible to all, including family, friends and the general community."

"I talked with a 60 something grandmother, who really enjoyed days looking after grandkids, but as disease progressed she found sometimes she needed to reduce the time a bit. You won't believe that her daughter in law suggested she would just bring them around less, 'you're always tired but you look really well', so I won't bother you as much. Shattering to the poor woman obviously, but again demonstrates the absolute lack of understanding of this debilitating disease. ***Looks well, so can't be too ill, except she's struggling to breathe and is on a journey with an inevitable end***."



Source: Bill van Nierop, https://www.facebook.com/kayakforlungs 28 September 2023

https://www.longkayakforlungs.com.au/

AdAlta's solution: AD-214 is being readied for Phase II clinical studies and partnering

A$45m investment to date has built strong value proposition

First in class molecule targeting validated mode of action in fibrotic disease
- ✓ Competitively positioned

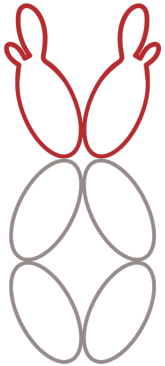
Pre-clinical efficacy in multiple animal models of fibrotic disease
- ✓ Led by Idiopathic Pulmonary Fibrosis (IPF): TAM US$4.3b
- ✓ Multiple indication potential: kidney, eye, cancer

Phase I successfully completed, extension underway
- ✓ Well tolerated, evidence of target binding

Target IV product profile verified; next generation SC product profile identified
- ✓ Intravenous (IV) every two weeks; subcutaneous (SC) every week

Strong intellectual property, regulatory position
- ✓ Patents protecting asset to 2036 and beyond
- ✓ US FDA Orphan Drug Designation for IPF
- ✓ 10-12 years market exclusivity (US, EU)

Next steps to realise value

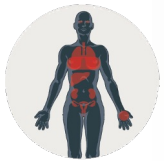


Phase I extension study underway
- Extend safety to higher, target doses for Phase II
- Add data to inform partnering

Planning for Phase II in lung fibrosis
- Intravenous (IV) route: fastest to proof of concept
- Subcutaneous (SC) route: parallel formulation development for Phase III use

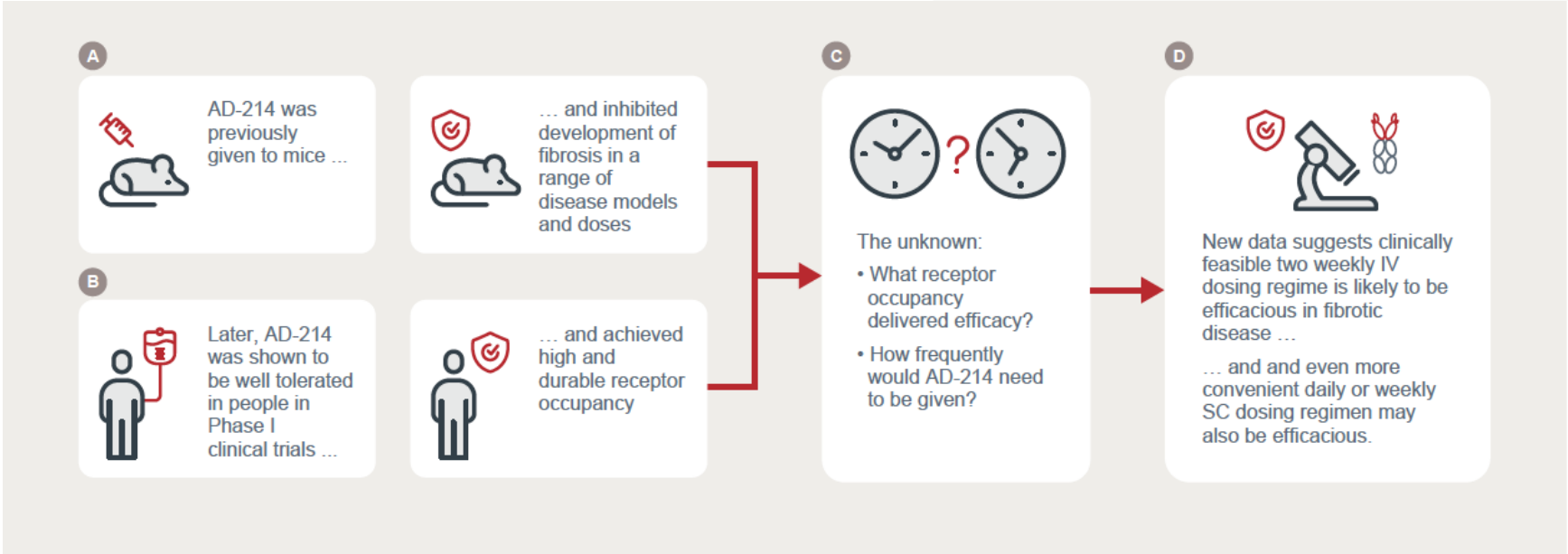
Advancing multiple Phase II financing options
- Out-licensing
- Co-investment/co-development



Sources: GlobalData; www.clinicaltrials.gov (accessed 7 and 17 October 2022)

Recent achievements #1: Potential IV efficacy verified at clinical dosing regimens; potential SC product identified



A. AD-214 has demonstrated efficacy in multiple animal models of fibrotic disease
B. In humans, AD-214 was able to maintain more than 60% receptor occupancy (blocking) for up to three weeks after IV infusion, depending on dose

C. Is this sufficient to achieve efficacy for target IV product profile (two weeks between doses)? Is a next generation SC product profile possible?

D. YES – new data shows that AD-214 does not require 100% receptor occupancy to meaningfully inhibit a model fibrotic process: efficacy of two weekly IV dosing regimens is plausible AND weekly or daily SC dosing regimens appear possible

Source: ASX release 7 July 2023

Recent achievements #2: Phase I extension study supporting partnering and Phase II

AD-214 multidose Phase I extension clinical study

Establishes safety of AD-214 at likely maximum dose to be used in Phase II studies

- ✓ 3x10 mg/kg doses well tolerated with no dose limiting toxicity
- ✓ Continues to demonstrate favourable safety profile
- ▪ 4th dose to confirm no adverse immune response – results Q1'24

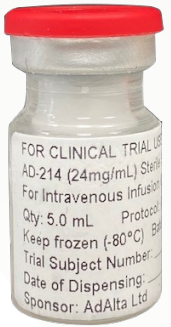
COMMENCED

Better informs dosing levels and schedule for Phase II

- ▪ Interim PK and PD (receptor occupancy) data due end Nov'23

Enhances partnering process

- ✓ Safety, immune response and PK data address typical questions
- ✓ Maintains product development momentum



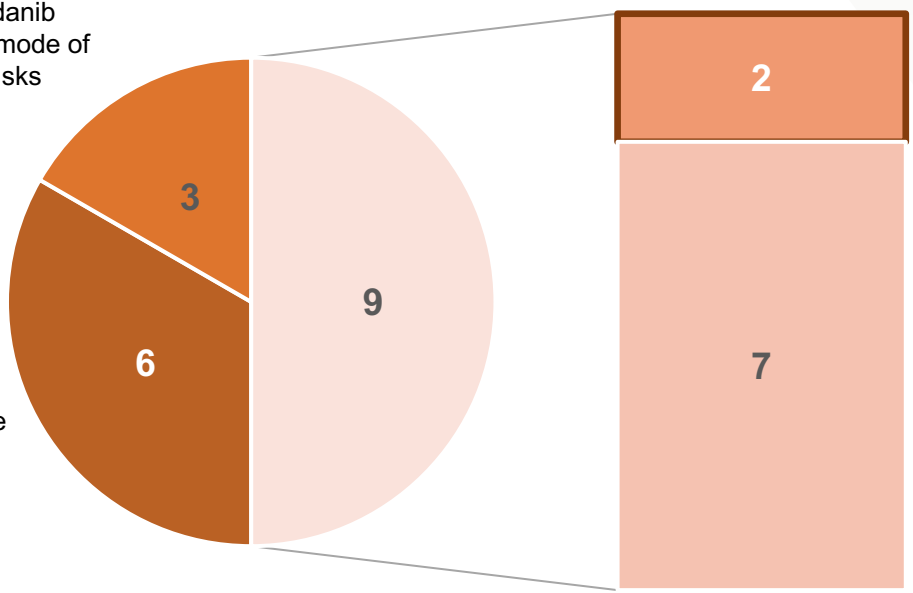
Competitive positioning: AD-214 takes a much needed, differentiated approach to fibrotic disease

18 active product candidates in Phase II or beyond*

AD-214 poised to enter Phase II as one of only three products targeting a novel but validated disease modifying pathway with no prior failures – **and the only product offering antibody-like precision**

Pirfenidone or nintedanib analogues – uncertain mode of action, tolerability risks

Products designed to manage symptoms – not disease modifying



Targeting novel pathways with no clinical failure to date

Targeting novel pathways where there have been prior clinical failures

* Excludes 11 studies categorized as Phase I/II, institution led or with <25 patients per arm which are unlikely to be powered to show efficacy
Source: GlobalData, clinicaltrials.gov, company press releases, AdAlta analysis

The value: pharma companies license fibrosis assets for significant prices: IPF examples

Date	Licensor/target	Licensee/acquirer	Transaction	Upfront payment to licensor	Contingent milestones	Clinical Phase at transaction
Feb 23	Redx	Jounce Therapeutics	Acquisition#	**US$294m**	N/A	2
Jan 23	Daewoong	CSPharmaceuticals 创新进中国	China only license	**US$76m^**	US$336m	2
Aug-22	Kiniksa	Genentech A Member of the Roche Group	License	**US$80m**	US$620m	2
Apr-20	curzion Pharmaceuticals	Horizon	Acquisition*	**US$45m**	Not disclosed	2
Nov-19	Promedior	Roche	License	**US$390m**	US$1,000m	2
Nov-21	Blade Therapeutics	Biotech Acquisition Company	Acquisition#	**US$254m**	N/A	2 (Ready)
Nov-21	OncoArendi Therapeutics	Galápagos	License	**Not disclosed**	€320m	2 (Ready)
Sep-21	Syndax	Incyte	License	**US$152m**	US$602m	2 (Ready)
Feb-21	泰德制药 TIDE PHARMACEUTICAL	Graviton Bioscience Corporation	License	**Not disclosed**	US$517.5m	1
Jul-19	bridgebio	Boehringer Ingelheim	License	**€45m**	€1,100m	1
Oct-22	DJS antibodies	abbvie	Acquisition	**US$255m**	Not disclosed	Pre-clinical (+ platform)

AD-214 almost Phase II ready

Source: Company press releases; * Lead indication was diffuse cutaneous systemic sclerosis which usually evolves into IPF; # Did not complete; ^ Includes development milestones

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Co-developed immuno-oncology programs: i-CAR-cell therapies

The need: multifunctional CAR-cell therapies

Therapy involves re-engineering patient's own immune cells to "see" cancer – **living drug, single dose, potentially curative**

>US$2.6 billion earned in 2022[3]

US$20.3 billion CAR-T market forecast for 2028[1]

6 FDA-approved CAR-T therapies since 2017 transforming outcomes:

Complete response rates: **83%** r/r pALL, **51-65%** r/r LBCL, **78%** r/r MM[4]

… but so far only for blood cancers

90% of cancers are solid tumours: harder to target, harder to access, immune suppressive … needs new multifunctional CAR cell therapies

>50% of CAR-T revenues from solid tumours by 2030[2]

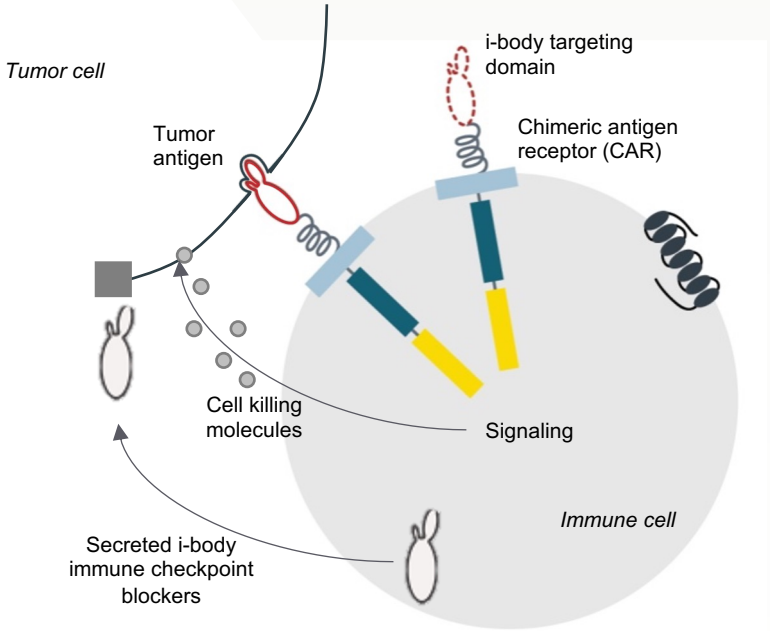
1. Grandview Research, "T-cell Therapy Market Size, Share & Trends Analysis" Feb 2021
2. Polaris Market Research, "CAR-T Cell Therapy Market Share, Size Trends, Industry Analysis Report", June 2021
3. Company websites and financial filings
4. Kymriah, Yescarta and Carvytki prescribing information; r/r = relapsed/refractory; pAML – paediatric acute lymphoblastic leukemia, LBCL = large B cell lymphoma, MM = multiple myeloma

AdAlta's solution: i-bodies enable superior CAR constructs (i-CARs) when combined with partner platforms

Tiny i-bodies take up LESS room in inserted gene, enabling TWICE the engineered functionality

Results in superior, multifunctional i-CAR products

- **Targeting**: novel tumor antigens
- **Targeting**: Dual and bi-specific CARs for enhanced specificity, reduced tumor escape
- **Persistence**: overcome immune suppression "checkpoints"
- **Performance**: stimulate immune cells, enhance trafficking and overcome "exhaustion"



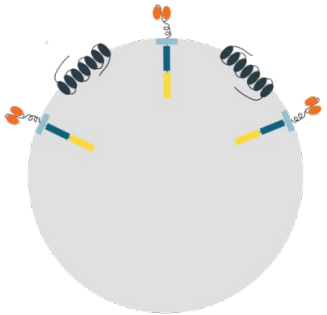
i-CAR-T: Valuable cell therapy partnering potential at pre-clinical proof of concept

AdAlta i-bodies + Carina cell therapy platform

AdAlta next generation protein therapeutics

carina biotech

i-CAR-Ts for solid tumor patients



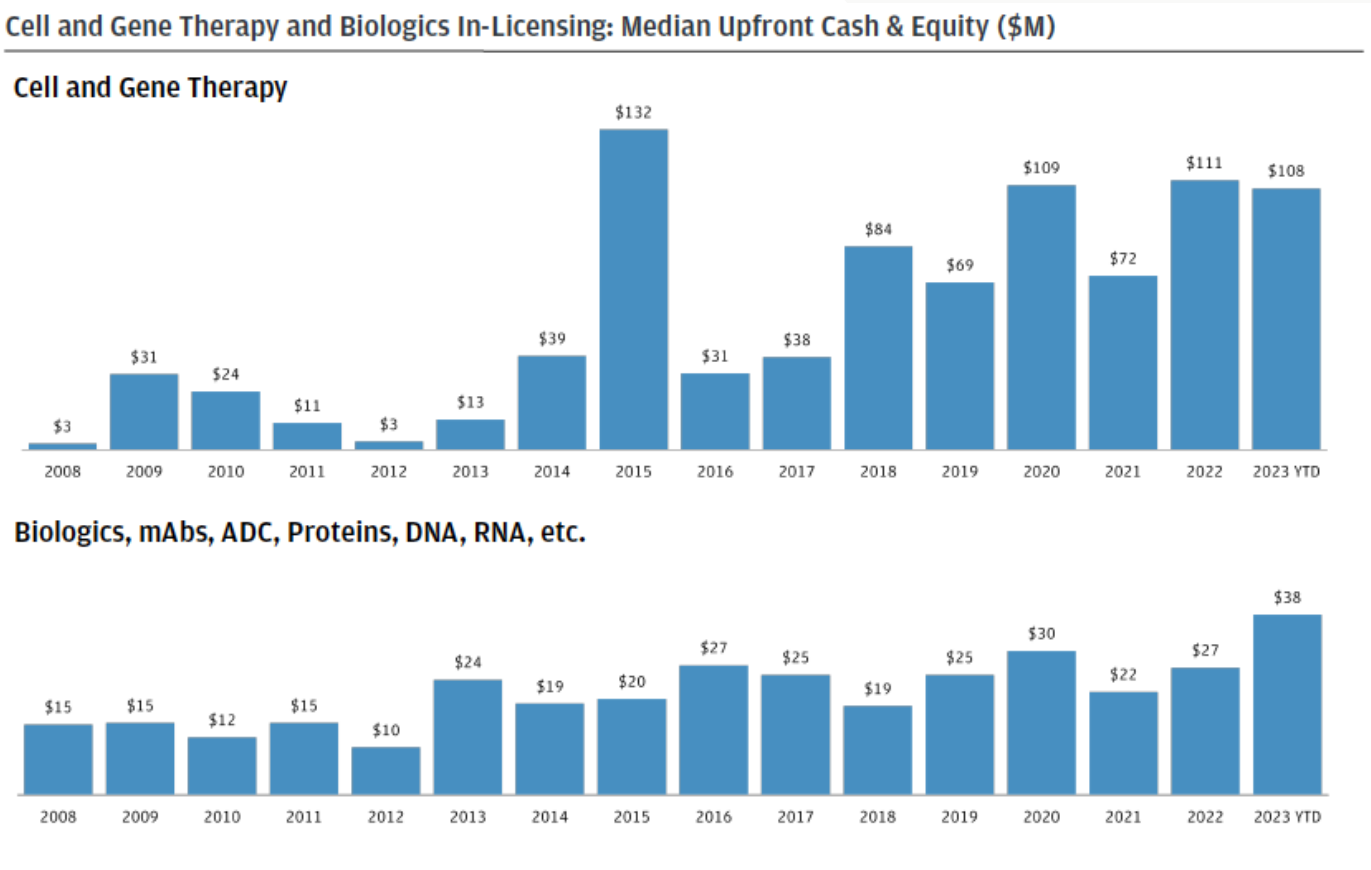
- ✓ i-body® enabled CAR-T (i-CAR-T) cells have successfully demonstrated *in vitro* cancer cell line killing (lysis)[1]
- ✓ Target A: 3 A-i-CAR-T cells progressed to *in vivo* proof of concept
- ✓ Next two targets (targets B and C): i-body discovery commenced Q2 2023

Significant industry interest from potential additional partners

Value could be realized at preclinical PoC

1. ASX release 29 November 2021

The value: cell therapy up front deal value higher than other protein therapeutics



Source: JPMorgan, Q2 2023 Biopharma Licensing and Venture Report, July 2023

J.P.Morgan

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Co-developed immuno-oncology programs: i-PET imaging

The need: Immuno-oncology (I/O) imaging

Immuno-oncology (I/O) drug market is worth **US$95 billion**[1] …

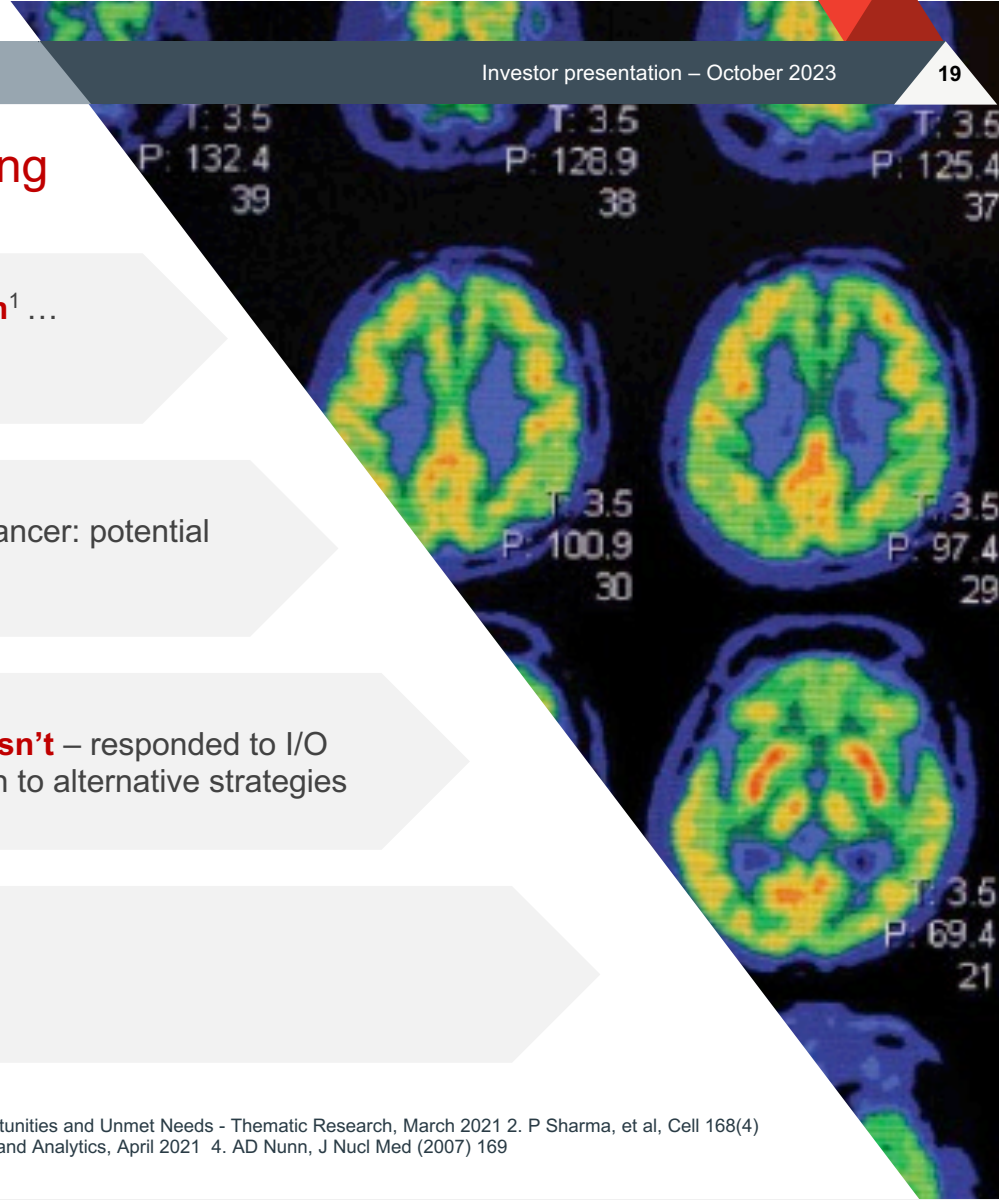
… but only **20-40%** of patients respond[2] to therapy

Granzyme B (GZMB) is produced by immune cells to kill cancer: potential biomarker of I/O drug activation of the immune system

PET imaging GZMB could help identify **who has – and hasn't** – responded to I/O drugs before their tumor progresses: enabling timely switch to alternative strategies

US$6.4billion[3] PET imaging agent market

>US$400m[4] annual sales for largest products



1. 2026 forecast by ResearchandMarkets.com, Immuno-Oncology - Market Analysis, Trends, Opportunities and Unmet Needs - Thematic Research, March 2021 2. P Sharma, et al, Cell 168(4) 707 (2017) 3. 2027 forecast by Global Industry Analysts, Imaging Agents: Global Market Trajectory and Analytics, April 2021 4. AD Nunn, J Nucl Med (2007) 169

AdAlta's solution: funded discovery, shorter timeline to royalties for GZMB i-PET imaging asset

AdAlta i-bodies + GE PET technology = GZMB i-PET asset to evaluate the effectiveness of immuno-oncology drugs

AdAlta next generation protein therapeutics | GE Healthcare

- ✓ Fully funded discovery program plus downstream milestones, royalties
- ✓ i-body optimization, manufacturing development, pre-clinical proof of concept studies continuing
- ✓ Shorter time to royalty revenue than therapeutic product development
- \- Further updates as commercially relevant milestones are achieved

Market feedback confirms value and importance of this target

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The investment opportunity

i-bodies are a powerful drug discovery tool to engage targets that traditional antibodies can't

Small Molecules

Avoid off-target issues of small molecules

Antibodies

~10% the size of human antibodies

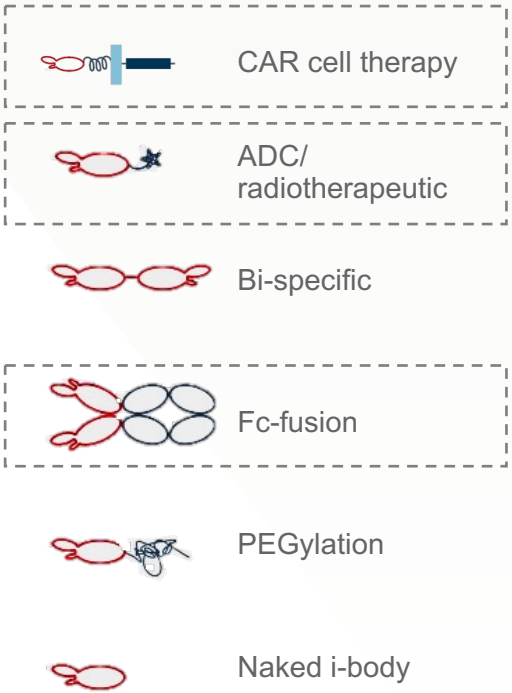
Enables access to novel targets and efficient payload delivery

i-bodies™

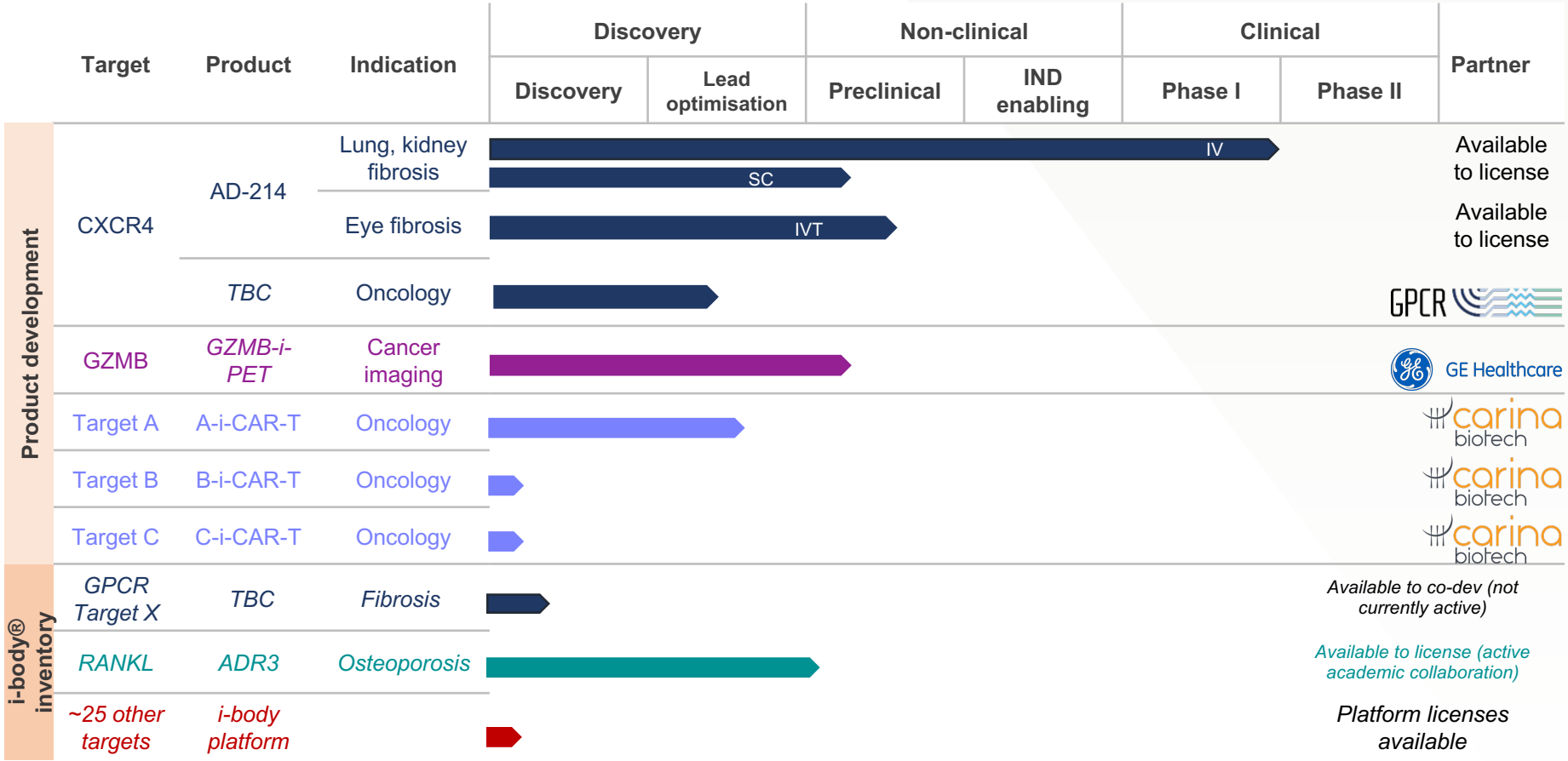
Unique binding capabilities drive unique pharmacology

Flexible, modular formats

Current pipeline focus



AdAlta's pipeline so far: five active assets plus growing i-body® inventory



Partnering momentum increasing to unlock asset value and reduce risk

- Illustrative recent progress

Out-licensing or co-investment for Phase II development

Generating return on investment to date
- 21 active evaluations post BIO2023
- One party testing AD-214 in own assays
- Fielding several co-investment enquiries

AD-214 Phase II

Adding to GEHC, Carina, GPCR Tx
- Focus on GPCRs and i-CAR cell therapy
- GPCR Target X: 2 inbound enquiries at BIO2023 + 6 requests for further information from outreach campaign

AdAlta partnering

In-licensing/acquiring clinical stage assets with i-body® synergies

Inbound assets

i-body® platform

Co-discovery/sponsored research using i-body® platform and "inventory" of new targets

Potential clinical stage pipeline
- Screening criteria: clinical inflection point achievable within two years, i-bodies can support next generation product
- Target: 4-5 assets under review

Upcoming FY24 milestones: AD-214 and i-CAR-T data + potential multiple transaction upside

Strategy	Milestone	Impact
Realise value of AD-214	✓ HREC approval, 1st participant Phase I extension (Q3 23) • Phase I extension (PK/PD Q4 23; full safety Q1 24) • Progress existing partnering discussions (through FY24)	*Generates new data for partnering, shortens Phase II study* *Potential first major ROI (return on investment)*
Extend i-CAR programs	• A-i-CAR-T *in vivo* efficacy studies (H1 24) ✓ Commence discovery on Carina B, C targets (Q2 23) • Progress co-development discussions (through FY24)	*Preclinical PoC; opportunity for early ROI* *Carina pipeline expansion – future value* *Potential non-dilutive financing for future programs*
i-PET progress	• Lead candidate preclinical efficacy (timing not forecast)	*Visibility to product potential, time to royalties*
Invest in i-body™ platform	• i-body2.0 and research excellence program • Evaluate synergistic technology, product transactions	*Maintain competitive advantage* *Expand clinical stage pipeline, accelerate growth, leverage costs and capabilities*

Corporate snapshot

Key financial details (23 Oct 2023)

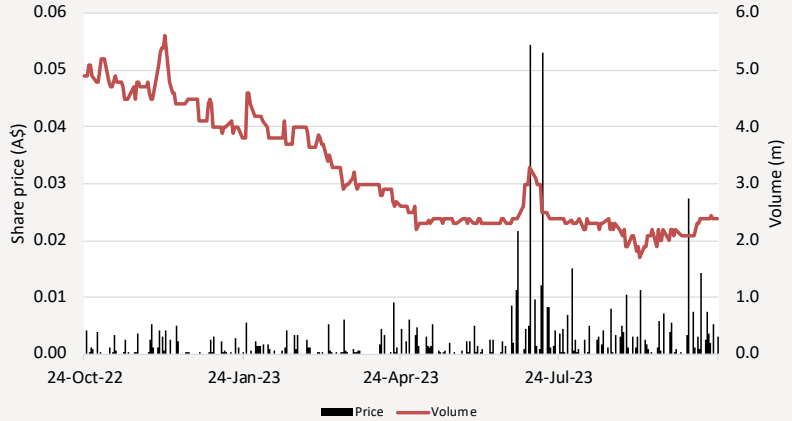
HQ and operations	Melbourne, Australia
Market capitalisation	**A$10.63m**
Share price (12 month closing range)	A$0.024 ($0.017 - 0.056)
12 month return	(51)%
Ordinary Shares (daily volume)	442,804,077 (246,590)
Listed Options	78,075,186
Unlisted Options	14,184,060
Cash (30 September 2023)*	**A$5.57m**

Largest shareholders (12 July 2023)

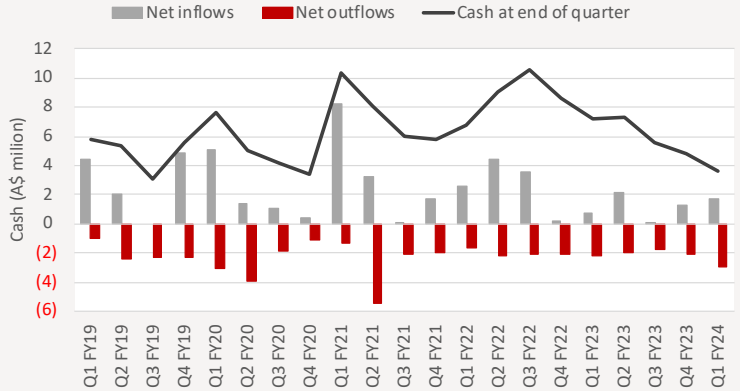
	%
Platinum International Healthcare Fund	18.7
Meurs Group	14.6
FMI Pty Ltd atf Commonwealth of Australia	7.4
Sacavic Pty Ltd	5.9
Radiata Super Pty Ltd	4.3
Other (1,358 total holders)	*49.1*
Total	**100%**

* Excludes $0.38m net proceeds of FY23 R&D Tax Incentive Rebate after repayment of $2m of a $4m loan facility with Victorian Government (facility due for full repayment April 2023)

Share price performance (ASX:1AD) (last 12 months)



Quarterly cash flows (A$ million)



Experienced, in-house team to execute from discovery through product development

BOARD

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CHAIR

Tim Oldham, PhD
CEO & MANAGING DIRECTOR

Robert Peach PhD
INDEPENDENT DIRECTOR

Dr. David Fuller
INDEPENDENT DIRECTOR

EXECUTIVE

Angus Tester, PhD
SENIOR MANAGER, PROJECTS AND PROGRAMS

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PULMONARY DRUG DISCOVERY & DEVELOPMENT

PARTNERS AND KEY CONTRACTORS

IN-HOUSE DISCOVERY & DEVELOPMENT TEAM

8 PhD/MSc Staff + La Trobe Uni location
Skills in protein chemistry, i-body discovery, product development, pre-clinical development

Investment proposition

i-body platform to create value

Strategy: invest to maintain competitive advantage

Fibrosis/inflammation
AD-214: Phase II and partnering in $4.3b market[1]

Strategy: realise near term return on investment

Immuno-oncology
2 co-development collaborations (4 programs) in $20b[2] and $6b[3] markets

Strategy: progress and extend collaborations

Demonstrated product development and partnering expertise

"Blue sky" catalyst opportunities

AD-214 out-licensing/co-investment
Additional platform transactions
Synergistic technology, product transactions

Steady news flow

Attractive current valuation with upside

1. GlobalData, Idiopathic Pulmonary Fibrosis Competitive Landscape, April 2023; kidney and eye fibrosis markets are larger 2. 2028 forecast by Grandview Research, "T-cell Therapy Market Size, Share & Trends Analysis" Feb 2021 3. 2027 forecast by Global Industry Analysts, Imaging Agents: Global Market Trajectory and Analytics, April 2021

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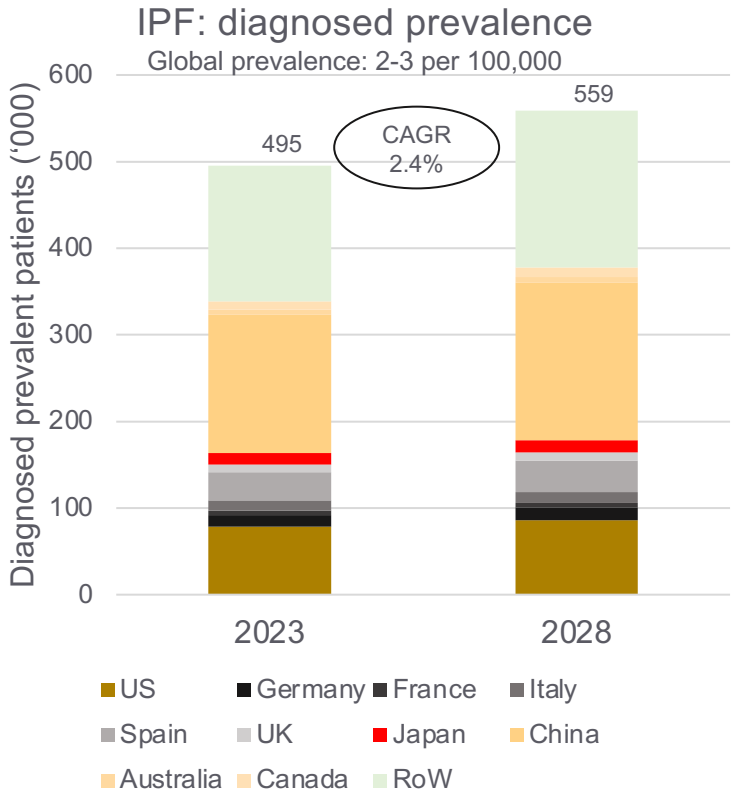
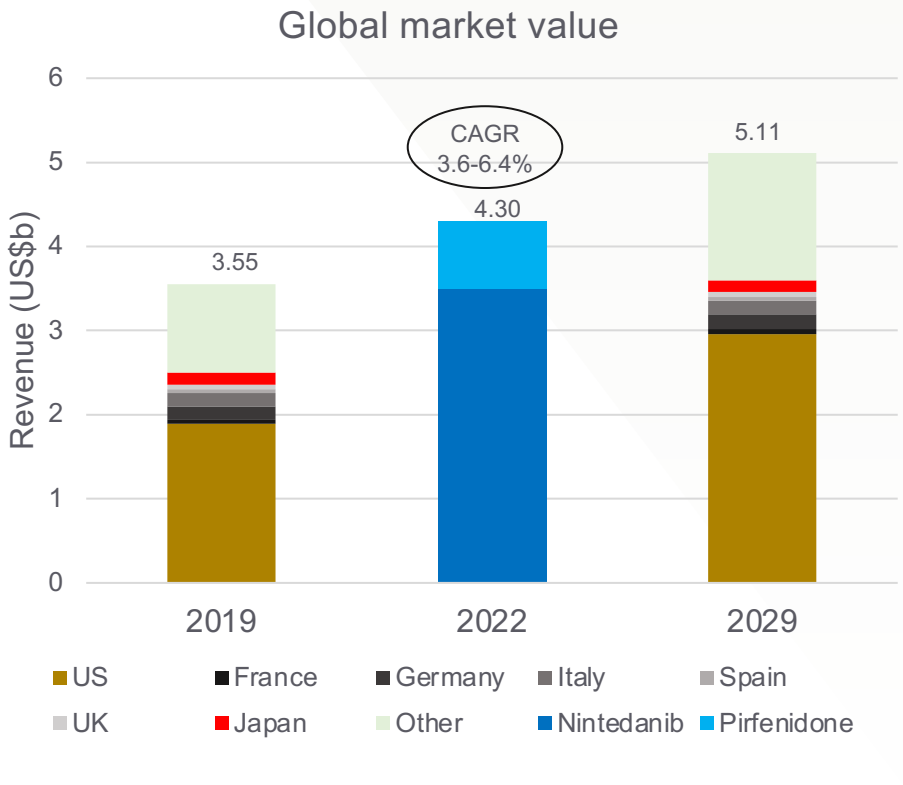
The market opportunity: US market dominates value today, with significant unmet patient needs in China





Source: GlobalData, Roche and Boeringher Ingleheim financial reports, AdAlta analysis

AD-214 is a first in class CXCR4 antagonist designed specifically for fibrotic disease

Product Profile: AD-214	
Disease Area	Fibrosis
Molecule class	Protein therapeutic (i-body-Fc-fusion)
Mode of action	First-in-class CXCR4 antagonist
Indications	Idiopathic Pulmonary Fibrosis and Interstitial Lung Disease (with kidney, eye and cancer indication extension potential)
Route of administration	Target: Intravenous (IV) Next generation: Subcutaneous (SC), inhaled
Clinical stage of development	Phase I complete; extension study under way Preparations for Phase II advancing
Regulatory	Orphan Drug Designation (US FDA) 10-12 years market exclusivity (US and EU)
IP	Composition of matter 2036 (granted) Method of treatment/dosing 2043 (pending)
Manufacturing	cGMP manufacturing at KBI Biopharmaceuticals, USA

Product development strategy

Target intravenous (IV) product profile

IV administration in clinic

Two weeks minimum between infusions: meets minimum product criteria for clinical adoption

Fastest, cheapest to clinical proof of concept

Progress to Phase II

Potential subcutaneous (SC) product profile

Patient self administration at home (like diabetes, arthritis)

Weekly or daily injections: maximum convenience, minimum costs

Enhanced market share, reduced COGS

Develop formulation, progress to Phase II

Choice of formulation to take through to Phase III

Based on relative success of each development

AD-214 offers a superior safety profile and potential efficacy compared with marketed products

Product attributes	AD-214	Ofev (nintedanib)	Esbriet (pirfenidone)
Sponsor	AdAlta	Boehringer Ingelheim	Roche
Development stage	Phase I/IIa	Marketed	Marketed
More specific, targeted format	Antibody	Small molecule	Small molecule
Less frequent administration	IV every 2 weeks/SC weekly	Oral twice daily (2 tablets)	Oral three times daily (9 capsules)
Highly targeted mode of action	CXCR4 antagonist	Multi tyrosine kinase inhibitor	Unknown
Efficacy	TBD – Safety profile supports being additive to marketed products	45-70% reduction in annual FVC decline No increase in survival	35% reduction in annual FVC decline No increase in survival
Compliance and discontinuation	IV > oral compliance (market research); tolerability supports compliance	Discontinuation within 1yr: 21-50%	Discontinuation within 1yr: ~37%
Superior tolerability and side effect profile	Phase I: No AE's > grade 2 (moderate) Most common: headache/dizziness, musculoskeletal discomfort and infusion related reaction	Liver function impairment (13-14%) Diarrhea (68-76%) Nausea (24-32%) and vomiting (12-25%) Vascular disorders/bleeding	Liver function impairment (4%) Photosensitivity/rash (9%) Diarrhea (26%) Nausea (36%) and vomiting (13%) Dyspepsia/abdominal pain (19-24%)
Potential synergies with nintedanib	May counter increased CXCR4 expression induced by nintedanib	May increase CXCR4 expression	N/A

Source: FDA prescribing information, literature review, GlobalData, AdAlta analysis

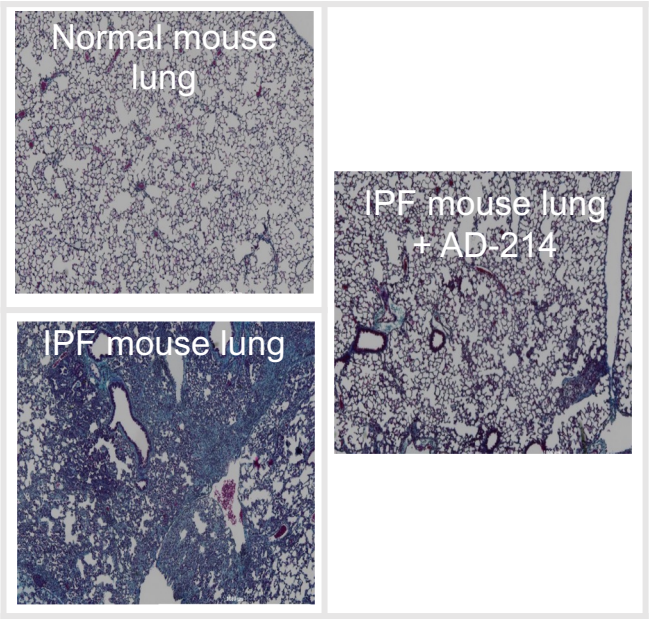
AD-214 offers a competitive and differentiated product profile compared with leading disease modifying products

Product attributes	AD-214	BI-1015550	BMS-986278	Bexotegrast
Sponsor	AdAlta	Boehringer Ingelheim	Bristol Myers Squibb	PLIANT THERAPEUTICS
Development stage	Phase I/II	Phase III	Phase III	Phase II
Format	Antibody IV every 2 weeks/SC weekly	Small molecule Oral twice daily	Small molecule Oral twice daily	Small molecule Oral once daily
Mode of action	CXCR4 antagonist	PDE4 inhibitor	LPAR1 antagonist	Dual αvβ1/6 integrin inhibitor
Novel, validated pathway, no prior failures	✓	✓	✗	✓
Antibody precision	✓	✗	✗	✗
Potential synergies with marketed products	✓	✗	✗	✗
ODD (US FDA)	✓	✓	✗	✓
Available/ accessible for partnering	✓	✗	✗	✓

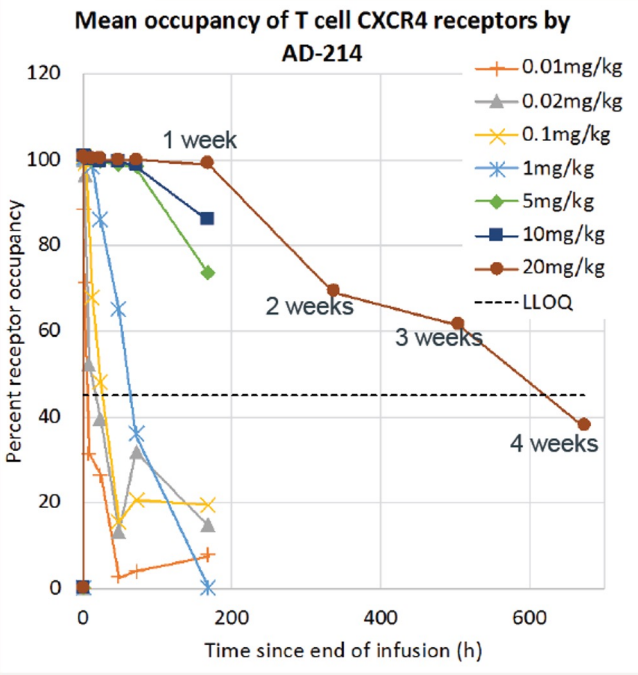
Source: GlobalData, clinicaltrials.gov, company press releases, AdAlta analysis

AD-214: efficacy validated in IPF mouse model; safety and target engagement in Phase I

AD-214 inhibited development of lung fibrosis in a mouse model at a wide range of doses and dose intervals[1]



AD-214 was well tolerated in Phase I clinical trials and demonstrated high and durable receptor occupancy[2]



[1] Murigenics_20210208. (Fibrosis induced by bleomycin at day 0; treatment commenced day 8; images from 10 mg/kg AD-214 every 4 days; statistical significance assessed using ANOVA and post-hoc Dunnett's test; ns (not significant) = p >0.05, * = p<0.05, ** = p < 0.01 relative to 21-day bleomycin vehicle; negative control is an i-body that does not bind specifically to CXCR4; error bars are standard error of the mean); test substances administered IV except pirfenidone and nintedanib orally

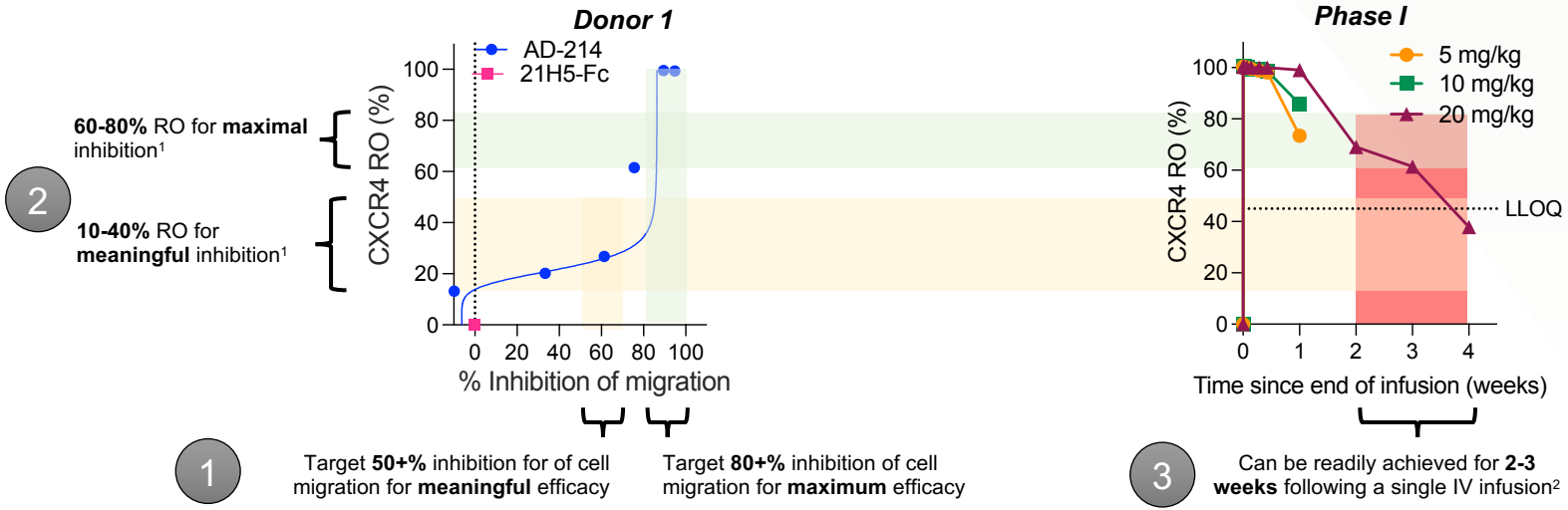
[2] Clinical Study Report: Protocol ID: ADA-AD-214-1A : Version 1 Dated 07 October 2022

Two weekly IV dosing regimens can maintain sufficient receptor occupancy to meaningfully inhibit fibrotic processes

1. ***Ex vivo* cell migration is a model fibrotic process and inhibition of migration is a model of efficacy**
   - Maximum efficacy at >80% inhibition of migration (green). Meaningful efficacy at >50% inhibition (yellow)

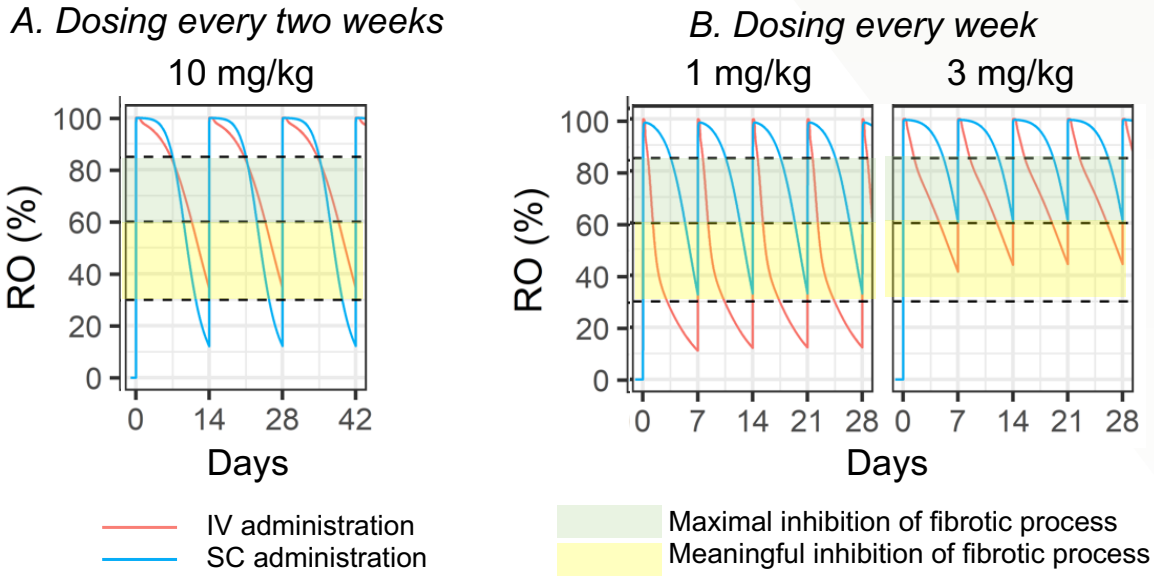
2. **Less than full receptor occupancy (CXCR4 RO) is required for efficacy (meaningful inhibition of cell migration)**
   - 60-85% receptor occupancy is sufficient for maximum inhibition of cell migration
   - Meaningful inhibition at receptor occupancy as low as 10-40%

3. **Maintaining efficacious receptor occupancy levels is the objective of dose selection**
   - **Efficacious receptor occupancy can be maintained for at least two weeks after an IV infusion in humans, a clinically viable dosing regimen[2]**



[1] AdAlta studies correlated AD-214 concentration with level of CXCR4 receptor occupancy and level of inhibition of SDF-1α induced migration *ex vivo* on human T cells. Ranges are average of results from three healthy donors, only one donor shown
[2] Clinical Study Report: Protocol ID: ADA-AD-214-1A : Version 1 Dated 07 October 2022

Two weekly IV and potentially weekly SC dosing regimens achieve target receptor occupancy



Simulated CXCR4 receptor occupancy following IV (red) and SC (blue) administration of AD-214 doses. Shading represents receptor occupancy (RO) required for maximal (green) and meaningful (yellow, more than 50%) inhibition of a model fibrotic process in ex vivo *experiments.*
Panel A: 10 mg/kg AD-214 administered every two weeks.
Panel B: 1 mg/kg (left) and 3 mg/kg (right) AD-214 administered every week.

Source: AdAlta analysis based on PK/PD model developed by LYO-X

i-body-like sdAb CAR-T therapies are an emerging, validated approach

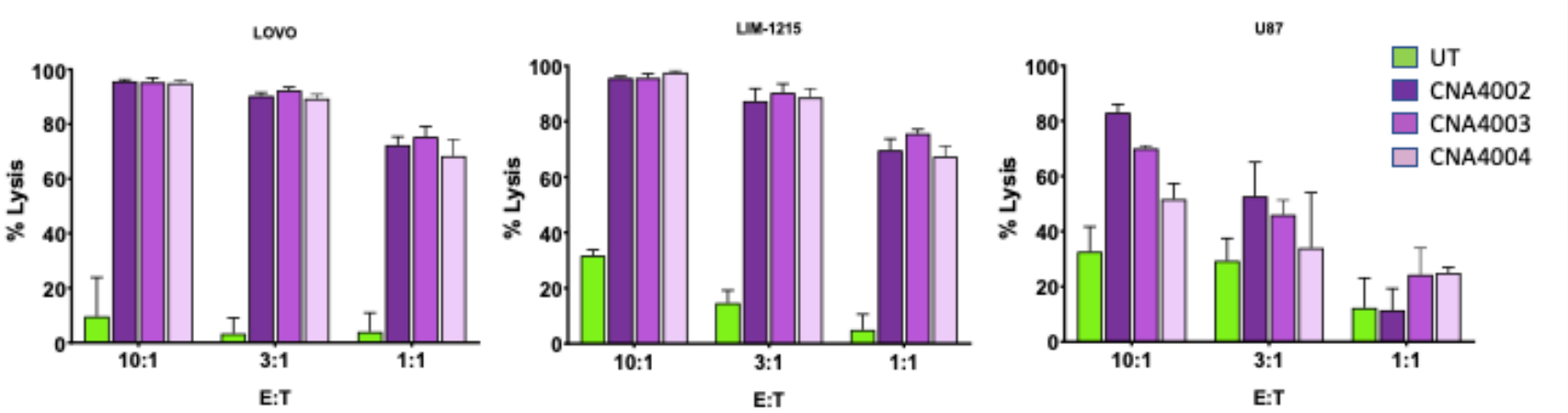
GROUP	YEAR	STAGE	SDAB CAR TARGET	AVAILABLE RESULTS
AdAlta Ltd/Carina Biotech	**2022**	**Proof of principle *(in vitro)***	**Undisclosed**	
Johnson and Johnson[1] Legend Biotech	2022	Market	anti-BCMA CAR-T (biepitopic)	P3 results for n=97 patients ▪ ORR: 97.9%; sCR 78.4% ▪ PFS: 77% (at 12 months) ▪ Overall survival: 89%
Shenzhen Pregene Biopharma[2]	2021	Phase 1 (complete)	anti-BCMA CAR-T	P1 results for n=34 patients: ▪ ORR: 88.2%; sCR/CR: 55.9% ▪ PFS(at 12 months): 53.7%; Median PFS: 12.1 months ▪ Overall survival at 12 months: 78.8%
PersonGen BioTherapeutics[3]	2020	Phase 1 (ongoing)	CD7	P1 results for n=3 patients: ▪ All patients had increased IL-6 ▪ PFS observed in 3/3; remission observed in 2/3 patients
PersonGen BioTherapeutics[4]	2022	Phase 1 (ongoing)	CD19	Not yet available
Legend Biotech[5]	2020	Phase 1 (ongoing)	Claudin 18.2	Not yet available
National Cancer Institute (USA)[6]	2022	Preclinical (mouse)	PD-L1	*In vitro* lysis of breast and liver tumor cells *In vivo* regression of liver tumor cells
Boston Children's Hospital[7]	2019, 2020	Preclinical (mouse)	PD-L1 EIIIB fibronectin	*In vivo* reduction of tumor growth and increased survival Improved activity of CAR-Ts secreting anti-CD47, anti-PD-L1 and anti-CTLA4 nanobodies

[1]https://www.clinicaltrialsarena.com/projects/carvykti-ciltacabtagene-autoleucel/
[2]https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.15_suppl.8025
[3]https://ascopubs.org/doi/10.1200/JCO.2020.38.15_suppl.3026
[4]https://clinicaltrials.gov/ct2/show/NCT04691349?term=car-t+single+domain+antibody&draw=2&rank=1
[5]https://clinicaltrials.gov/ct2/show/NCT04467853
[6]https://www.cell.com/molecular-therapy-family/oncolytics/fulltext/S2372-7705(22)00032-8#secsectitle0020
[7]https://www.pnas.org/doi/10.1073/pnas.1817147116; https://pubmed.ncbi.nlm.nih.gov/32019780/

Building the first iCAR-T cell therapy: proof of principle results

i-body enabled CAR-T (iCAR-T) cells have been successfully generated by Carina and demonstrate *in vitro* cell killing (lysis)[1]

carina biotech AdAlta next generation protein therapeutics



Experimental details

- LOVO and LIM1215 are colorectal cancer cell lines; U87 is a glioblastoma cell line
- 3 different Carina CAR-T constructs incorporating i-body against a single target “X” (CNA4002/CNA4003/CNA4004)
- UT is an unmodified T-cell that does not result in significant killing (lysis) of these cell lines
- i-CAR-T cells manufactured with 97% transduction (i-body CAR insertion) efficiency
- i-CAR-T cells included 60-70% CD4+ (helper) and 20-30% CD8+ (cytotoxic – killer) T cells

1. 210921 Carina iBody Datapack SB (2021) – previously unpublished data

i-CAR-T: Valuable cell therapy partnering potential at pre-clinical proof of concept

Date	Licensee	Licensor	No. of assets	Upfront/target (US$m)	Deal value/target (US$m)
Jun-22	Bristol Myers Squibb	immatics	2	30	730
Jul-20	SANOFI	Kiadis pharma	1	20	988
Feb-20	GSK	immatics	2	25	300
Nov-19	Allogene	Notch THERAPEUTICS	1	10	304
Oct-18	Roche	SQZ BIOTECH	1	45	1702
Median value				**25**	**730**

Source: GlobalData, company press releases, AdAlta analysis