Transforming treatment outcomes for cancer patients

BIO June 2023

Dr. Fiona McLaughlin, Chief Scientific Officer

Avacta Group plc

Our purpose is to improve patients' lives and grow shareholder value by developing novel cancer therapies and powerful diagnostics using our proprietary AFFIMER®® and pre|CISION™ platforms

Therapeutics

Harnessing our proprietary technologies to deliver innovative oncology drugs that transform treatment outcomes and improve cancer patients' lives.

Diagnostics

M&A led strategy to build an integrated and differentiated in-vitro diagnostics (IVD) business with global reach serving professionals and consumers

Avacta Group plc Overview

Avacta Group plc
LSE: AVCT
~£300M market capitalisation

Therapeutics Division

- Clinical stage oncology drug company based in White City, London, UK
- R&D Centre: ~30 staff – majority PhD
- Clinical Development Group established including Translational Sciences, CMC, Clinical Operations
- In-house pre-clinical and clinical pipeline of novel cancer therapies based on the proprietary AFFIMER® and preCISION technologies
- Global partnerships (oncology, autoimmune, cell and gene therapy)

Affimer® preCISION™

Diagnostics Division

- In-vitro diagnostics company based in Wetherby and Kent, UK
- R&D Centre and plc Headquarters
- ~100 staff
- £18M revenue (FY23e)

Affimer® LAUNCH

Avacta Group plc Leadership

Dr Eliot Forster

Non-Executive Chairman

- Over 25 years experience in pharma and Biotech.
- 2015 – 2018 CEO of Immunocore Limited.
- 2018 - 2023 CEO F-Star.
- Held a number of senior roles in Pfizer where he became Head of Development and Operations for the EU and Asia.
- Joined Avacta in 2018.

Dr Alastair Smith

Chief Executive Officer

- Over 18 years experience as a life sciences public company CEO.
- Science background with 13 years in academia – established a leading UK biophysics group.
- Founded Avacta in 2006.
- World class scientific and technical knowledge with a highly commercial mindset.

Tony Gardiner

Chief Finance Officer

- Over 20 years senior financial and operational experience across multiple sectors.
- 4 years as CFO of AIM listed Fusion IP plc, 5 years as Finance Director of Aedas/AHR Architects.
- Joined Avacta in 2016.

Therapeutics Division Leadership

Dr Fiona McLaughlin, Chief Scientific Officer

Fiona is a highly experienced oncology drug developer, bringing over 25 years' experience in research and translational drug development in the pharmaceutical and biotech sectors, having led teams from early research through to clinical development. Fiona started her career at GlaxoSmithKline and has subsequently held leadership positions in multiple biotech companies including Vice President, Translational Research at Antisoma plc and Director of Pre-clinical Development at BTG plc (now part of Boston Scientific).

. Fiona received a PhD from the Haematology Department at Cambridge University and has a BSc in Biochemistry from Glasgow University.

Neil Bell, Chief Development Officer

Neil has over 30 years' experience in drug development across a range of therapeutic areas including oncology. During this time Neil has held senior leadership positions in large to mid-sized global pharmaceutical companies and emerging biotechs. Neil has led several development programmes from pre-clinical to clinical leading to successful market approvals in Europe, US and Japan. Prior to joining Avacta, Neil was a member of the senior management team at Autolus, a leading CAR-T cell company, and played a major role in building a global and fully integrated organisation and in parallel implementing several CAR T-cell programmes across Europe and the United States.

Karen Harrison - Chief Operating Officer

Karen Harrison is the Chief Operating Officer for Avacta Life Sciences. She is responsible for people and talent initiatives and processes. Karen has over 30 years of experience and has held notable positions throughout her career such as VP Global Talent for Astellas Pharmaceuticals, SVP Global Partnerships for Cielo Talent Inc and Managing Director for Wright Research (a talent mapping organisation). Karen brings with her expertise in talent acquisition, learning and development and culture and leadership. Karen is also a qualified Executive Coach.

Avacta Therapeutics

Improving cancer patients' lives through innovation and partnership

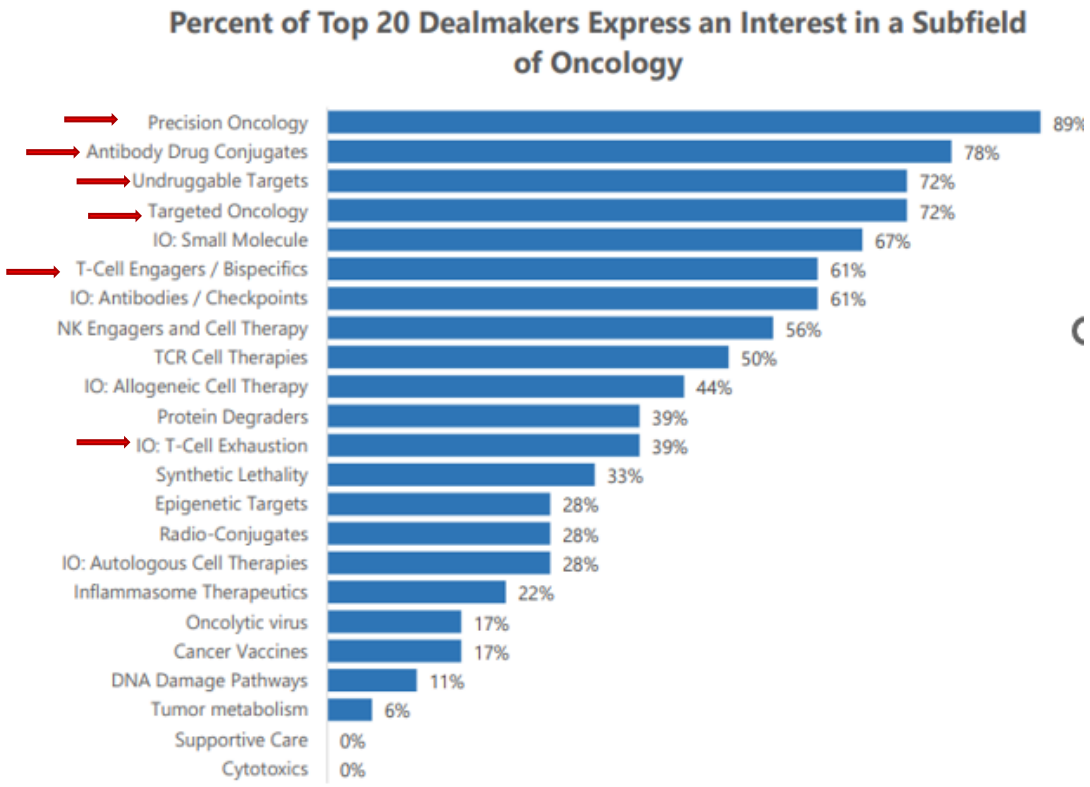
VISION

Our vision is to deliver innovative oncology drugs that transform treatment outcomes to improve cancer patients' lives.

STRATEGY

- Use our proprietary pre|CISION™ and AFFIMER® platforms to develop best-in-class and first-in-class cancer therapies.
- Grow our clinical pipeline alongside selective and focused out-licensing.
- Combine our in-house drug development expertise with a focused partnership strategy.

Addressing the Hottest Areas in Oncology



Source: Torreya meetings with various players at ASCO and later, reviews of ASCO presentations, partnering presentations and web site discussions of partnering/M&A interest.

Avacta®

preCISION™

Targeting the tumour microenvironment

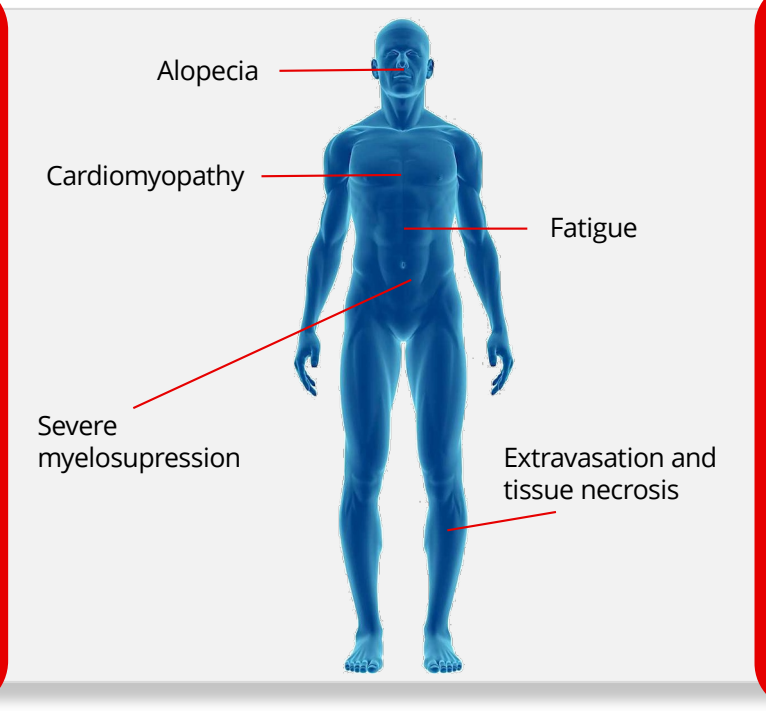
Targeting Payloads to the Tumour

Reducing systemic toxicities of chemotherapies and improving tolerability for patients through tumour-specific activation

The Problem

- Chemotherapy, cytotoxic agents and immunotherapies are not tumour selective.
- Systemic toxicities and tolerability for patients limit the therapeutic index of most oncology drugs.
- There is an urgent unmet need to differentiate between tumour and normal cells.

Common Doxorubicin Toxicities



preCISION

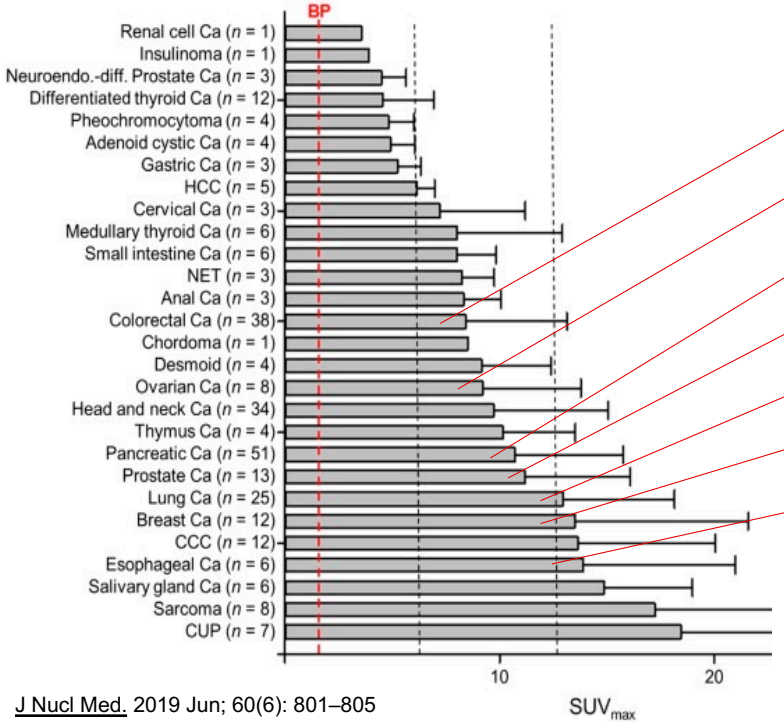
- Targets the tumour tissue and limits systemic exposure.
- Selectively activated in the tumour microenvironment by an enzyme that is in high concentration in most solid tumours.
- Designed to enhance safety and tolerability and increase efficacy.

What is pre|CISION™?

Targeting the tumour microenvironment through fibroblast activation protein alpha

- pre|CISION™ is a highly specific substrate for fibroblast activation protein-α (FAPα), an extracellular enzyme that is upregulated in most solid tumours.
- pre|CISION™ prevents chemotherapeutics from entering cells rendering them inert until it is removed in the tumour microenvironment by FAP.
- **pre|CISION™ is specific to FAP and not cleaved by any other human enzyme.**
- pre|CISION™ can also be incorporated into a drug conjugate linker for release of the targeted warhead in the tumour microenvironment.
- pre|CISION™ is exclusively licensed from Tufts University Medical School.

FAP Concentration in a Range of Solid Tumours



J Nucl Med. 2019 Jun; 60(6): 801–805

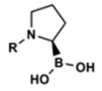
Prevalence (US)

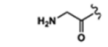
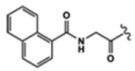
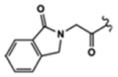
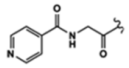
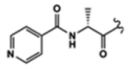
Renal cell Ca (n = 1)	1,286,971
Insulinoma (n = 1)	191,915
Neuroendo.-diff. Prostate Ca (n = 3)	86,756
Differentiated thyroid Ca (n = 12)	3,229,152
Pheochromocytoma (n = 4)	541,204
Adenoid cystic Ca (n = 4)	3,481,062
Gastric Ca (n = 3)	10,973

SEER Database, 2019
https://seer.cancer.gov/

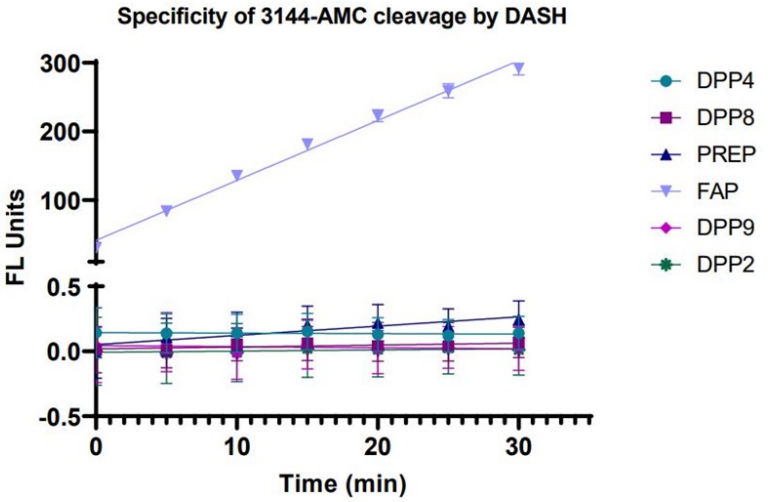
Development of a FAP specific linker

- Identification of a FAP specific linker comes from work analyzing substrate specificity and development of selective inhibitors
- Fibroblast activation protein (FAP) is a type II, membrane bound serine protease and uniquely has both exo and endopeptidase activities



Compound	R	IC_{50} (nM) DPPIV	DPP8	DPP9	FAP	PREP	FAP selectivity
1		13 ± 2.1	180 ± 32	98 ± 20	52 ± 9.2	47,000 ± 45,000	900
2		>100,000	1200 ± 300	420 ± 130	2.3 ± 0.4	1.8 ± 0.3	0.8
3		–	–	–	2900 ± 600	130 ± 19	0.04
4		–	–	–	93 ± 11	7.2 ± 1.0	0.08
5		2800 ± 740	1,900 ± 260	1000 ± 570	0.47 ± 0.05	5.0 ± 0.7	11
6		>100,000	5600 ± 1300	3400 ± 800	36 ± 4.8	13,000 ± 4300	360

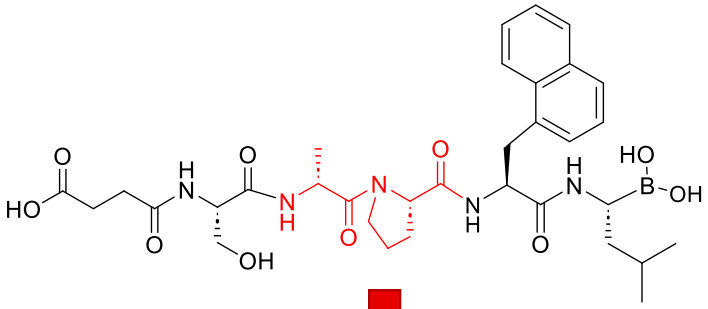
"The FAP selectivity is equal to IC_{50}(PREP)/IC_{50}(FAP). IC_{50} values are expressed with ±SEM.



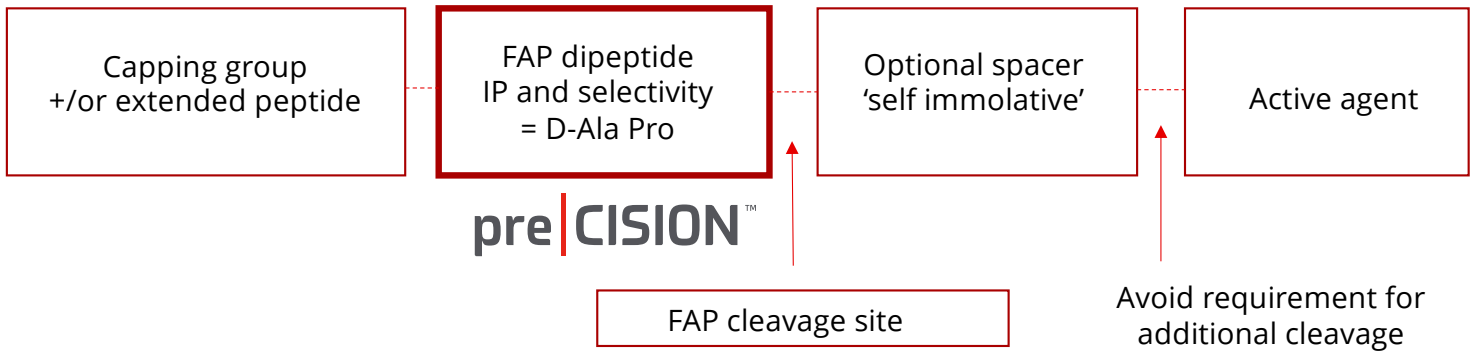
Synthetic substrate 3144-AMC =(quinoline-4-carbonyl)-D-Ala-L-Pro-AMC in which AMC is the fluorogenic leaving group, 7-amino-4-methylcoumarin

The D-Ala-Pro sequence provides exquisite selectivity for cleavage by the protease FAPα

General Concept for a pre|CISION™ Tumour Targeted Therapy



4-component molecule

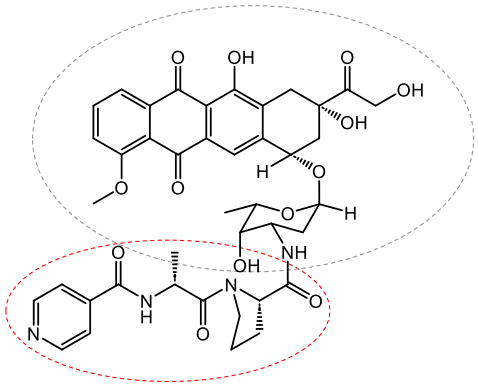


AVA6000: Lead Programme

Reducing the side-effects of doxorubicin through tumour-specific activation using the pre|CISION™ technology

AVA6000

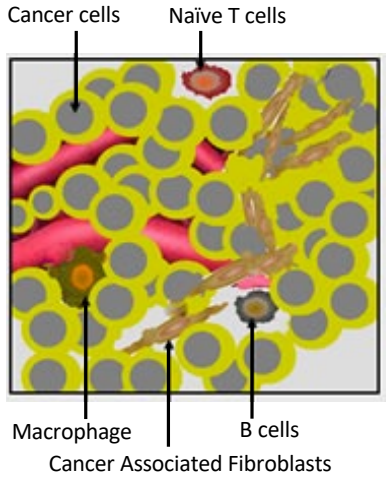
Doxorubicin



pre|CISION™

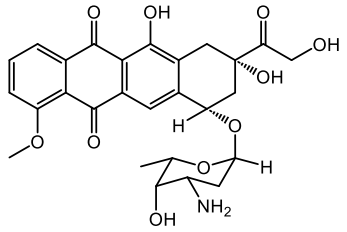
Prevented from entering cells by pre|CISION modification

Tumour Microenvironment

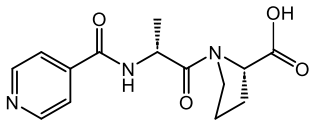


FAPα +ve fibroblasts and cancer cells

Release of Active Doxorubicin



FAPα



FAP mediated release of doxorubicin

AVA6000: Ongoing Phase 1 Dose Escalation & Expansion Trial

Phase 1a Dose Escalation

Primary Objectives

- Safety and tolerability of AVA6000.
- Maximum tolerated dose and/or recommended phase 2 dose of AVA6000.

Patient Population

- Locally advanced or metastatic selected solid tumours.
- 20-30 patients.

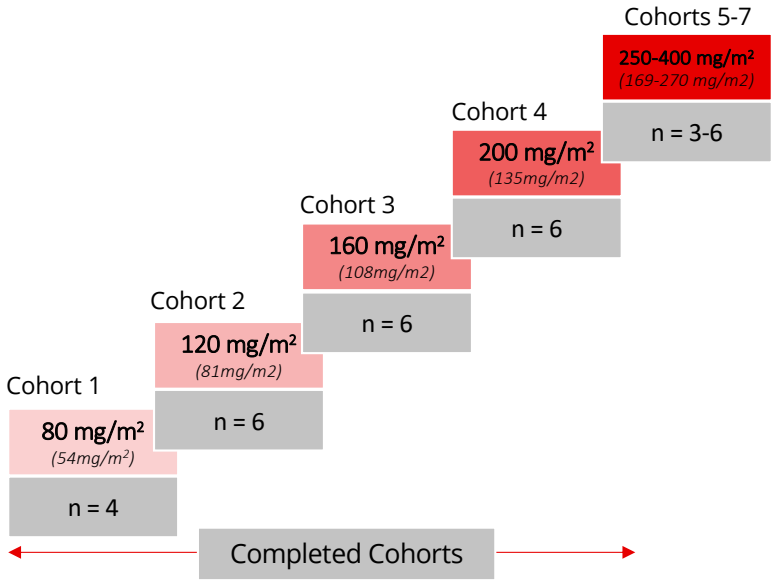
Endpoints

- Dose limiting toxicities, safety, tolerability & cardiac safety.
- Pharmacokinetic profiles for cycles 1 & 2.
- Optional biopsies (AVA6000/Dox levels).
- Tumour assessments.

Centres

- 5 UK (open) & 2 US (opened post-period end)

AVA6000 Dose Regimen - 3 weekly cycles *(Doxorubicin Equivalent Dose)*



"n" = number of patients in cohort

AVA6000 vs Doxorubicin Safety Profile

AVA6000 shows a marked reduction in frequency and severity of treatment emergent adverse events

Treatment-Emergent Adverse Event (TEAE)	[1] AVA6000 (80-200mg/m² Q3W) N = 19 Median No. Cycles = 2 (Range 1-8)	[2] Doxorubicin (75mg/m² Q3W) N = 249 Median No. Cycles = 7 (Range 1-8)
	Grade ≥3	Grade ≥3
Nausea	0	6 (2.4)
Fatigue	0	12(4.8)
Lethargy	0	NR
Decreased appetite	0	1 (0.4)
Vomiting	1 (5.3)	2 (0.8)
Constipation	0	2 (2.8)
Diarrhoea	0	3 (1.2)
Abdominal Pain	0	3 (1.2)
Weight Decrease	0	NR
Mucositis	1 (5.3)	NR
Stomatitis	0	NR
ALT increase	0	4 (1.6)
AST Increase	0	NR
Bilirubin	1 (5.3)	NR
Anaemia	0	31 (12.4)
Neutropenia	1 (5.3)	122 (49)
Thrombocytopenia	0	21 (8.4)
Lymphopenia	1 (5.3)	NR
Alopecia	0	1 (0.4)
Heart Failure	0	NR
Dyspnoea	0	2 (0.8)
Pyrexia	0	0
Cough	0	1 (0.4)
Rash	0	0
Troponin T increase	0	NR
Upper respiratory tract Infection	0	1 (0.4)
Urinary Tract Infection	1 (5.3)	1 (0.4)
Arthralgia	0	NR

Observations

- Low incidence of grade 3 or above AVA6000 TEAEs compared with doxorubicin.
- No dose related increase in frequency or severity of AVA6000 TEAEs.
- AVA6000 tumour types: heavily pre-treated metastatic CRC (11), pancreatic (5), STS (1), ovarian (1) & oesophageal (1).
- Doxorubicin tumour type: first line metastatic soft tissue sarcoma.

Treatment-Emergent Adverse Events

TEAEs are undesirable events not present prior to medical treatment, or an already present event that worsens either in intensity or frequency following the treatment. TEAEs may therefore be treatment-related or unrelated as assessed by the treating physician.

TEAE Grades

Grade 1: mild; Grade 2: moderate; Grade 3: severe or medically significant but not immediately life-threatening; Grade 4: life-threatening; Grade 5: death related to TEAE.

References

[1] *Ongoing Phase 1 Dose Escalation Study in metastatic solid tumours (ALS-6000-101:* ClinicalTrials.gov Identifier: NCT04969835

[2] *Tap WD, Wagner AJ, Schöffski P, et al. Effect of Doxorubicin Plus Olaratumab vs Doxorubicin Plus Placebo on Survival in Patients With Advanced Soft Tissue Sarcomas: The ANNOUNCE Randomized Clinical Trial. JAMA. 2020;323(13):1266–1276. doi:10.1001/jama.2020.1707*

Tumour Biopsy Data

Significantly higher levels of released doxorubicin in tumour biopsies compared with plasma at the same time point

Cohort	AVA6000 (Dox Dose) mg/m²	Patient	DOX Plasma @24h ng/ml	DOX Biopsy @24h		DOX Ratio* Biopsy:Plasma	Biopsy Source
				ng/g	nM		
Cohort 1	80 (54)	101-006 (1st)	4.9	135	248nM	28:1	Liver
		101-006 (2nd)	4.9	43	79nM	9:1	Liver
Cohort 3	160 (108)	103-021	4.4	376	690nM	85:1	Liver
		103-022	2.4	270	496nM	113:1	Liver
		102-023	7.5	875	1607nM	117:1	Liver
Cohort 4	200 (135)	103-017	15.9	553	1015nM	35:1	Liver
		102-018	10.5	1317	2419nM	125:1	Lung

*ng/ml ~ ng/g

Doxorubicin Target Activity	DOX IC50
DNA adduct formation [1]	25nM
Free radical formation/cardiomyocyte apoptosis[1]	100nM
Topoisomerase Inhibition[1]	400nM
In vitro cytotoxicity[2]	30nM-3μM

[1] doi:10.1007/s11095-018-2456-8
[2] internal data

Summary of ALS-6000-101 Phase I Dose Escalation Data

Positive safety profile and biopsies confirm release of doxorubicin in the tumour tissue at therapeutic levels

- 22 patients with a range of solid tumours dosed across four dose escalation cohorts.
- Currently dosing patients in the fifth cohort at 250mg/m^2.

Safety and Tolerability

- AVA6000 is well tolerated across first four cohorts.
- Marked reduction in the incidence and severity of the usual doxorubicin related toxicities (alopecia, nausea, myelosuppression, mucositis) including the most serious (neutropenia, thrombocytopenia, anaemia).
- Despite administering the equivalent of more than double the normal dose of doxorubicin to patients in cohort 4, the typical drug-related cardiotoxicity of doxorubicin has not been observed.

Biopsy Analysis

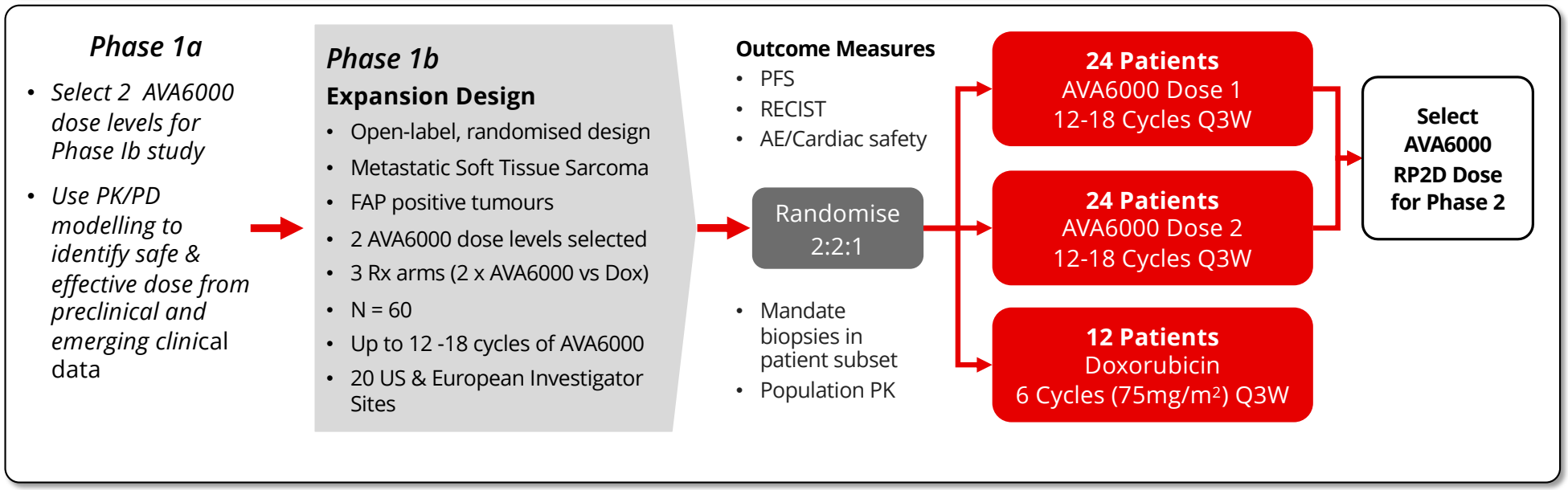
- Analysis of tumour biopsies taken from 6 patients confirms pre|CISION™ can deliver therapeutically significant levels of doxorubicin to tumour tissue compared to systemic levels at same timepoint.

AVA6000: Phase Ib Study

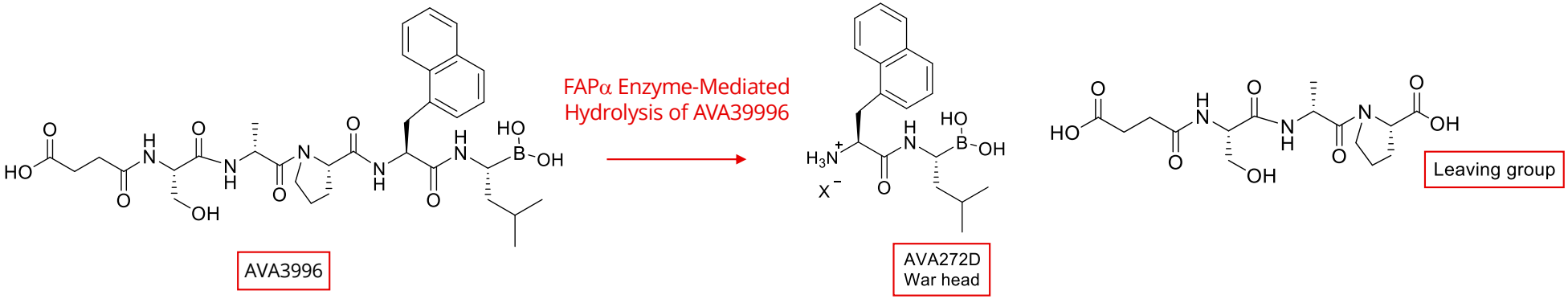
Clinical development in Soft-Tissue Sarcoma (Phase 1 to 2)

Development Rationale in Soft Tissue Sarcoma (STS)

- Advanced, Metastatic STS tumours
- Doxorubicin is the only therapy indicated for first-line monotherapy in advanced STS
- No current or near future competition for doxorubicin in 1st line STS
- Conventional doxorubicin has marginal efficacy (18% ORR; 6mth PFS) & Rx limitation due to cumulative dose limit (450mg/m^2 – 6 cycles maximum)
- AVA6000 has potential to safely increase Rx duration beyond 6 cycles (18 weeks) by x2-3 times (12-18 cycles – 36-54 weeks) with increased efficacy



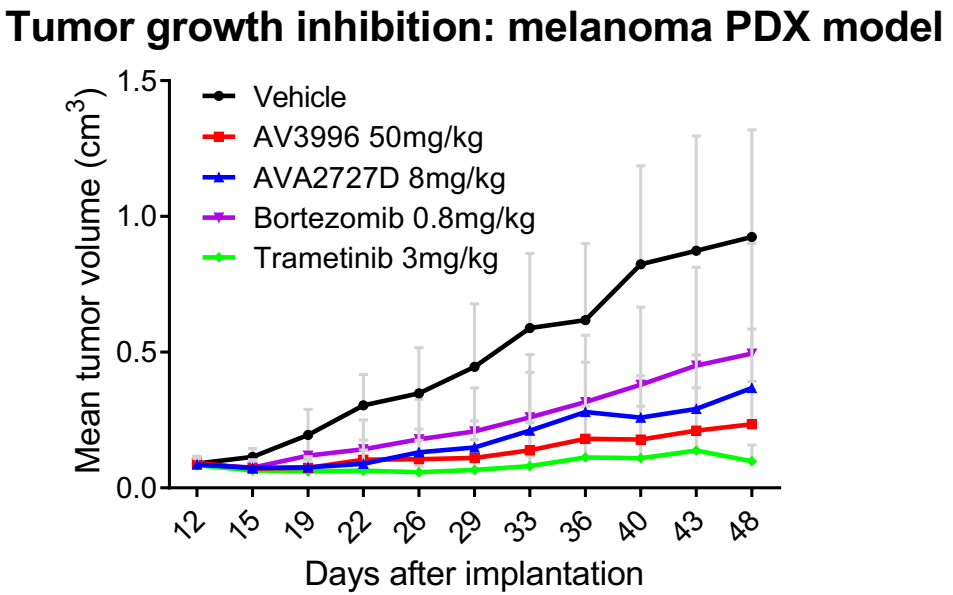
AVA3996: 2nd pre|CISION™ Candidate



- FAP activated proteasome inhibitor
- New Chemical Entity
- Proven specificity for FAPα versus other proteases
- Delivers proteasome inhibitor directly to the tumour microenvironment
- In IND enabling studies
- FIH planned 2024

AVA3996: In-vivo Efficacy

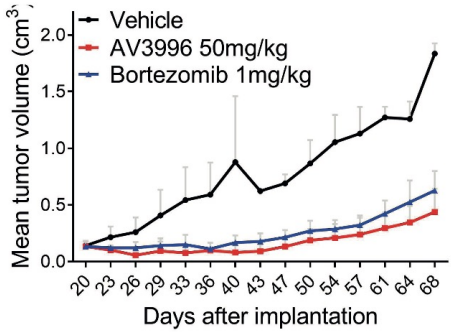
- AVA3996 reduces tumour growth in several animal models including melanoma, sarcoma and colorectal patient derived xenographs
- Currently testing whether AVA3996 shows synergy with anti-PD-1 checkpoint blockade
- A collaboration is ongoing with the Beatson Institute focusing on cholangiocarcinoma (bile duct cancer)
- Demonstrated proof of concept, now pushing forward with IND studies with aim to take into Phase I



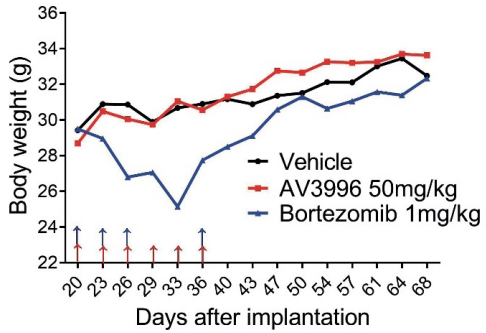
AVA3996: In-vivo Efficacy in Multiple Tumour Models

Melanoma Model

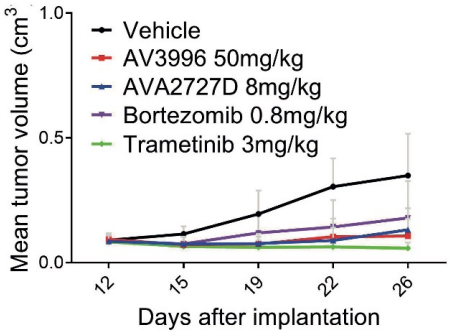
Tumour growth inhibition: melanoma PDX model



Body weight: melanoma PDX model



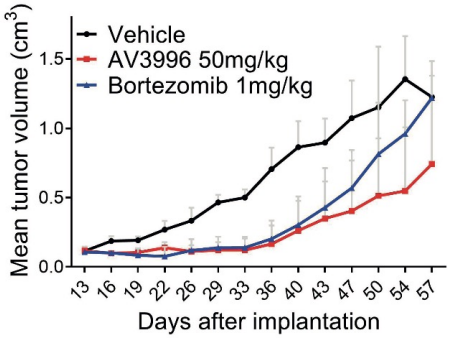
Tumour growth inhibition: melanoma PDX model



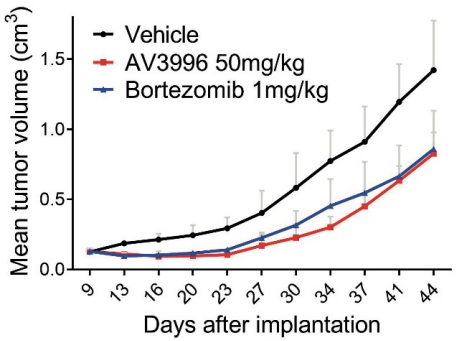
Key Takeaways

- AVA3996 is as effective in these different mouse PDX models as bortezomib and, in the case of the melanoma model, as trametinib.
- Mice did not show the same toxicities when treated with AVA3996 as when they were treated with 1mg/kg bortezomib.

Tumour growth inhibition: sarcoma PDX model



Tumour growth inhibition: colorectal PDX model



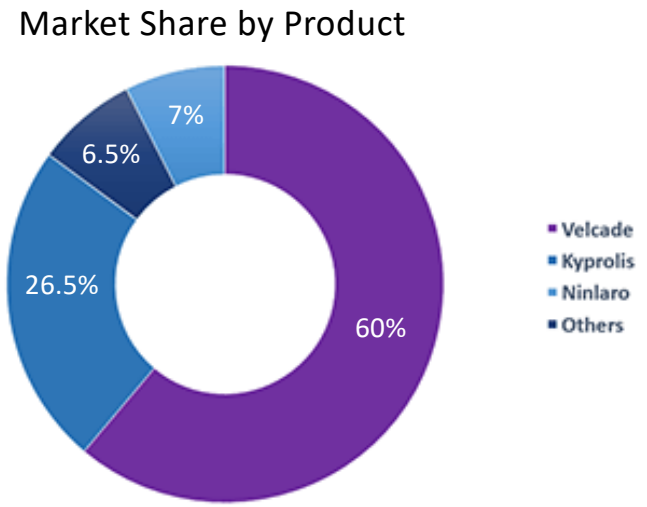
Proteasome Inhibitor Market

Opportunity for first-in-class proteasome inhibitor targeted to solid tumours

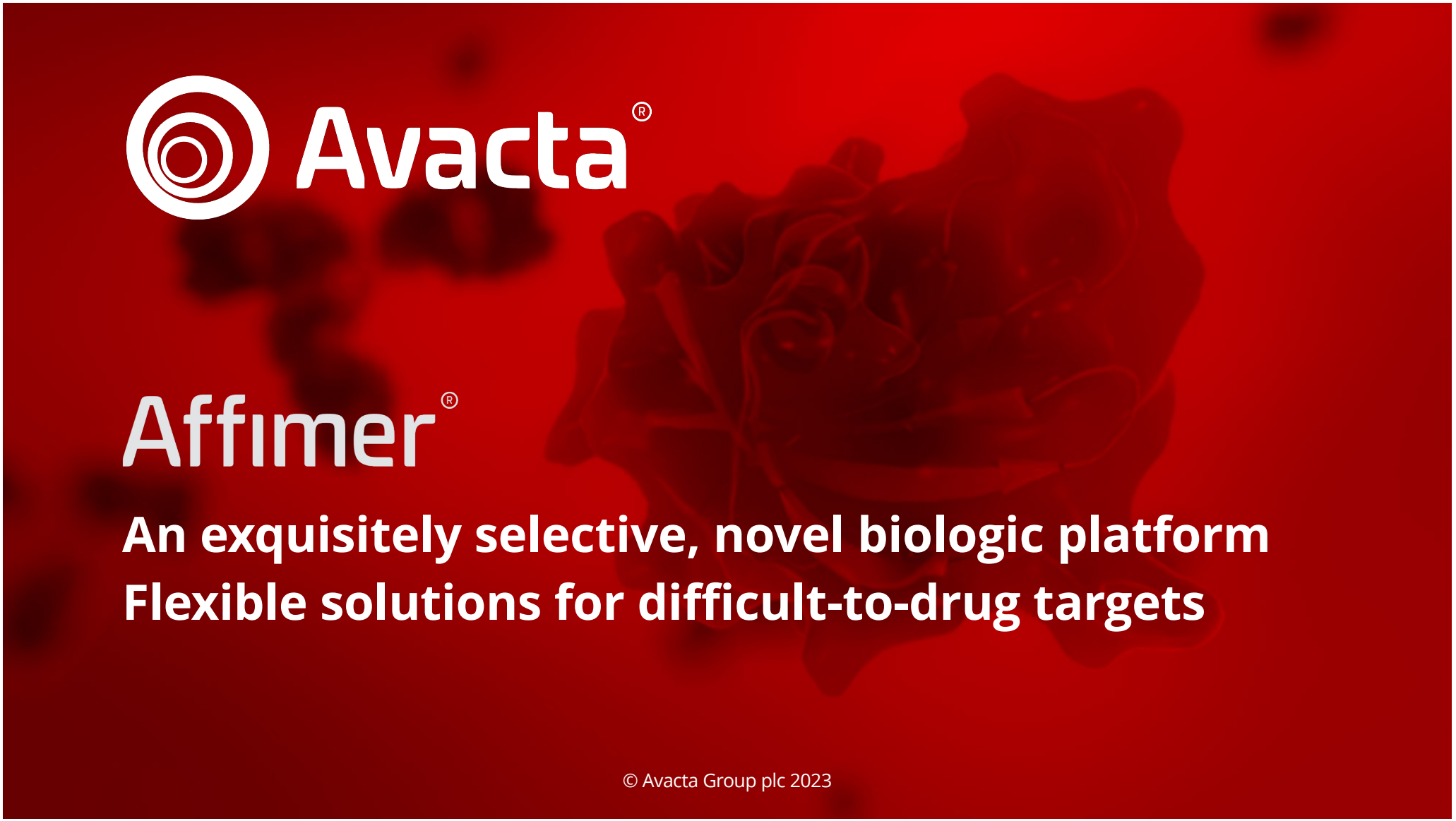
- The **global proteasome inhibitors market** is expected to grow at a CAGR of 8.4% (2023-2028) to reach nearly USD 2.3 billion by 2026[1].
- Proteasome inhibitors have severe dose limiting toxicities which have restricted their approval.
- Three are approved for treating multiple myeloma:
  - Bortezomib (*Velcade*) was approved in 2003. This was the first proteasome inhibitor approved for use in the U.S. AVA2727D is very similar but not identical to bortezomib.
  - Carfilzomib (*Kyprolis*) was approved by the FDA for relapsed and refractory multiple myeloma in 2012.
  - Ixazomib (*Ninlaro*) was approved by the FDA in 2015 for use in combination with lenalidomide and dexamethasone for the treatment of multiple myeloma after at least one prior therapy.

1. (https://www.expertmarketresearch.com/reports/proteasome-inhibitors-market)

Global Proteasome Inhibitors Market 2022 (~$1.7billion)

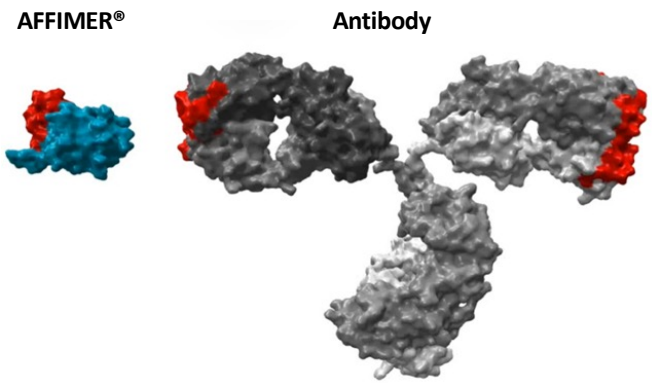


Source: https://www.expertmarketresearch.com/reports/proteasome-inhibitors-market



hSteA and Development of AFFIMER® Display Libraries

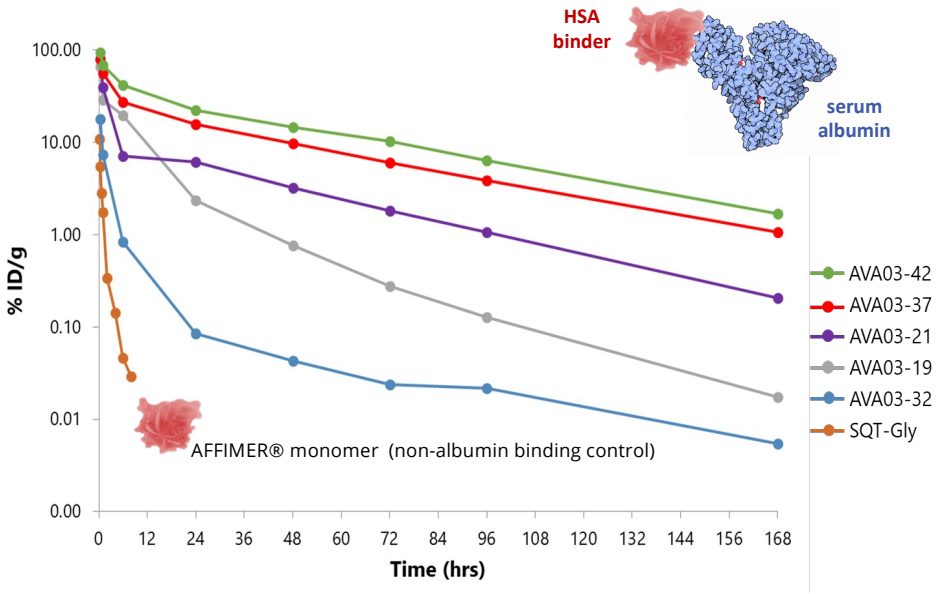
- Different iterations of libraries based on extensive mutagenesis and structural analysis
- Latest libraries are high diversity based on rational design
  - Structural liabilities eliminated
  - Optimised sequences for efficient screening processes
  - StefinA functions eliminated



- Libraries are available with one or two binding loops and with a choice of inserted loop sizes
- Libraries and AFFIMER® technology owned by Avacta with IP coverage of the platform
- Highly customisable with rapid discovery and validation

AFFIMER® Formatting: Pharmacokinetics

- AFFIMER® proteins have a short serum half-life when administered intravenously due to renal clearance
  - This may be of benefit for in vivo imaging and some therapeutic approaches
- AFFIMER® proteins may also be formatted as in-line fusions
- Fusion to an albumin-binding AFFIMER® increases serum half-life to alter PK properties



AFFIMER® proteins labelled with I^{125} and dosed at 10 mg/kg (IV).

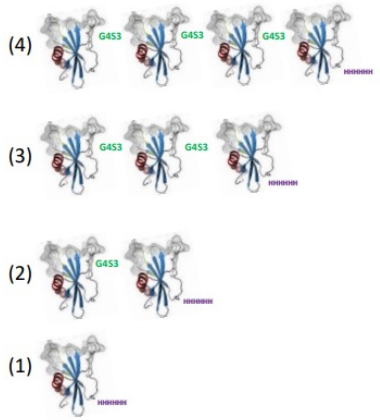
Clone	$t_{1/2}$ (hrs)	AUC 0-t h*µg/mL
AVA03-42	38.2	5,670
AVA03-37	37.7	3,435
AVA03-21	30.6	1,401
AVA03-19	24.3	1,059
AVA03-32	29.0	112
Non-binder	1.6	18.1

AFFIMER® Formatting: Affinity

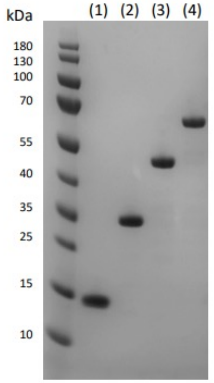
- Multiple AFFIMER® units may be linked as in-line fusions: protein productivity and quality remain high
- Addition of repeat AFFIMER® units increases avidity of binding to target

Expression and yield

In-line fusion proteins representation

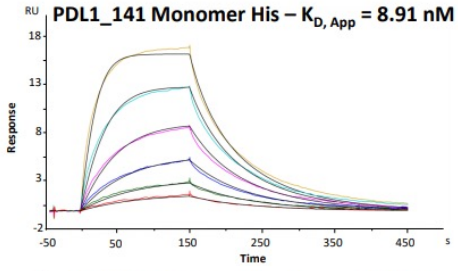


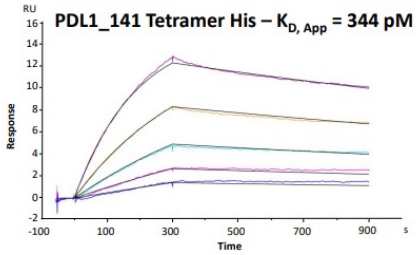
SDS-PAGE



Format	Predicted Mass (kDa)	Yield after one-step purification (mg/L)
Monomer His	14	270
Dimer His	25	278
Trimer His	42	212
Tetramer His	56	205

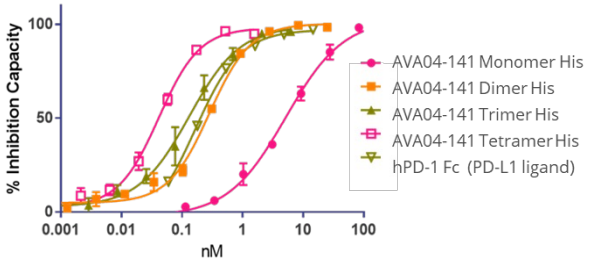
Biacore sensorgrams





Protein	k_a (1/Ms)	k_d (1/s)	Apparent K_D (nM)
Monomer His	2.81E+06	2.51E-02	8.9
Dimer His	1.12E+06	5.35E-04	0.5
Trimer His	1.13E+06	4.73E-04	0.4
Tetramer His	1.01E+06	3.48E-04	0.3

PD-L1/PD-1 Competitive ELISA



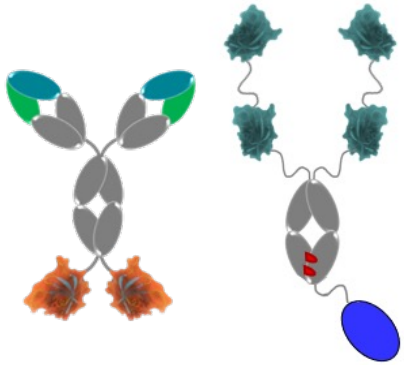
IC_{50} (nM)				
hPD-1 Fc	Monomer His	Dimer His	Trimer His	Tetramer His
0.17	2.5	0.28	0.13	0.04

AFFIMER® Formatting: Multi-specificity and Fusions

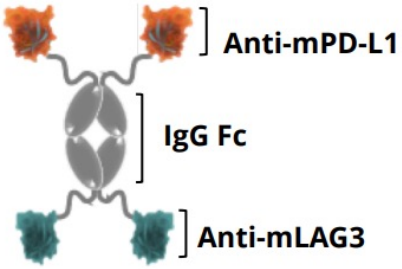
- Multiple AFFIMER® units which bind distinct targets may be linked with optimal linker sequences: binding to both target proteins is maintained
- AFFIMER® proteins may be linked to Fc domains, cytokines or other proteins of interest

Multi-specific binders

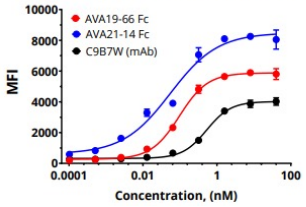
Fc or antibody fusions



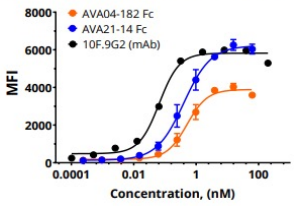
Other multi-specific binders



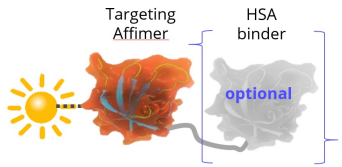
A. Binding on mLAG-3 DO-11-10 Cells



B. Binding on mPD-L1 LK35.2 Cells



Drug conjugates



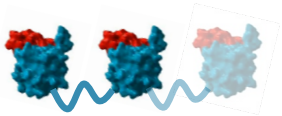
Powerful and Flexible Formatting

Flexible multi-specific formatting, excellent expression levels, stability and purity, and half-life extension using hFc or proprietary serum albumin binders

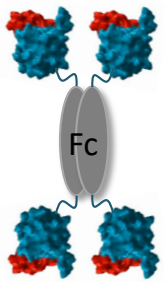
AVA004 PD-L1 Antagonist

In-line fusion with AFFIMER® XT, and as an Fc fusion or "AffmAb" to generate pM binding affinity and good serum PK.

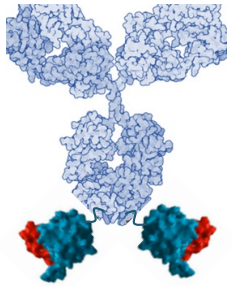
"In-line" AFFIMER® Fusions



Fc AFFIMER® Fusions

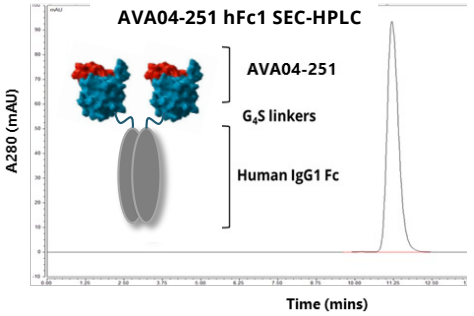


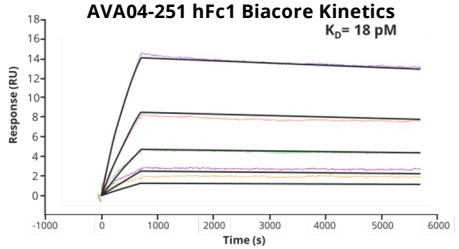
AFFIMER® mAb Fusions



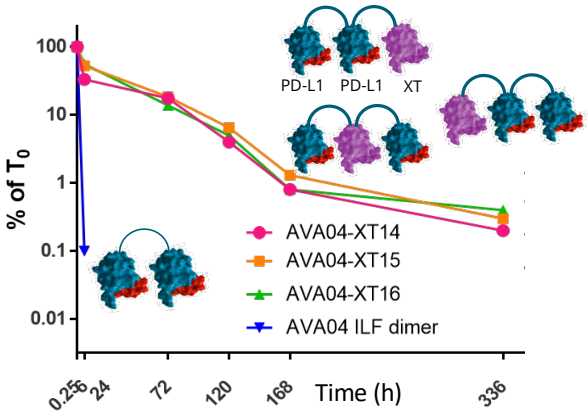
AVA004 Expression and Solubility

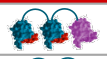
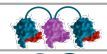
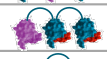
Typical (unoptimized shaker flask) expression yields of in-line (up to pentamers) and Fc fusions in the range 200-500 mg/l. Solubility up to 500mg/ml.





AFFIMER® XT Half-life Extension in Mice



AFFIMER® Clone	Format	$t_{1/2}$ (h)
AVA04 XT14		23.8
AVA04 XT15		24.2
AVA04 XT16		24.2
AVA04 ILF dimer		3.3

Comparator Technologies

AFFIMER® proteins exhibit all the properties of a best-in-class therapeutic protein platform

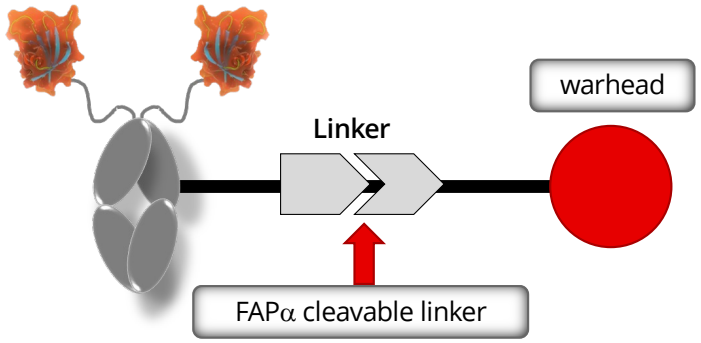
Key Attributes of a Therapeutic Protein Platform	AFFIMER®	DARPIN®	ANTICALIN®	NANOBODY®	Antibody
Small, monomeric, full length human protein, no disulphide, no PTM	Y	N	Y	N	N
Rapid discovery process yielding highly specific nM binders routinely	Y	N	Y	N	N
Low immunogenicity risk	Y	Y	Y	Y	Y
Flexible formatting for multi-specifics	Y	Y	N	Y	N
High expression of monomers and multimers in a range of cells, human tissues and in *e. coli.*	Y	N	N	N	N
Tunable pharmacokinetics	Y	Y	Y	Y	N
Very high solubility (>250mg/ml PBS) with low viscosity	Y	N	N	N	N
Simple, unencumbered IP, with freedom to operate around antibody IP	Y	Y	Y	N	N

Tumour Microenvironment Activated Conjugates

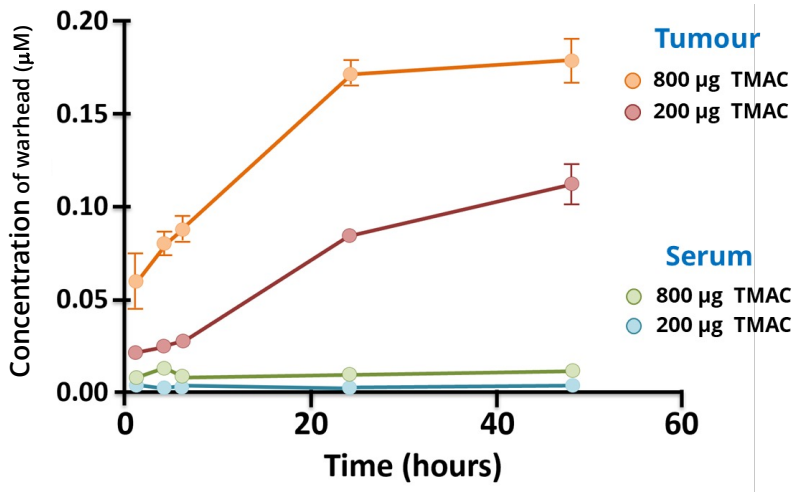
Tumour microenvironment activated conjugate brings together the pre|CISION™ and AFFIMER® platforms

Tumour Microenvironment Activated Conjugates and Targeting AFFIMER® proteins

- Cytotoxin linked to AFFIMER® immunotherapy/targeting by pre|CISION™ linker
- Cytotoxin released in the TME/stroma by FAP
- Undisclosed AFFIMER® targets
- Targeting first-in-class therapies



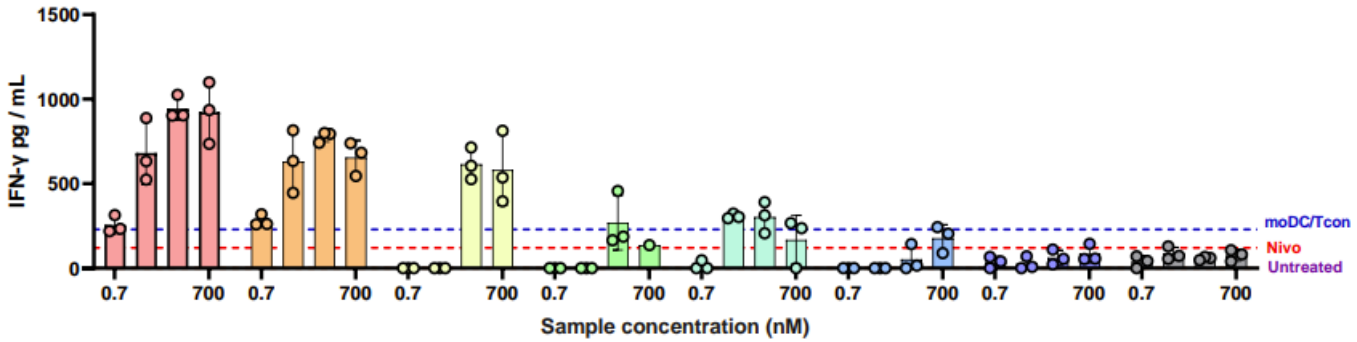
Proof of concept – FAPα release of warhead in tumour vs serum



- CT26 tumours engineered to overexpress FAPα
- PD-L1 AFFIMER® targeted TMAC with toxic warhead (talabostat)
- High levels of warhead detected in CT26 tumours– very low levels in mouse serum

AVA3x – PD-L1 Immunocytokine

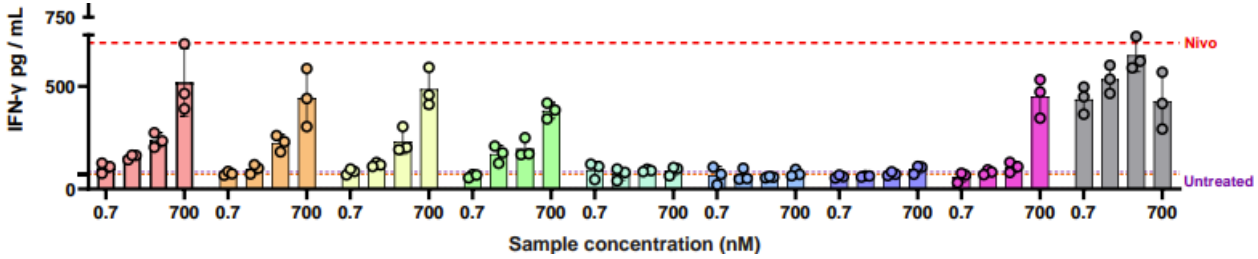
- Cytokine linked to anti-PD-L1 AFFIMER®
  - Stimulates NK cells and CD8+ T cells which can kill tumour cells, with no increase in Tregs
- PD-L1 directs the molecule to the tumour and is itself a checkpoint inhibitor
- Demonstrated *in vitro* efficacy, now evaluating *in vivo* tolerability, PK and efficacy



Mixed lymphocyte reaction assay with primary cells
Reversal of T cell exhaustion exhibited

AVA21- PD-L1/LAG3 Bispecific

- LAG3 – PD-L1 AFFIMER® bispecific
  - PD-L1 is an established checkpoint inhibitor: blocking interaction with PD-1 increases T cell activity
  - LAG3 interacts with its ligand MHCII to disrupt TCR interaction and hence inhibit T cell signalling
  - Multiple modalities active in a mixed lymphocyte assay (upregulate T cell activation)
- Constructs are being tested for *in vivo* activity



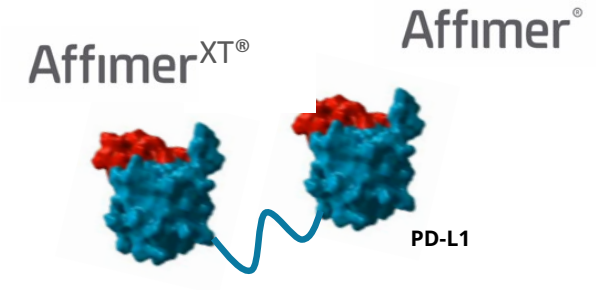
Mixed lymphocyte reaction assay with primary cells

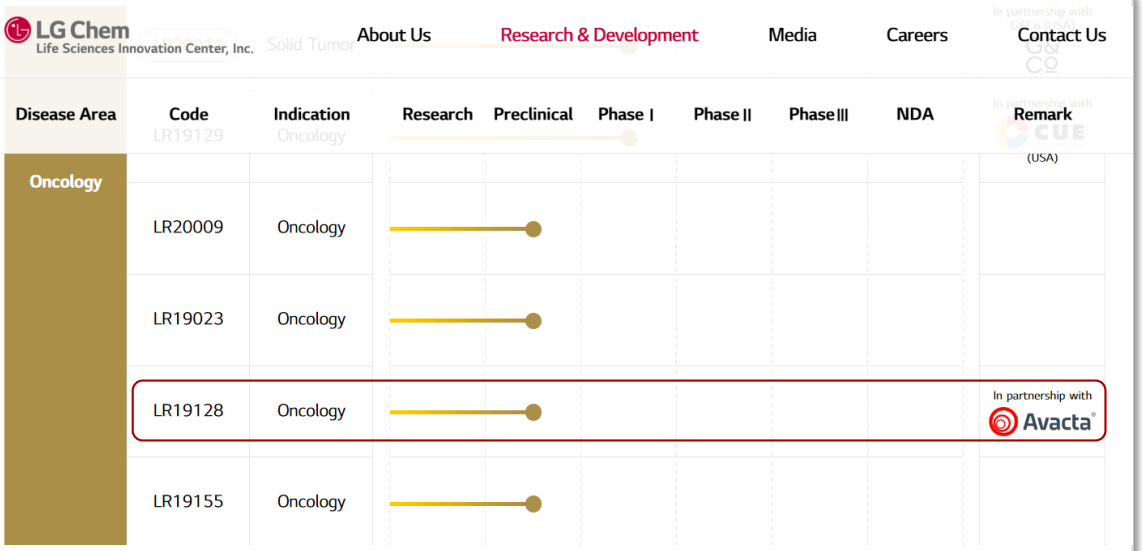
LG Chem – Multi-target Partnership

A multi-target development partnership and licensing deal worth up to $310 million with a focus on oncology and inflammatory diseases

PDL1/XT Antagonist

- PD1/PDL1 axis AFFIMER® inhibitor
- Half-life extension using AFFIMER® XT a human serum albumin binder
- Small size potentially leads to better tumour penetration



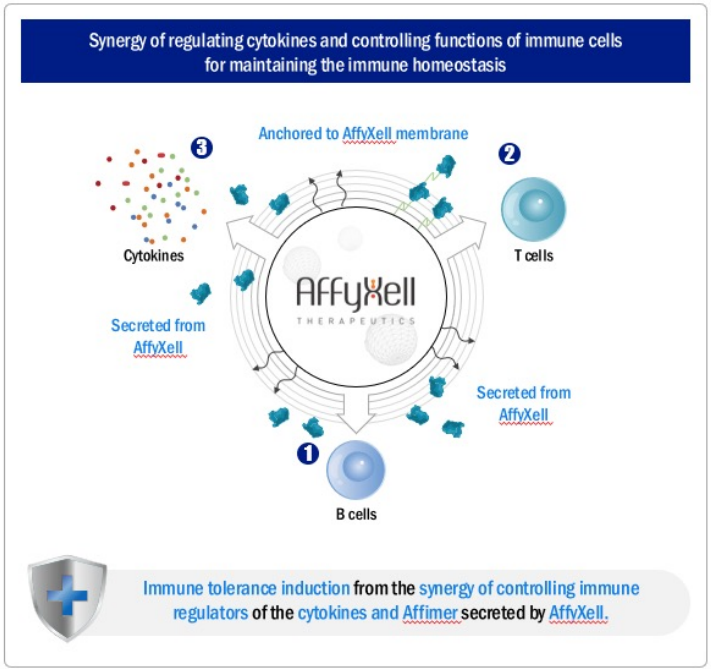


During the reporting period;

- LG Chem Life Sciences ('LG Chem'), the life sciences division of the South Korean LG Group, exercised its renewal option as part of the ongoing collaboration with Avacta, triggering a licence renewal fee payment to Avacta of $2 million.

Joint Venture in the Cell & Gene Space

A joint venture in South Korea with Daewoong Pharmaceutical to develop engineered mesenchymal stem cells that express and secrete immuno-modulatory AFFIMER® molecules to treat autoimmune diseases



Next-generation Stem Cell Therapies

Renewable "off the shelf" mesenchymal stem cells

AFX001: MSC secreting anti-CD40L AFFIMER® for use in GvHD

AFX002: MSC membrane bound agonist AFFIMER® for use in MS

AFX003: Undisclosed target

Program		Disease	Discovery	Lead Op	IND Enabling
Prioritized Program					
AFX-001	anti-CD40L	Graft versus Host Disease			
AFX-002	Undisclosed	Multiple Sclerosis			
AFX-003	Undisclosed	Undisclosed			

AFX-001 *In vivo* Efficacy in GvHD Mouse Models

AFX-001 secretes an AFFIMER® CD40L antagonist

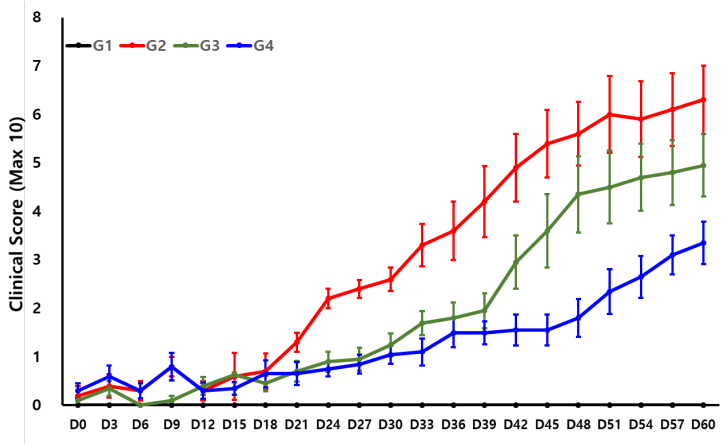
AFX-001 demonstrates superior efficacy in mouse acute GvHD model

AFX-001 MoA confirmed in *in vitro* and *in vivo* proof-of-concept (PoC) studies

Human PBMC $2x10^6$ cells

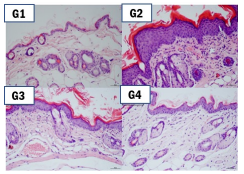
Group	Animal Model	Test Article	Injection Volume	Injection Interval
G1	Normal control	-	-	-
G2	GvHD	Vehicle	200 µL	D0 and D7
G3	GvHD	Naïve MSCs	200 µL	D0 and D7
G4	GvHD	AFX-001	200 µL	D0 and D7

Clinical Score in GvHD

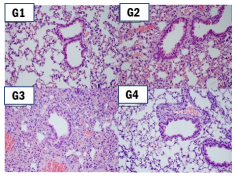


Histopathology

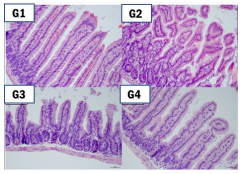
Skin (H&E)



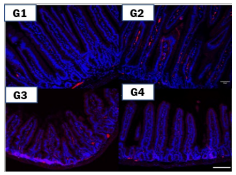
Lung (H&E)



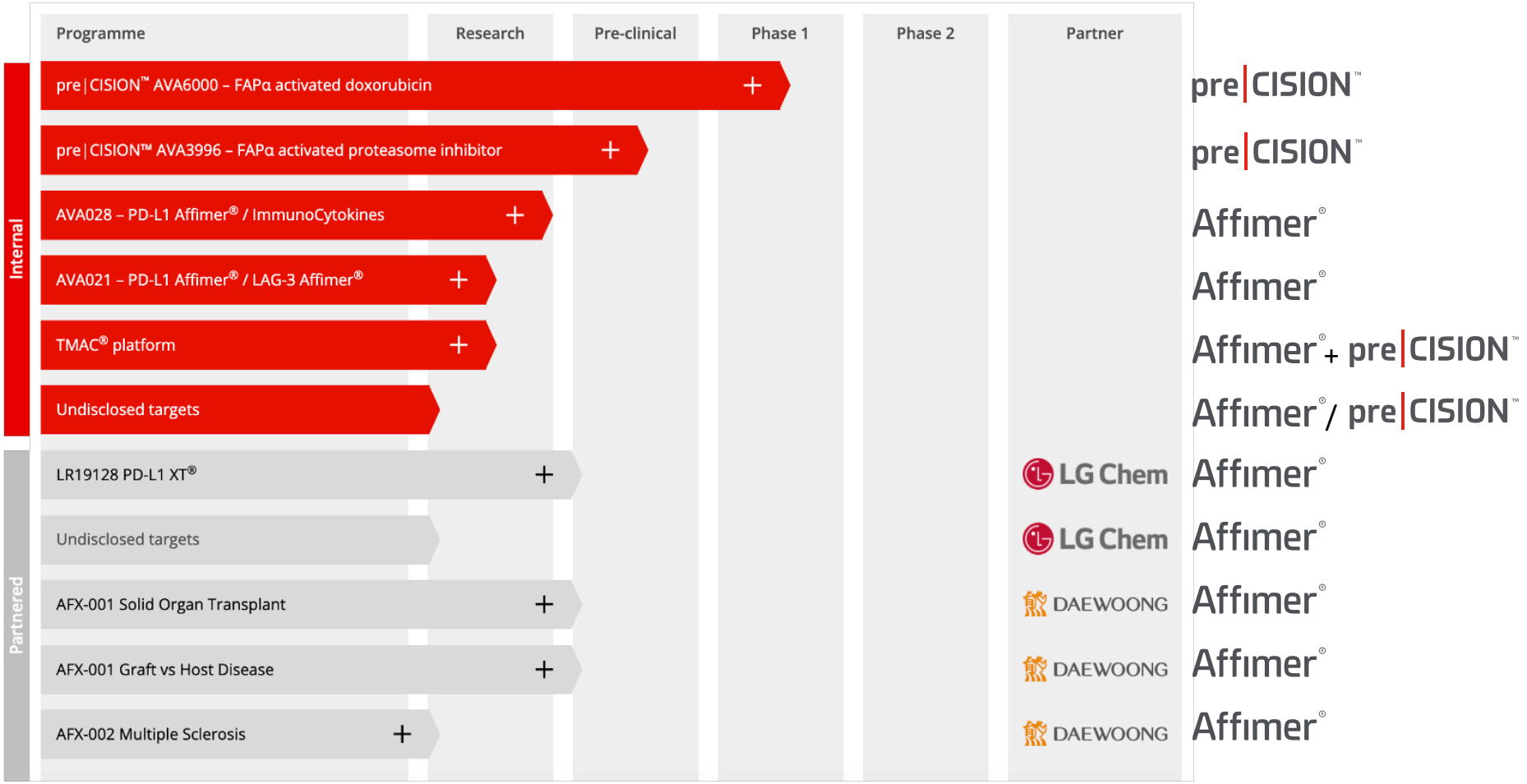
Small Intestine (H&E)



CD3+ T cell in Small Intestine



Avacta Therapeutics Pipeline – 2023



Intellectual Property

Affimer®

1st generation AFFIMER® technology for Therapeutics
- Mutated stefin A framework for novel binders including libraries for screening
- WO2006/131749; WO2009136182
- Licensed from University of Leeds and MRC

2nd gen AFFIMER™® technology for Research and Diagnostics
- Framework for novel binders derived from plant cystatins
- WO2014/125290
- Licensed from University of Leeds

Next gen AFFIMER™® technology for Therapeutics
- Stefin A framework for novel binders with improved biophysical properties and binding
- WO2019/008335 and unpublished patent filings

AFFIMER™® target binding IP
- PD-L1 binders: WO2019/197583; WO2023/057567
- HSA binders: WO2022/023538
- FAP-activated serum half life extenders: WO2022/094262, WO2022/094237
- CD33 binders: WO2022/234003
- Unpublished patent filings

preCISION™

FAP Cleavable Drug Conjugates
- Platform technology comprising having a drug linked to a leaving group through a FAP cleavable linker
- WO2015/192123 – FAP-Activated Therapeutic Agents
  - Broad platform patent filing
  - Includes ranted claims to AVA600.
  - Licensed from Tufts University
- WO2013/033396 – FAP-activated proteasome inhibitors.
  - Includes granted claims to AVA3996.
  - Licensed from Tufts University
- WO2022/094262, WO2022/094237 - FAP-activated serum half life extenders.
  - Covers drugs linked to half life extenders such as HSA binding AFFIMER™ proteins through FAP cleavable linkers
  - Co-owned with Tufts University
- Unpublished patent filings

Tumor Microenvironment-Activated Drug-Binder Conjugates (TMAC)
- Platform technology comprising a drug linked to a cell binding group through a FAP cleavable linker
- WO2019/236567 – TMAC binder conjugates
  - Covers platform TMAC technology.
  - Co-owned with Tufts University


Avacta®
www.avacta.com