Avacta®

Affimer®

pre|CISION™

Innovative Cancer Therapies

January 2020

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Investment Highlights

Affimer®
pre|CISION™

Addressing the lack of a durable response to existing immunotherapies through combinations of two proprietary therapeutic platforms: Affimer® - best-in-class antibody mimetic platform - and pre|CISION™ tumour targeted chemotherapy.

Near-term value inflection points including phase I clinical trial (3Q20) of AVA6000, a pre|CISION pro-drug form of Doxorubicin, that is only activated in the tumour improving the safety and therapeutic index of this chemotherapy.

Pipeline of pre|CISION targeted chemotherapies and novel tumour microenvironment activated drug conjugates (TMACs).

Validating partnerships in place with LG Chem, Moderna Therapeutics, ADC Therapeutics, Daewoong Pharmaceuticals and Tufts University, and new discussions with additional third parties ongoing.

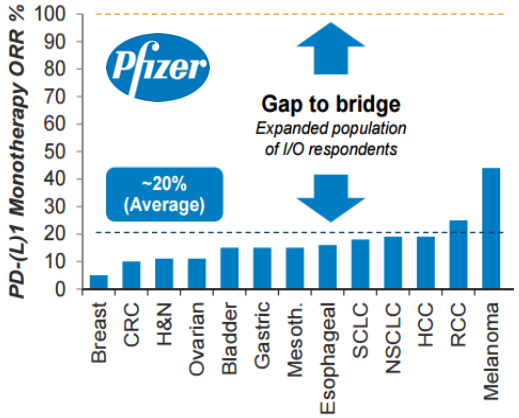
Based in Cambridge and Wetherby UK and listed on the London Stock Exchange (AVCT)

The Cancer Immunotherapy Challenge

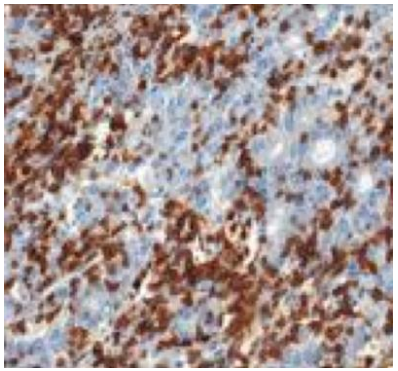
Affimer®
pre|CISION™

Only ~20% of patients respond to current immune checkpoint monotherapies

PD-1 Monotherapy Response Rates

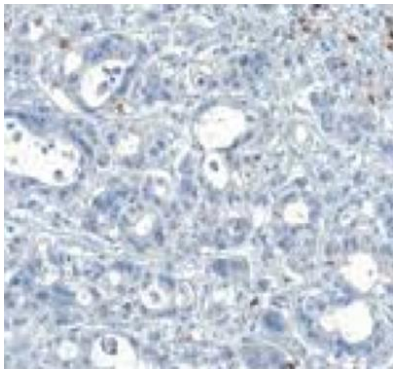


"Inflamed tumours" respond well to checkpoint inhibitors



20-30% patients

"Non-inflamed" tumours do not



70-80% patients

Avacta is uniquely placed to address this gap in cancer immunotherapy market through **clinically differentiated combinations of pre|CISION pro-inflammatory drugs and Affimer immune checkpoint modulators**

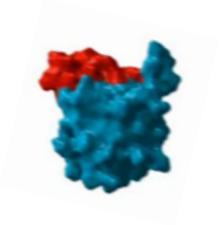
Technology and Strategy Overview

Affimer®
pre|CISION™

Two proprietary platforms well positioned to generate multiple clinically differentiated products addressing the gap in cancer immunotherapy

Affimer®

Mono- and bi-specific immunotherapies

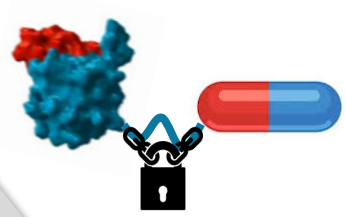


pre|CISION™

Chemotherapy pro-drugs activated in the tumour

Clinically Differentiated Cancer Therapies

Novel TME activated drug conjugates



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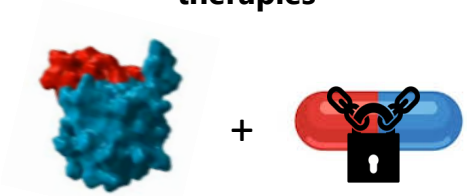
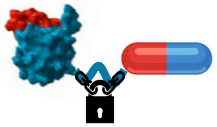
Co-administered combination therapies



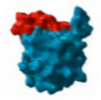
Lead Programmes

AVA6000
pro-doxorubicin prodrug
Phase I 3Q20

AVA004/100
anti-PD-L1 + DPP8/9 inhibitor drug conjugate



AVA004
anti-PD-L1 antagonist

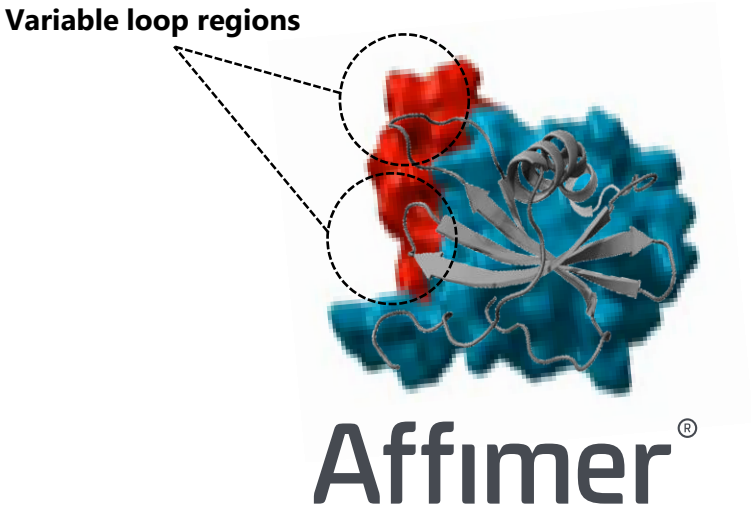


Affimer®
Avacta's Proprietary Biologics Platform

Affimer® pre|CISION™

What is an Affimer?

- Based on a **naturally occurring human protein** (stefin A) and engineered to **display two loops that create an antigen binding surface.**
- **Variable loop regions of 9 amino acids each are randomised** to create very large (10^{10}) libraries for phage selections.



Technical Advantages

- **Smaller, simpler and more robust, soluble and stable** than antibodies.
- **High affinity** Affimer® generated for new targets in a matter of weeks, **much quicker** than antibodies.
- **Flexible formatting** for multi-specifics, agonism, drug conjugates.
- **High expression levels** in a range of cells and tissues.
- **Fully human: lower immunogenicity risk.**

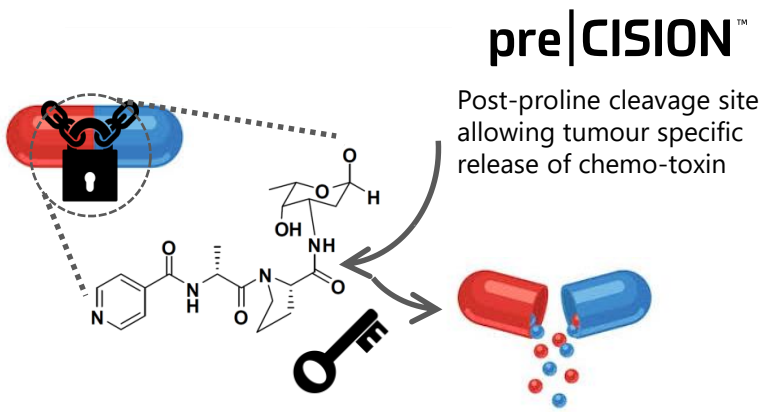
Commercial Advantages

- **Proprietary and unencumbered IP.**
- **Freedom to operate** where there is antibody IPR.
- **Security of supply.**
- **Cheaper to produce (*E.coli*).**

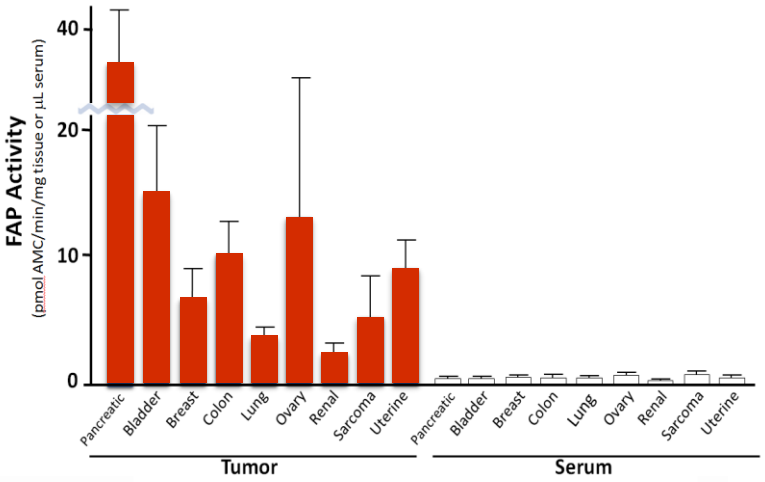
pre|CISION™
Avacta's Proprietary FAPα Sensitive Substrate

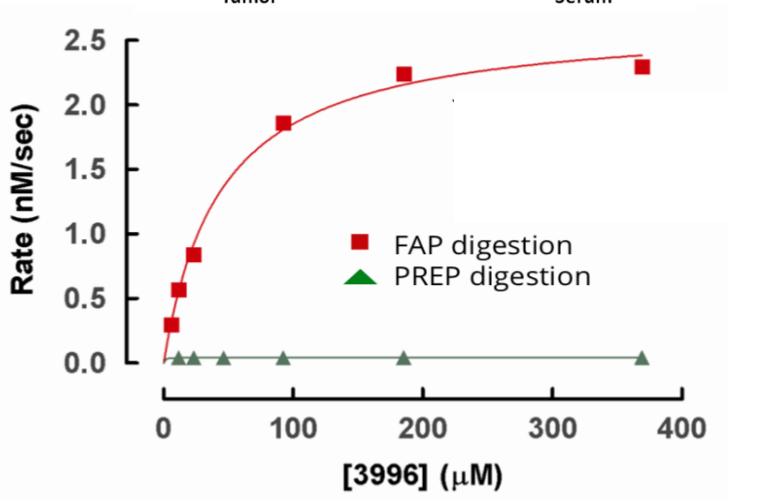
Affimer®
pre|CISION™

- pre|CISION is **highly specific** to cleavage by an enzyme, **fibroblast activation protein-α (FAPα)** that is **highly upregulated in the tumour microenvironment of most solid tumours**
- pre|CISION substrate prevents chemotoxins from entering cells **rendering them inert until activated in the tumour** by FAP
- Substrate can also be incorporated into a **drug conjugate linker**
- Substrate exclusively licensed from Tufts University



Average Induction of FAPα Activity in Tumour Relative to Sample Matched Serum





pre|CISION™ Chemotherapies activated only in the tumour

AVA6000 Pro-doxorubicin – an FAP activated form of Doxorubicin aimed at dramatically improving the safety profile and therapeutic index of this standard-of-care treatment for advanced soft tissue sarcomas, and providing POC for the pre|CISION platform.

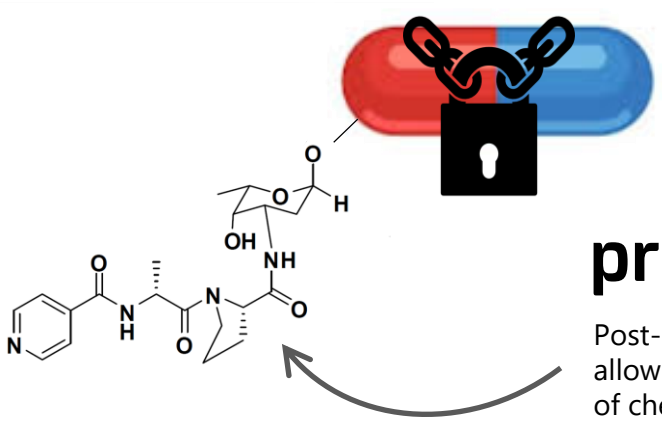
FAP Activated pre|CISION Pro-drugs

Affimer®
pre|CISION™

Tumour specific activation limits systemic exposure, improves safety and therapeutic index for stand-alone chemo and in combination with checkpoint therapies

Circulating pro-drug cannot enter cells

Activation of drug by FAP in TME



pre|CISION™

Post-proline cleavage site allowing tumour specific release of chemo-toxin by FAPα

Increased Maximum Tumour Exposure (MTE) of Active Drug and Improved Therapeutic Index (TI)

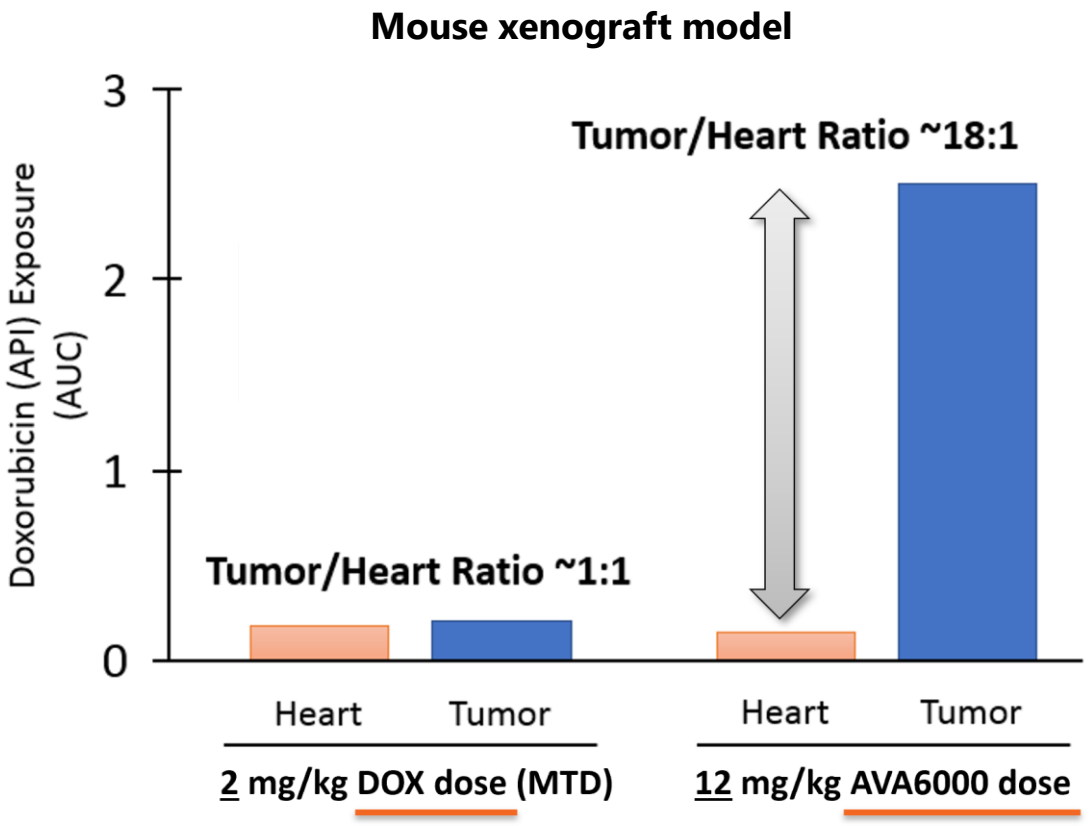
pre|CISION prodrugs are designed to address dose-limiting toxicities and side-effects across a wide range of drug classes, including:

Anthracyclines – cardiotoxicity
Proteasome Inhibitors – peripheral neuropathy

Taxanes – neutropenia and peripheral neuropathy
AKT Inhibitors – erythematous and stomatitis

AVA6000 Pro-doxorubicin Pre-clinical Safety

Differential intra-tumoural exposure relative to cardiac tissue creates substantial opportunity for improved therapeutic index for chemotherapies



AVA6000 Pro-doxorubicin Efficacy

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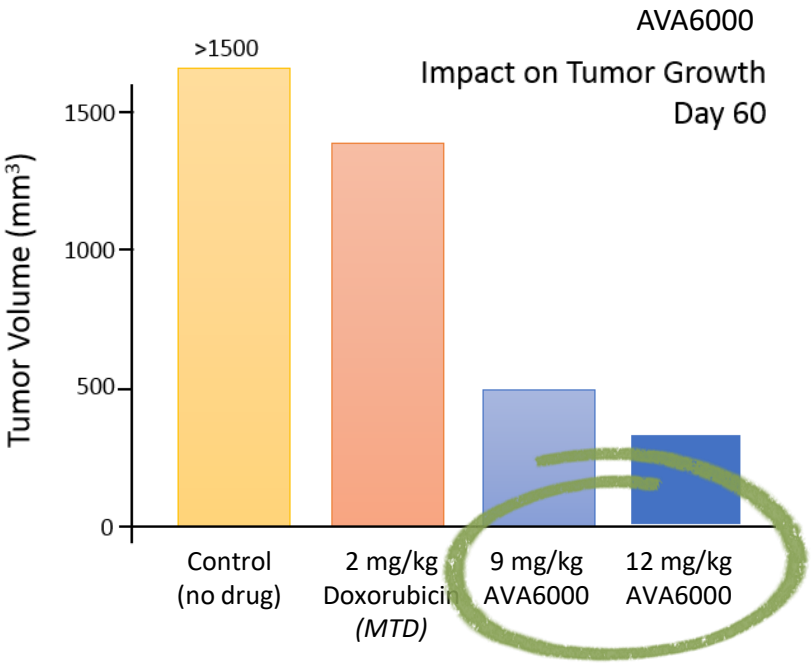
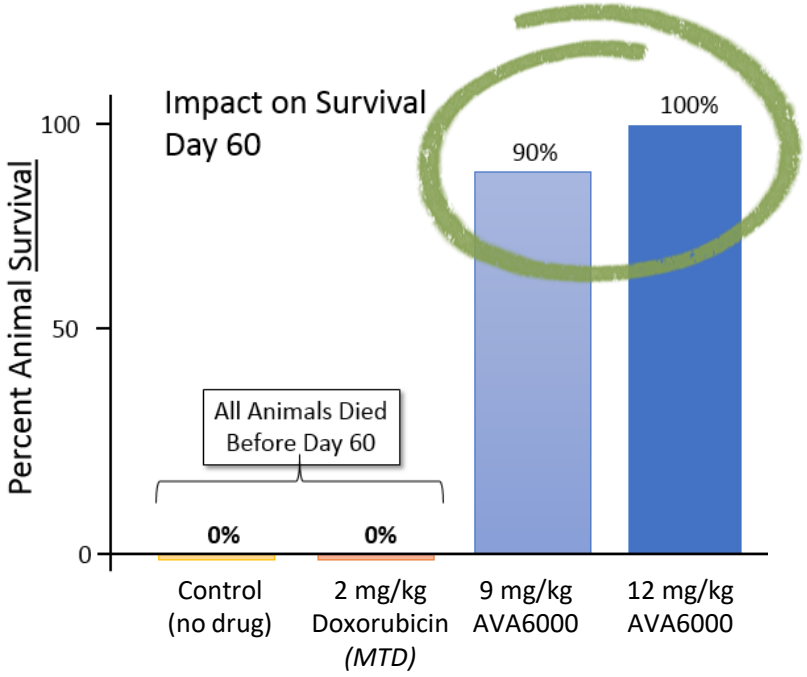
pre|CISION™

AVA6000 Pro-doxorubicin permits higher doses than the MTD for doxorubicin resulting in better anti-tumour activity in mouse xenograft model



AVA6000 can be dosed at higher concentrations than the MTD for doxorubicin



AVA6000 significantly reduced tumour volume and improved survival, relative to doxorubicin

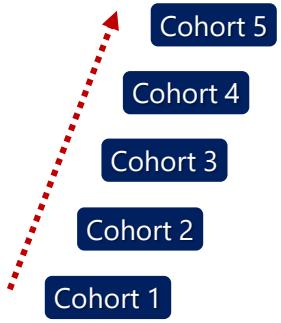
Overview of Clinical Development Plan to Market Authorization

Affimer®
pre|CISION™

First-Patient-In Q3/4 2020

Phase 1a – Dose Escalation/Expansion
AVA6000 in Solid Tumours
Safety, PK, PD and preliminary efficacy

Dose Escalation Cohorts



MTD or recommended dose expansion

Phase 1b & 2 in Combination

Phase 1b – Safety Expansion
PD(L)1 Inhibitor Combination
Phase 2 Expansion Cohorts per Indication (below)

- Advanced Gastric Cancer 2L
- Platinum resistant Ovarian Cancer
- Advanced NSCL Cancer 2/3L
- Advanced Pancreatic Cancer 2/3L
- Advanced Colorectal Cancer 3L
- Advanced Bladder Cancer 1L
- Advanced unresectable Triple Negative Breast Cancer (TNBC) 2L
- Advanced Head and Neck cancer 2L

Phase 3 | Pivotal

AVA6000 + Anti-PD-(L)1:
Advanced Gastric Cancer 2L
Randomized versus paclitaxel.
200-300 patients per arm
Primary endpoint: Overall Survival (OS)
100 sites, Global

AVA6000 + Anti-PD-(L)1:
Ad. Platinum Resistant Ovarian Cancer
Randomized versus liposomal doxorubicin,
100-200 patients per arm
Primary endpoint: Overall Survival (OS)
100 sites, Global

AVA6000 + Anti-PD-(L)1:
Other potential pivotal trials in advanced solid tumors according to signal in phase 2 expansions, TBD

AVA6000 Single Agent Pivotal Expansion
First line for Advanced Soft Tissue Sarcoma
Primary endpoint: Overall Survival (OS). 100 patients, 25 sites US/EU

AVA6000 Potential Partnering Opportunities

Affimer®
pre|CISION™

Standard Doxorubicin is a generic drug with a ~$1bn market despite severe cardiotoxicity

Companies with Existing Doxorubicin Products

Companies with sales forces and relevant doxorubicin commercialization experience and contacts

- **Approved Generic Doxorubicin HCl**
  - Brand Names: Adriamycin, Adriamycin RDF, Rubex, Adriamycin PFS
  - **Most notable companies include BMS, Pharmachemie and Abraxis**
- **Approved Liposomal Doxorubicin Formulations**
  - Brand Names: Doxil, Dox-SL, LipoDox, Evacet, Nudoxa, Myocet
  - **Most notable companies include J&J, Sun Pharma, Teva**

Companies with Ongoing Checkpoint Inhibitor + Doxorubicin Clinical Studies

Large pharma testing combinations of antibodies/ receptor traps with doxorubicin (including liposomal Dox)

- **Involving Checkpoint Inhibitors**
  - **AstraZeneca/Medimmune, BMS, Merck, Roche/Genentech, Pfizer** (PD-L1/PD-1)
  - **BMS, AstraZeneca/Medimmune**: (CTLA-4)

Companies with Other Ongoing Doxorubicin Clinical Studies of Note

- **Roche, Biocon and/or Mylan**: Trastuzumab (anti-HER2)
- **Genentech**: Bevacizumab (anti-VEGF-A)
- **Eli Lilly/Merck KGaA**: Cetuximab (anti-EGFR)

AVA6000 Market Opportunity

- Market expansion through increasing number of treatment cycles per patient
- Market expansion in existing indications not readily addressed by current doxorubicin formulations because of age-related risks
- Market expansion in indications not normally addressed by current doxorubicin formulations because of patient fragility (i.e. not age per se)
- Opportunity for combinations with checkpoint inhibitors`

Expansive pre|CISION Pro-drug Pipeline

Affimer®
pre|CISION™

The pre|CISION technology can be applied to a broad range of other chemotherapies beyond doxorubicin to improve their safety and tolerability

A pipeline of pre|CISION tumour activated pro-drugs has alreadybeen generated and substantial pre-clinical data including PK and efficacy has been generated for a FAP activated proteasome inhibitor (AVA3996):

- FAP-activated proteasome inhibitor (AVA3996)
- FAP-activated Gemcitabine
- FAP-activated Capecitabine
- FAP-activated Taxanes
- FAP-activated PARP inhibitors
- FAP-activated Platins
- FAP-activated small molecule PD-1 Inhibitor
- FAP–activated AKT inhibitors (FAP-activated MK-2206)
- FAP-activated Balixafortide

pre|CISION™

TMAC™

Lead tumour microenvironment (TME) activated drug conjugate (TMAC) progamme

AVA004/100 PD-L1/I-DASH – a novel TME activated drug conjugate incorporating the pre|CISION FAP sensitive substrate in the linker to release the I-DASH warhead in the TME.

AVA004/100 seeks to synergistically combine stimulation of the innate immune response by a pro-inflammatory DPP8/9 inhibitor (AVA100 I-DASH) with induction/maintenance of the adaptive immune response using the Affimer PD-L1 blockade (AVA004).

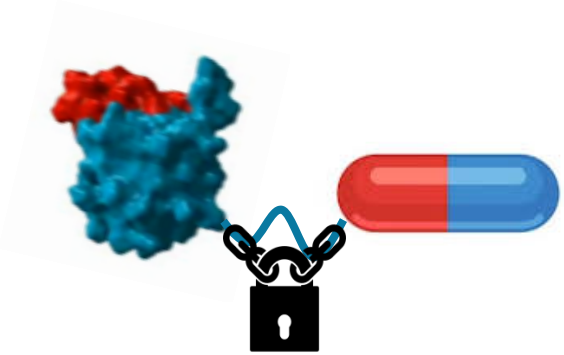
Tumour Microenvironment Activated Drug Conjugates (TMAC™)

Affimer®
pre|CISION™

Targeting and release of pro-inflammatory drugs <u>in the tumour microenvironment</u> synergises the innate and adaptive immune responses

First TMAC Programme

Affimer®
PD-L1 inhibitor



“I-DASH”
DPP8/9 inhibitor warhead

pre|CISION™ **FAPα sensitive linker**

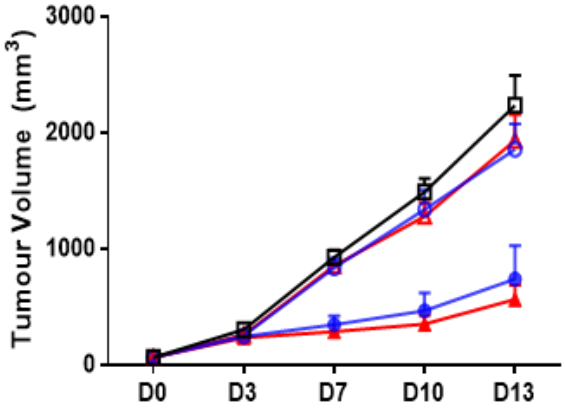
Patent Application July 2018: *Tumor Microenvironment – Activated Drug-Binder Conjugates, and Uses Related Thereto.* US Patent Application Serial Number 62/680,300

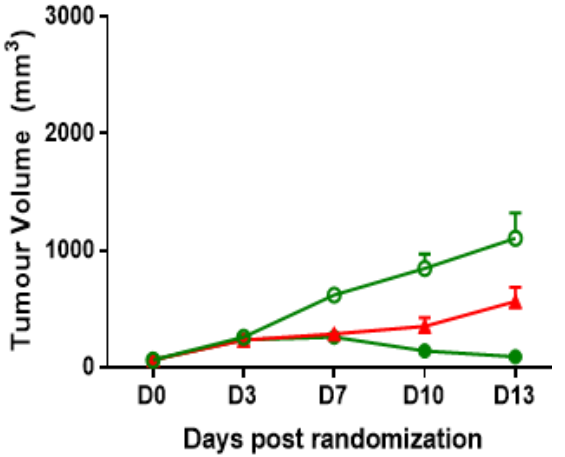
AVA004 + AVA100 (anti-PD-L1 + I-DASH) Combination Shows Improved Anti-tumour Activity

Affimer®
pre|CISION™

Affimer PD-L1 antagonist in combination with AVA100 I-DASH inhibitor in MC38 humanized PD-L1 model shows improved tumour response

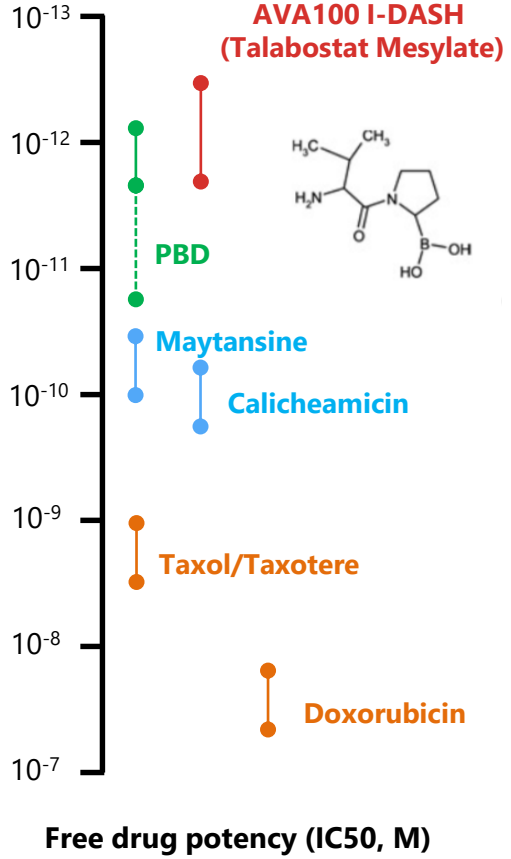
Affimer PD-L1 + AVA100 Combination in MC38 Model





- Vehicle
- Control IgG1 5 mg/kg
- SQT Gly Fc 10 mg/kg
- Atezolizumab 5 mg/kg
- hAVA04 Fc 10 mg/kg

- SQT-Gly Fc 10 mg/kg + AVA100
- hAVA04 Fc 10 mg/kg
- hAVA04 Fc 10 mg/kg + AVA100

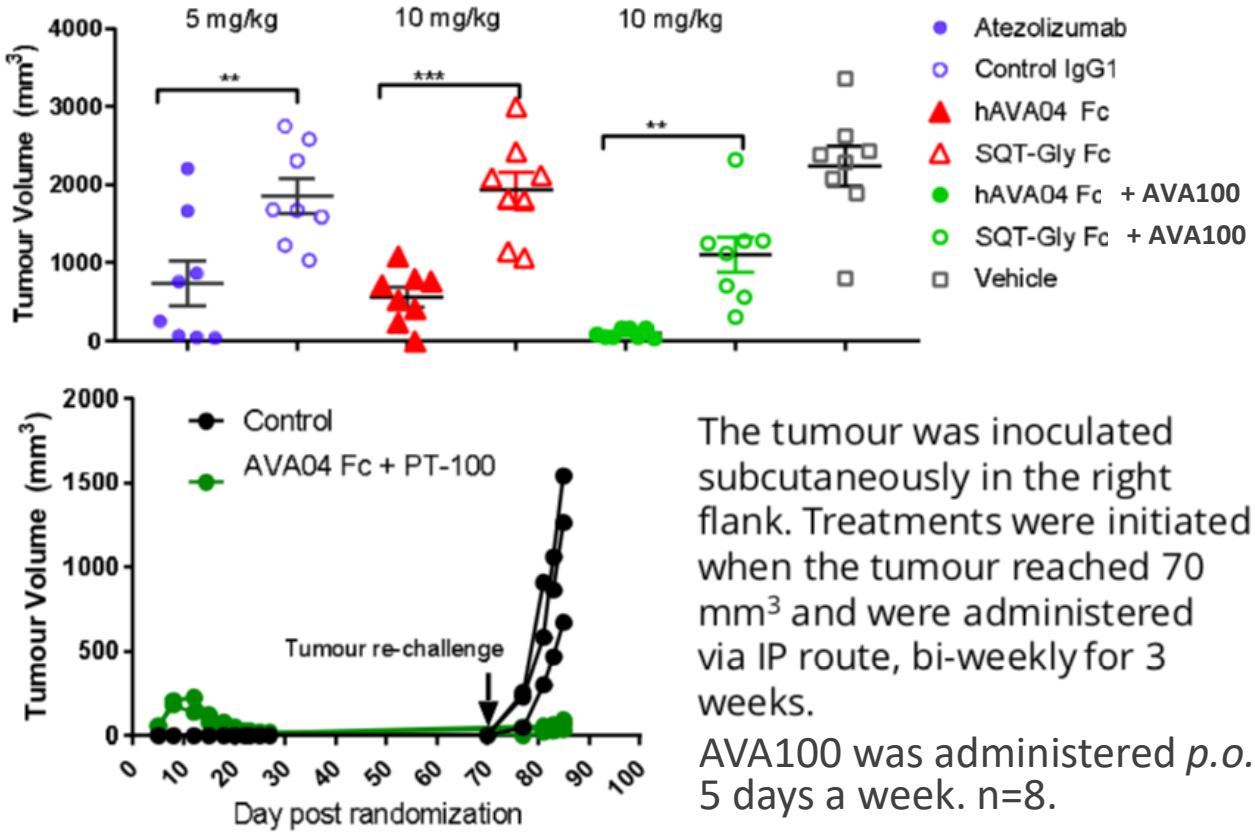


AVA004 + AVA100 (anti-PD-L1 + I-DASH) Combination Shows Immunity to Re-challenge

Affimer®
pre|CISION™

Affimer PD-L1 antagonist in combination with AVA100 I-DASH inhibitor in MC38 humanized PD-L1 model shows immunity to re-challenge

Affimer PD-L1 + AVA100 Combination in MC38 Model



The tumour was inoculated subcutaneously in the right flank. Treatments were initiated when the tumour reached 70 mm^3 and were administered via IP route, bi-weekly for 3 weeks.

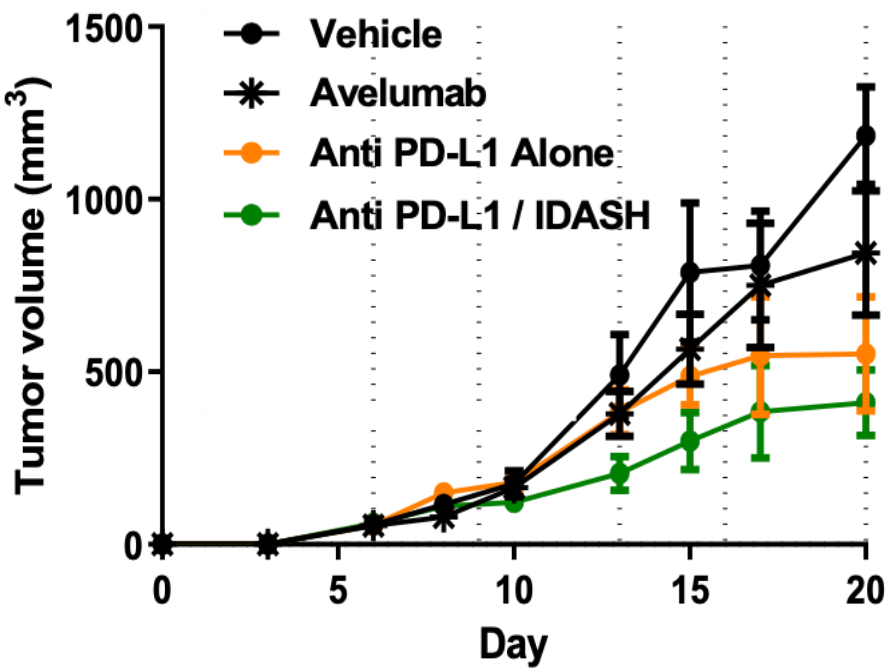
AVA100 was administered *p.o.* 5 days a week. n=8.

AVA004/100 (anti-PD-L1/I-DASH) TMAC Conjugate Shows Potent Anti-tumour Activity

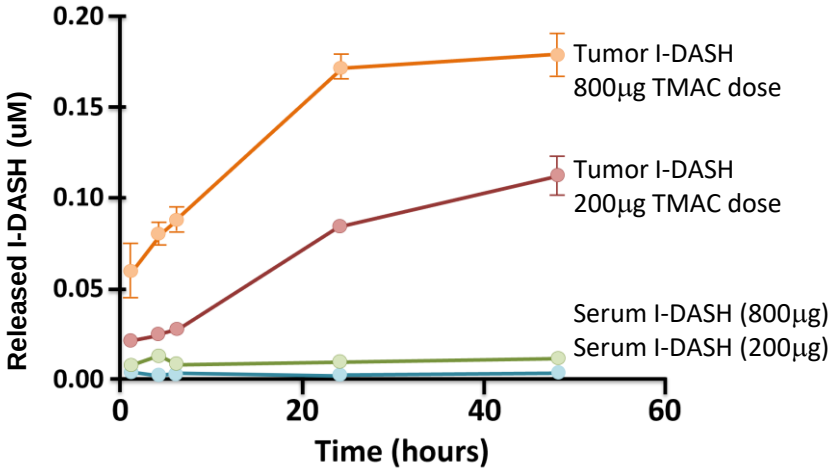
Affimer®
pre|CISION™

PD-L1/I-DASH TMAC shows potent anti-tumour activity in mFAP+ CT26 syngeneic mouse colon carcinoma model and preferential intra-tumoral exposure of FAP released I-DASH warhead

Efficacy in CT26 Model



Tumor and Serum PK of Released I-DASH from High TMAC



Tumour Microenvironment Activated Drug Conjugates (TMAC™)

Affimer®
pre|CISION™

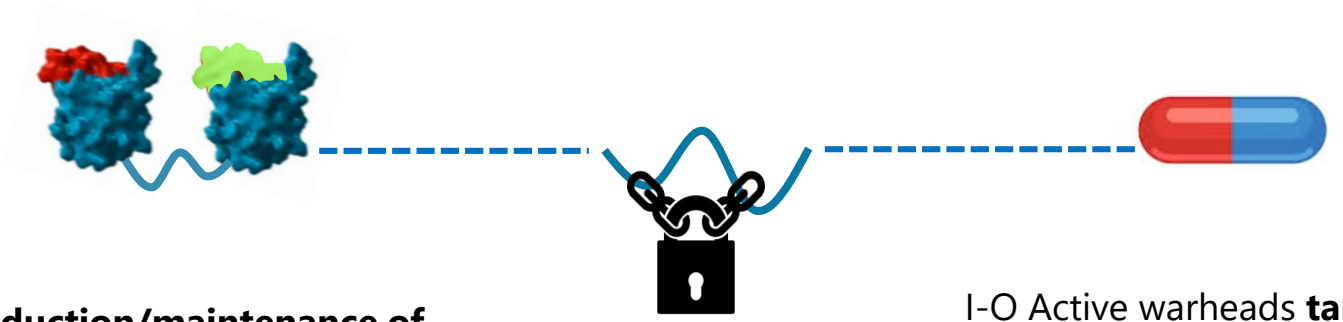
Targeting and release of pro-inflammatory drugs <u>in the tumour microenvironment</u> synergises the innate and adaptive immune responses

Future Developments

Affimer I-O Targeting

pre|CISION™
FAP Sensitive Linker

Synergistic Toxins



Induction/maintenance of adaptive immune response overcoming immune evasion.

- PD-L1, other immune-checkpoints, bispecifics and costimulatory receptors
- Additional tumour targeting

I-O Active warheads **targeting "bystander" cells**, including macrophage, NK cells, etc. and supporting tumor stroma – e.g:

- I-DASH = DPP8/9 inhibitor
- Proteasome; AKT; CDK inhibitors
- STING; TLR7/8 agonists

Patent Application July 2018: *Tumor Microenvironment – Activated Drug-Binder Conjugates, and Uses Related Thereto.* US Patent Application Serial Number 62/680,300

Wholly Owned Pipeline and Fully Funded Partnerships

Affimer®
pre|CISION™

Discovery/Lead Optimisation	Clinical Candidate	IND	Phase 1

- AVA6000 PRO-DOXORUBICIN preCISION prodrug
- AVA3996 PRO-VELCADE preCISION prodrug
- AVA004 PD-L1
- AVA004-100 PD-L1/I-DASH Drug Conjugate
- AVA030 PD-L1/TGFβR Trap BISPECIFIC

Tufts University School of Medicine

Tufts University School of Medicine

Undisclosed (Oncology/Inflammatory)	LG Chem Life Sciences	Multi-target development partnership and licensing deal worth up to $310m with $2.5m upfront, $5.5m in near-term milestones, royalties on future products and full research costs
Undisclosed	moderna	Multi-target research collaboration initiated 2015. Commercial option exercised 1Q19 to take one or more Affimer lead molecules into clinical development.
Affimer Drug Conjugate	ADC THERAPEUTICS	Three target deal to develop Affimer-drug conjugates incorporating ADCT's proprietary PBD warheads. Fully funded by ADCT with development milestones and royalties on future sales.
Cell and Gene Therapies	DAEWOONG PHARMACEUTICAL CO.,LTD.	Established JV January 2020 to develop next generation engineered stem cell therapies that secrete immuno-modulatory Affimer proteins, with an initial focus on autoimmune diseases.

Summary

Affimer®
pre|CISION™

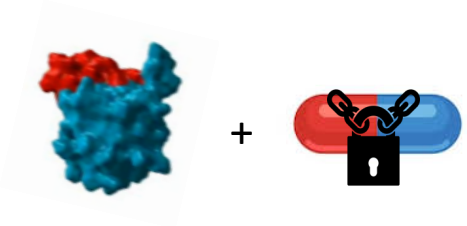
Addressing the lack of a durable response to existing immunotherapies experienced by most patients through combinations of two proprietary therapeutic platforms: Affimer® - best-in-class antibody mimetic platform - and pre|CISION™ tumour targeted chemotherapy.

Phase I clinical trial (3Q20) of AVA6000, a pro-drug form of Doxorubicin.

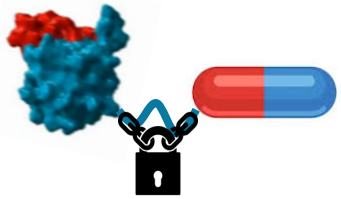
Pipeline of pre|CISION targeted chemotherapies and Affimer immunotherapies to be developed as co-administered combinations and in novel tumour microenvironment activated drug conjugates (TMACs).

Clinically Differentiated Cancer Therapies

Co-administered combination therapies of pro-drug chemotherapies and ICP therapies



Novel drug conjugates with tumour microenvironment activated warheads synergising with ICP inhibitors



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Appendix

Introductions

Dr Eliot Forster, Non-Executive Chairman

- Over 25 years experience in pharma and Biotech.
- 2015 – 2018 CEO of Immunocore Limited.
- 2018- 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 Jose Saro, CMO

- Over 20 years' experience in the pre-clinical, translational and early clinical development of oncology assets.
- Joined Avacta from Roche Innovation Center Zurich where he was Senior Translational Medicine Leader.
- Previously in senior roles at Bristol Myers Squibb, Novartis, Eisai and Wyeth.
- Joined Avacta in 2018.

Dr Alastair Smith, CEO

- Over 12 years experience as a public company CEO.
- A leading UK biophysicist - founded Avacta in 2006.
- World class scientific and technical knowledge with a highly commercial mindset.

Dr Amrik Basran, CSO

- Over 10 years' experience of both the biotech and pharma industries.
- Director of Protein Biosciences at Domantis, Head of Topical Delivery (Biopharm) at GSK.
- Joined Avacta in 2013.

David Wilson, Commercial Director (Diagnostics)

- >25 years commercial experience of in-vitro diagnostics.
- Led the sales, marketing and business development functions at Genzyme Diagnostics
- Joined Avacta in 2019.

Tony Gardiner, CFO

- 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.

Matthew Vincent, VP Business Development (Therapeutics)

- Senior executive with over 25 years' experience in biotech.
- Joined Avacta from Arisaph Pharmaceuticals where he led corporate development and therapeutic innovation strategy.
- Trained as a lawyer and patent attorney.
- Joined Avacta in 2017

Dr Matt Johnson, CTO

- Genetics & Microbiology Molecular Biology.
- 8 years at Abcam becoming global Head of R&D.
- Joined Avacta in 2014.

Comparator Technologies

Affimer®
pre|CISION™

Affimers exhibit all the properties of a best-in-class therapeutic protein platform

Key Attributes of a Therapeutic Protein Platform	Avacta Affimer®	Molecular Partners Darpin®	Pieris Anticalin®	Ablynx (Sanofi) 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