

Let's Make Cancer History!



inside out bio

science for living well

© InsideOutBio

alan.herbert@insideoutbio.com
1.617.584.0360

Team



Alan Herbert, MBChB and PhD

- **MIT, Research Scientist:** Fundamental Discoveries in Genetic Regulation, Z-DNA, Flips, Cancer Biology
- **Boston University, Associate Professor:** First Human Genome Wide Analysis – Framingham Heart Study
- **Merck, Associate Principal Scientist:** Pre-clinical programs in Immune Diseases and Immuno-oncology
- **InsideOutBio, Founder & CEO:** Complement Therapeutics



MERCK



BOSTON
UNIVERSITY



Philip Jeng (Advisory)

- **Genentech, Associate Engineer:** Process Development Rotational Program (PDRP)
- **ZS Associates, Associate:** Healthcare consulting – Strategy, Forecasting, Market Research, Market Access
- **Harvard Blavatnik Fellowship, Fellow:** Fellowship in life science entrepreneurship
- **Neurophth Tx, Corp Dev:** Gene Therapy for Ophthalmic Diseases

Genentech
A Member of the Roche Group



InsideOutBio's Targets the Complement C3 Checkpoint in Cancer

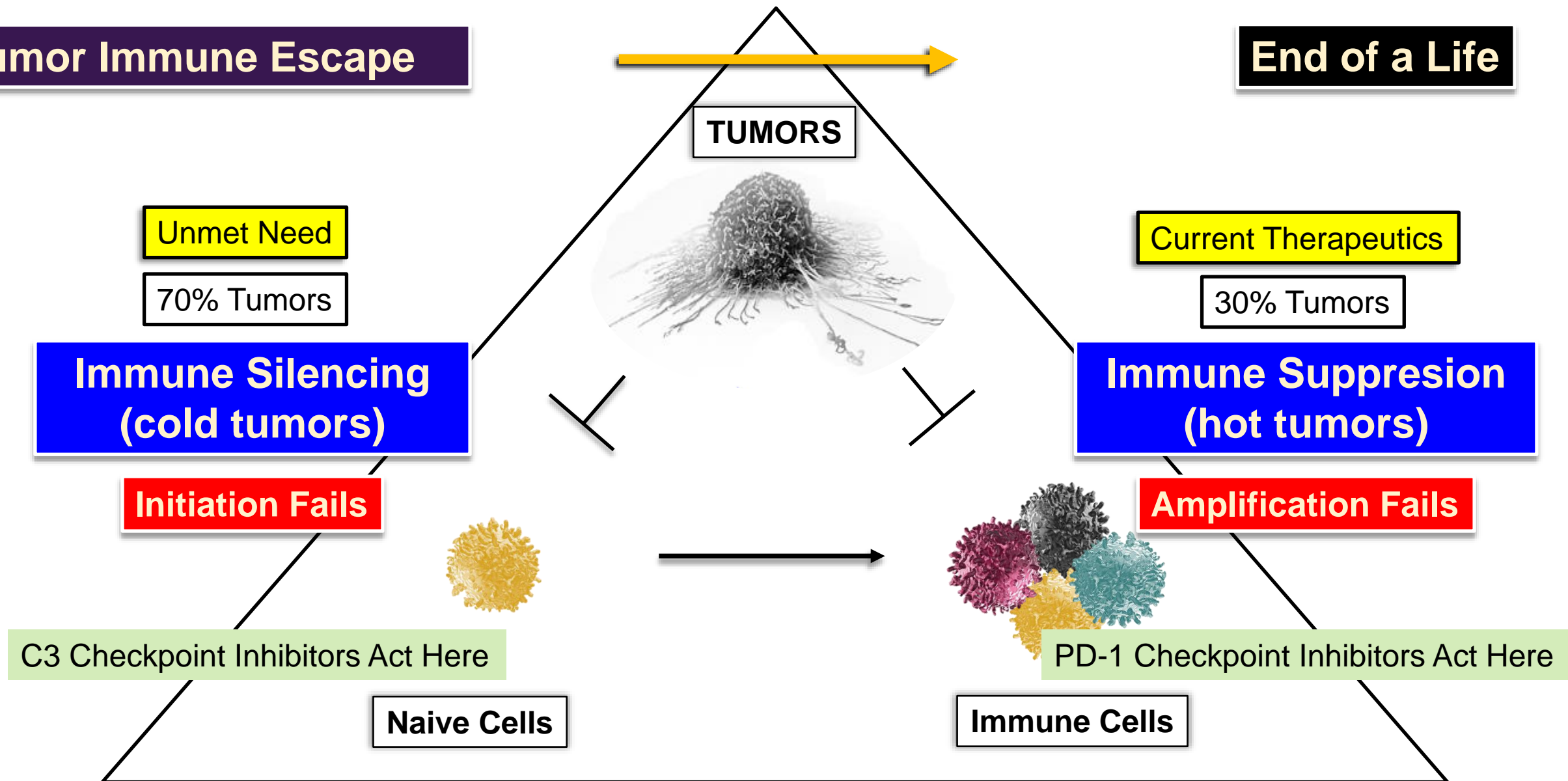
- We have a ***Novel*** therapeutic to attack the 70% of tumors not responding in the clinic today
- We target the complement ***C3 checkpoint*** that regulates the immune response against tumors
- We are the first to discover the C3 checkpoint and ***own the iP*** surrounding the therapeutic
- We have ***Human Genetic Validation*** and proof of biology
- Our current virtual model is ***capital efficient*** and sponsorship by Millipore Sigma at Lab Central

What we need

- We are looking for a 2 year runway to get to IND and partners
 - who can get us to the clinic faster
 - with synergistic technologies

Tumor Immune Escape

End of a Life



inside out bio

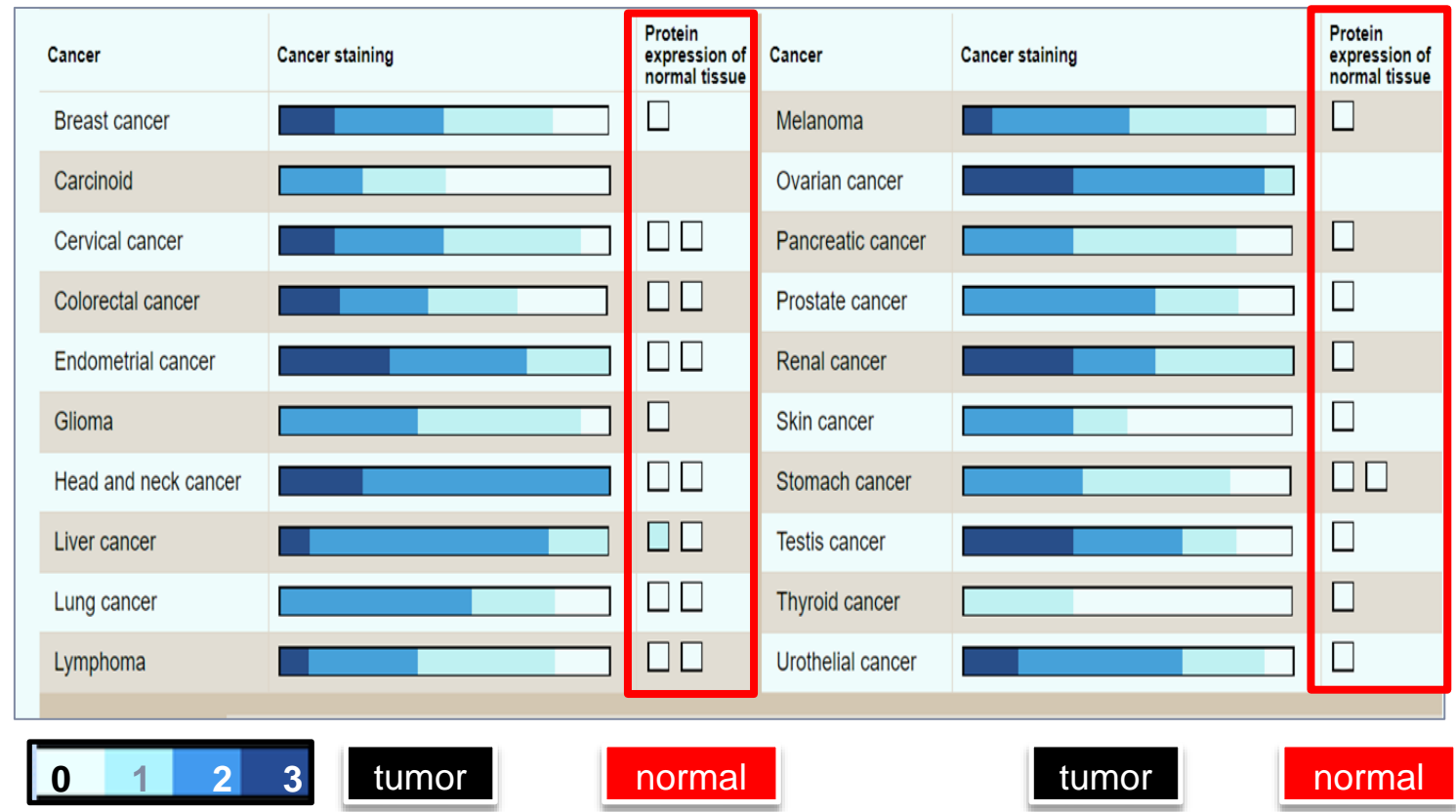
science for living well

NON-CONFIDENTIAL June 2020

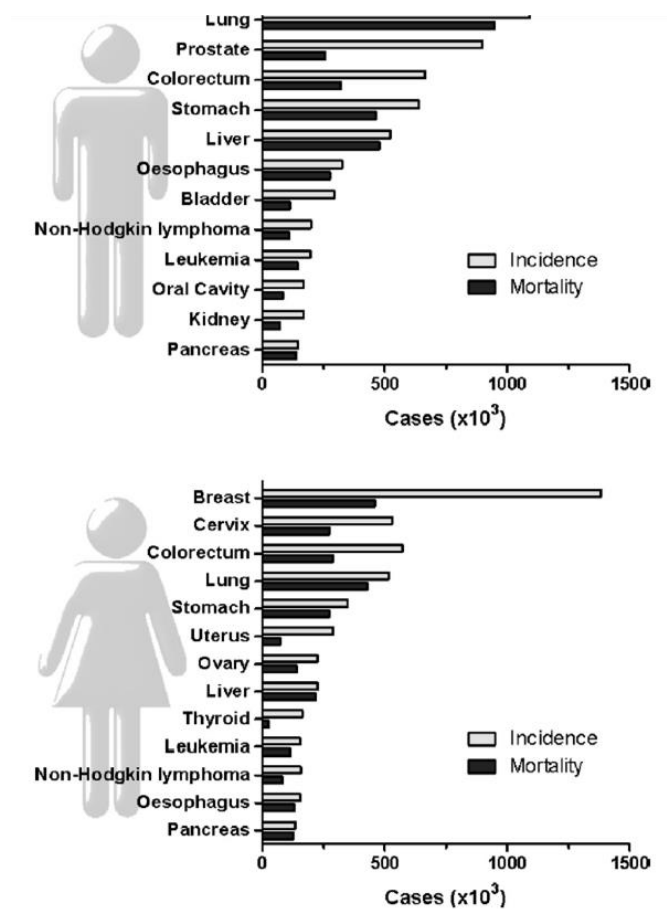
■ The C3 checkpoint versus the PD-1 checkpoint

Many Cancers Overexpress an Components of the Complement C3 Checkpoint

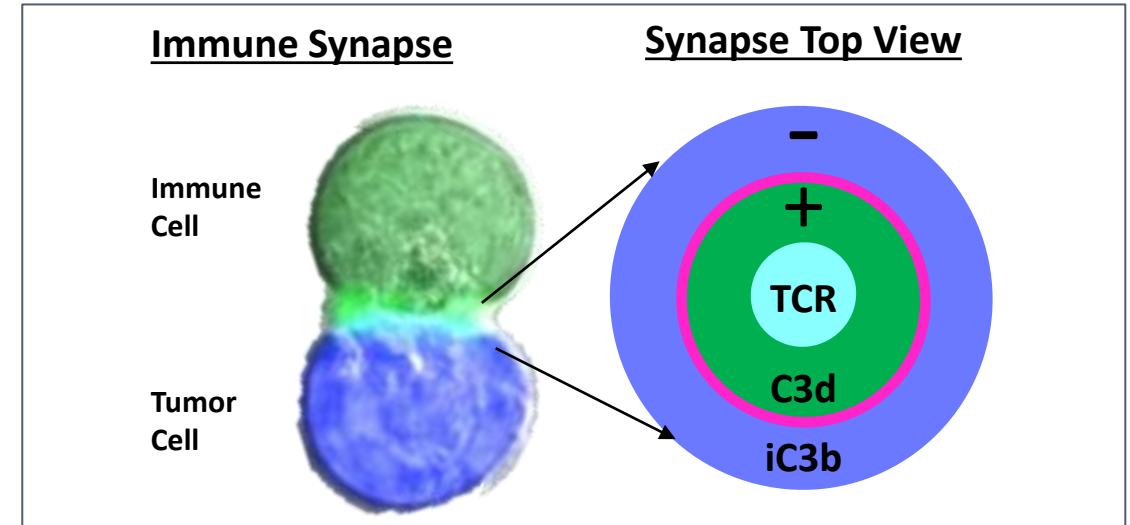
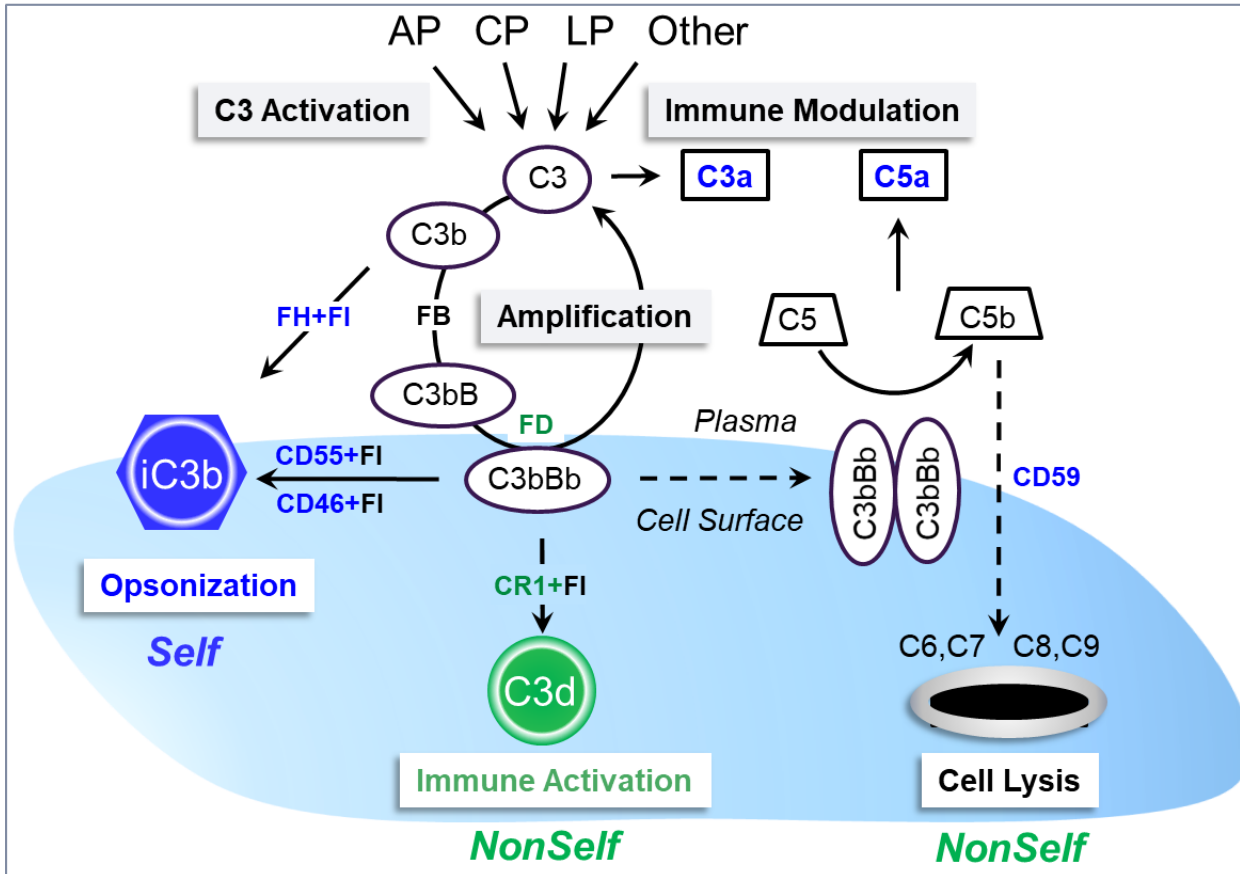
Complement C3 Protein Level
(normal versus Tumor)



Cancer Incidence & Mortality
(potential Indications)



The Complement C3 Checkpoint Regulates Initiation of anti-tumor Responses

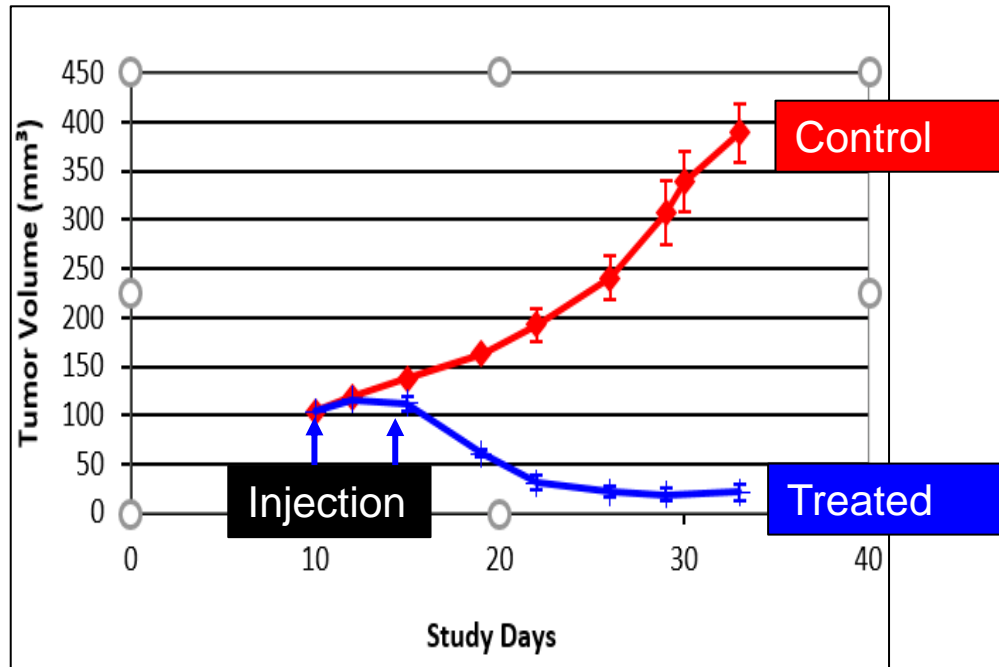


- iC3b inhibits synapse formation by immune cells
→ tumor induce immune suppression
- C3d promotes antigen-specific immune responses
→ tumor-specific immunity

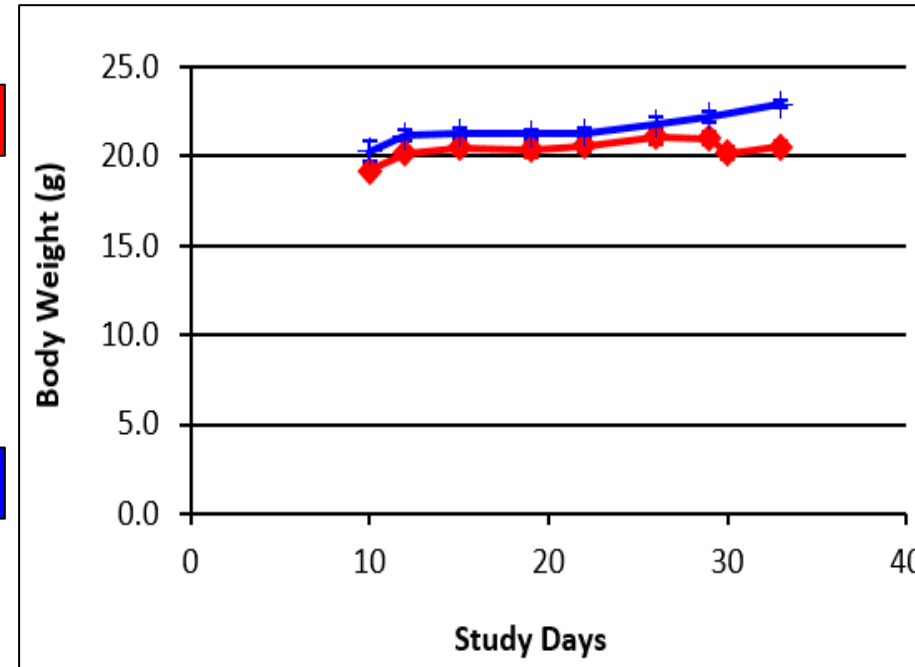
InsideOutBio Complement C3 Checkpoint Therapeutic Regresses Tumors

Tissue from Survivors is Normal

Efficacy: Tumor Volume



Safety



The InsideOutBio therapeutic in a pre-clinical animal model
(786-0 clear cell Renal Carcinoma in Balb/c Nude mice (5 per group))



inside out bio

science for living well

NON-CONFIDENTIAL June 2020

Current Development Pathway for the C3 Checkpoint Therapeutic

- Our Current Proof of Biology C3 Checkpoint Therapeutic is Delivered by Local Injection
- We are developing versions for Systemic Delivery
- One example uses mutant PD-1 for targeting as it works for xenograft and syngeneic tumor models



A Mutant PD-1 Targets Both Human and Mouse Checkpoint Ligands

	huPD-1	huA132L	mPD-1	mA132L
huPD-L1	6.36 ± 0.57	0.14 ± 0.01	4.02 ± 0.06	0.48 ± 0.02
huPD-L2	0.19 ± 0.019	0.0065 ± 0.0014	10.69 ± 0.83	1.18 ± 0.08
mPD-L1	3.81 ± 0.08	0.23 ± 0.01	5.43 ± 0.08	2.78 ± 0.03
mPD-L2	0.27 ± 0.01	0.029 ± 0.004	2.80 ± 0.15	0.47 ± 0.02

Our IP and Trade Secrets

Method & Compositions

Proprietary Therapeutics

- MOA differs from tumor vaccines, oncolytic viruses, siRNA, CRISPR and current Standard-of-Care immunotherapeutics

Proprietary Knowhow

- Bioinformatic Algorithms to Identify Biomarkers:
 - Diagnostics
 - Patient Selection
 - Treatment Response

InsideOutBio wholly owns this Intellectual Property

- a) WO2019051443 METHODS AND COMPOSITIONS TO ENHANCE THE IMMUNOGENICITY OF TUMORS
- b) WO2019222036 GENETICALLY ENGINEERED ARGONAUTE PROTEINS WITH ENHANCED GENE SILENCING
- c) WO2020092140 METHODS AND COMPOSITIONS TO INDUCE OR SUPPRESS IMMUNE RESPONSES
- d) US 62/848,345 MODULAR THERAPEUTICS FOR THE TREATMENT OF INFLAMMATION DISEASES AND CANCER.
- e) US 62/913,994 METHODS AND COMPOSITIONS FOR THE MANUFACTURE AND USE OF DNA ENCODED THERAPEUTICS.
- f) US 62/947,563 METHODS AND COMPOSITIONS FOR TARGETED DELIVERY OF NUCLEIC ACID THERAPEUTICS



inside out bio

science for living well

NON-CONFIDENTIAL June 2020

Foundational IP is Wholly Owned by IOB

InsideOutBio Intellectual Property

Foundational IP has wide applicability

Therapeutic Strategies	Delivery Strategy	Pros	Cons	Model Tested
Complement-Targeted DNA Therapeutic	DNA Delivery Vector	Delivers Therapeutic Systemically	Needs Human Validation	Renal Cell Carcinoma (by CRO)
Methods to enhance immune responses by other approaches	Ex Vivo Vaccine Product Enhancement for Car-T Oncogenic Viruses	Easy Add On to Existing Rx	Identifying Antigens Hard No Existing Data	Supplied by Partner
Immunosuppressive Modules	Add on to SOC Antibodies	Prevent Anti-drug Antibodies Life Cycle Management	No Data	Supplied by Partner
Protein Delivery Platform	Systemic, either with DNA that encodes protein therapeutic or with Protein	NDA required (pre-PTC)	NDA required (pre-PTC)	In development

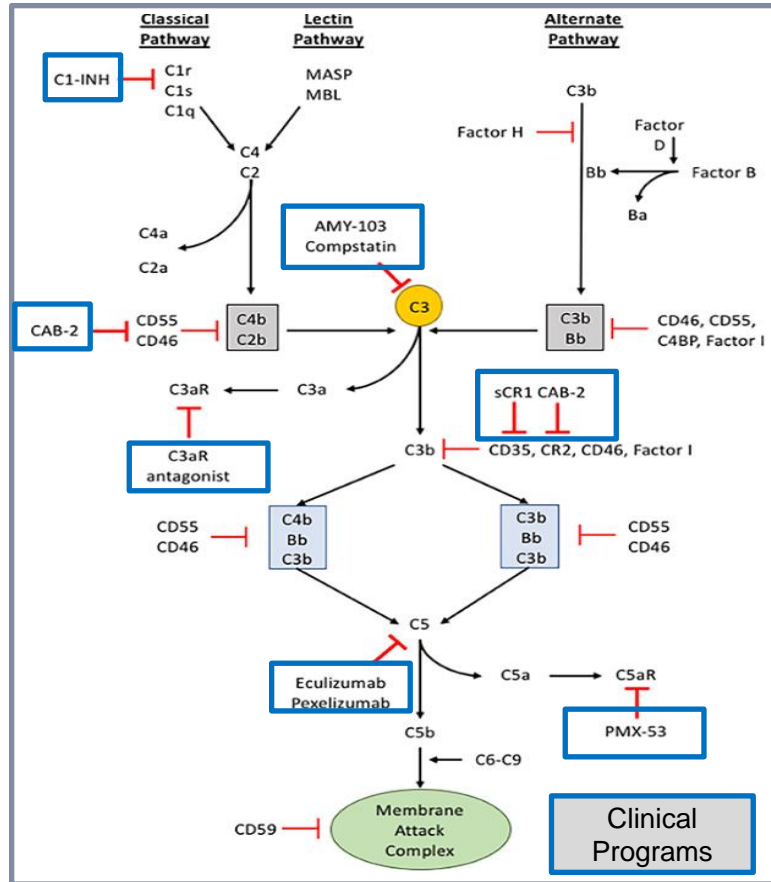
inside out bio

science for living well

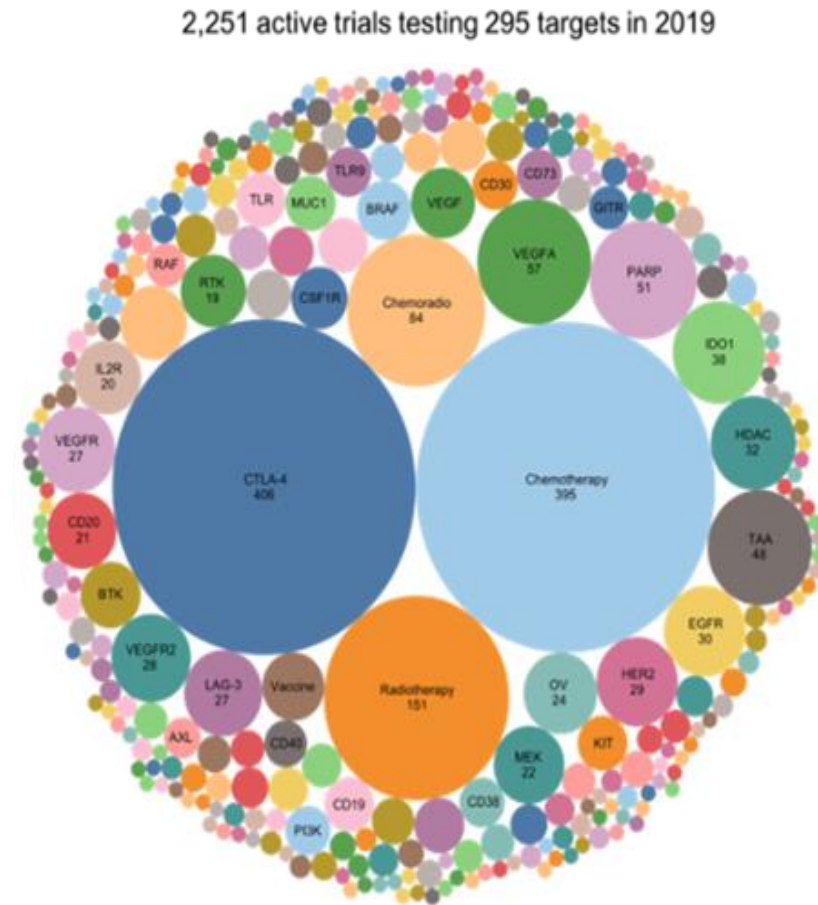
NON-CONFIDENTIAL June 2020

Competing Approaches do not target the Complement C3 Checkpoint

Complement Modulators



Immunotherapeutics: None target tumor complement production



Market is USD 77.44 Billion in 2026 (VerifiedMarketResearch.com)