agenus

May 8, 2018

Forward-Looking Statements

This presentation contains forward-looking statements. These forward-looking statements are subject to risks and uncertainties, including the factors described under the Risk Factors section of our most recent Annual Report on Form 10-K or Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission and made available on our website at www.agenusbio.com. When evaluating Agenus' business and prospects, careful consideration should be given to these risks and uncertainties. These statements speak only as of the date of this presentation, and Agenus undertakes no obligation to update or revise these statements. This presentation and the information contained herein do not constitute an offer or solicitation of an offer for sale of any securities.

Agenus Today – Innovation and Speed

I-O Capabilities & Portfolio

- **4** Therapeutic modalities
  CPMs, Vaccines, Cell Therapy*, Adjuvants
- **6** Technology platforms
  Mammalian, Yeast, Phage, Bispecific, PTTs, Cell therapy*
- **5** Ongoing trials^
- **5** Partnerships

Speed & Efficiency

- **5** INDs^
  Filed in 2016 – 2017
- **6** INDs^
  On track for 2018 filing
- **2** Additional INDs^
  On track for 1H2019 filing
- **2** Manufacturing sites
  Commercial grade^^
- **>12** Pipeline Candidates

Optimal Combinations

- **I-O backbone**
  CTLA-4 and PD-1
- **Novel targets**
  Next gen CTLA-4
  Tumor microenvironment conditioners (BiSpecifics)**
- **CPMs + vaccine**
  PD-1 + CTLA-4 + ASV™
- **CPM + CPM**
  Novel CPM + CTLA-4 + PD-1
- **CELL THERAPY***
  IND planned for 2019

*Program advancing through a separate subsidiary, AgenTus Therapeutics

^Includes 2 programs partnered with INCY

^^Commercial grade CTLA-4; PD-1 anticipated 1H2018

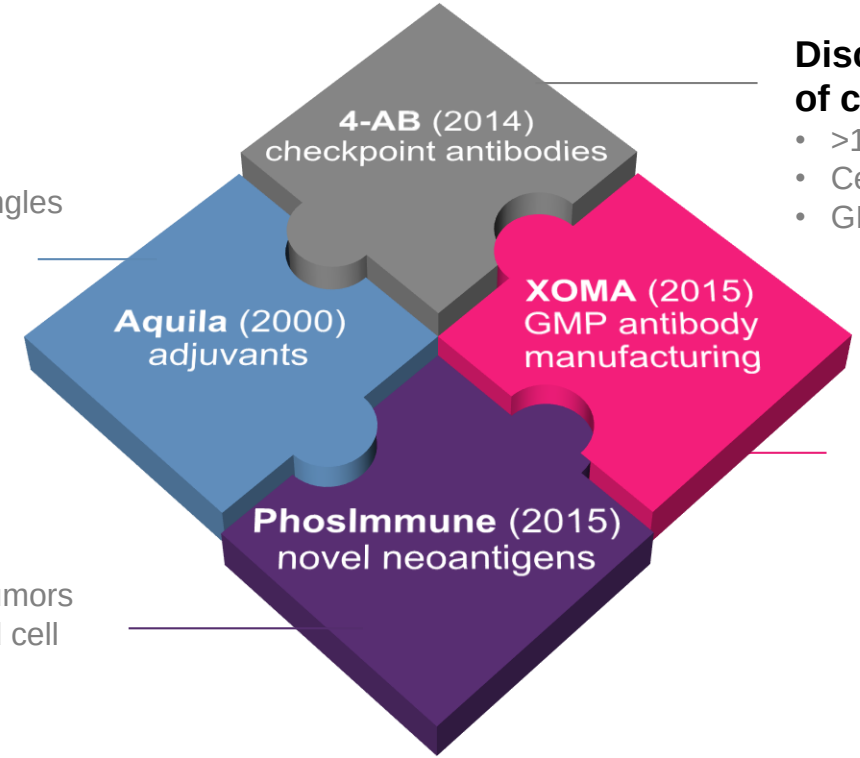
Key Acquisitions

QS-21 Stimulon®

- Most powerful adjuvant
- Adjuvant in most effective Shingles vaccine (SHINGRIX)

Proprietary targets

- Novel targets common across tumors
- Proprietary targets vaccines and cell therapy



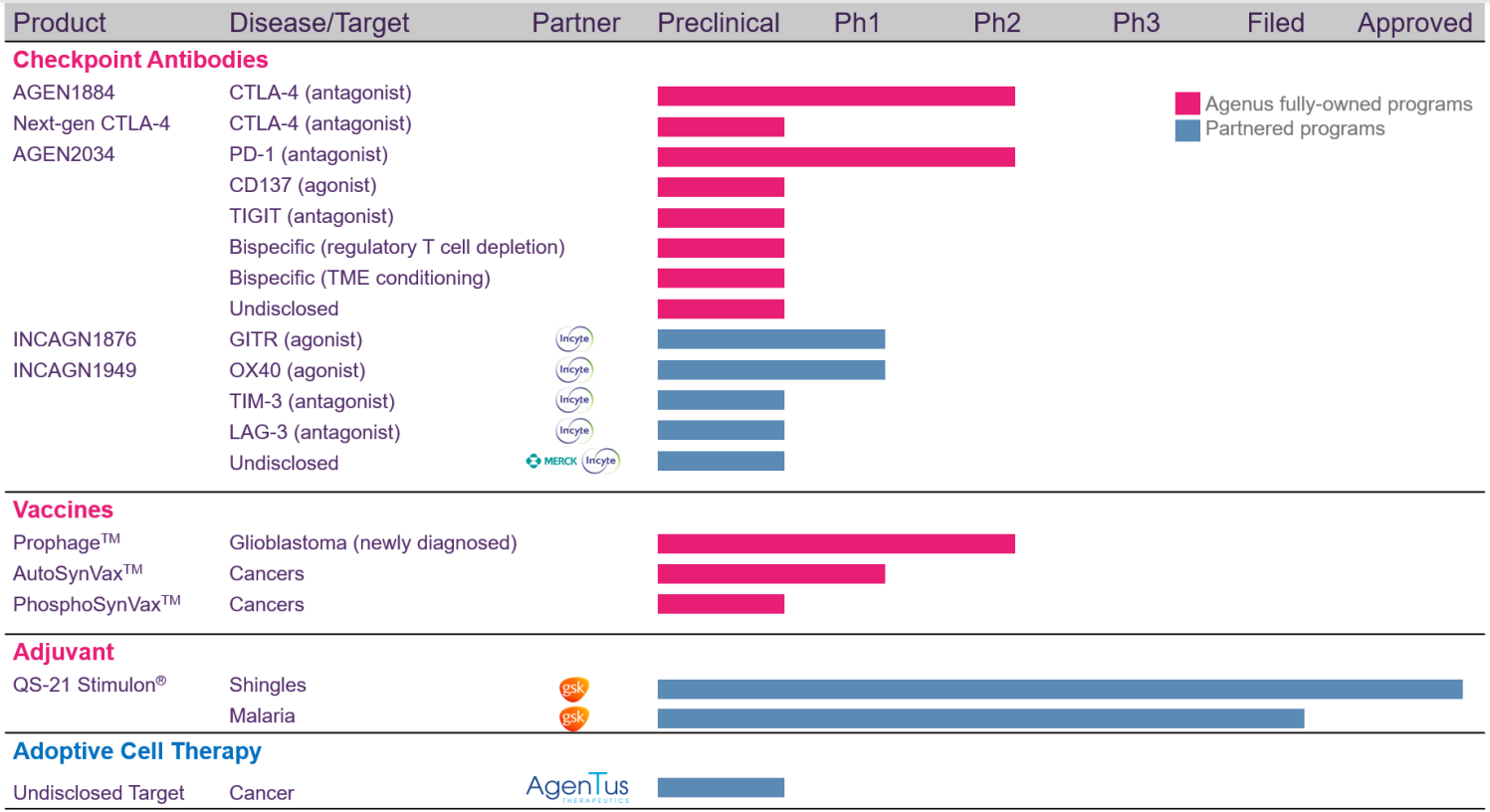
Discovery and development of checkpoint antibodies

- >12 programs
- Cell line development
- GMP manufacturing

Integrated GMP Antibody Manufacturing

- Rapid discovery to clinical material
  - Less than 12 months from clone evaluation to product fill

Portfolio Designed for Rapid BLA, Effective Combinations & Opportunistic Market Expansion



Notes: AGEN1884 and AGEN2034 are being evaluated in 2L cervical cancer and undisclosed tumors
AGEN1884 and AGEN2034 are partnered with Recepta for certain South American rights

Delivering on Our Partnerships



Shingrix with Agenus QS-21 Stimulon®

- Most effective Shingles vaccines (up to 97% efficacy)
- Initial FY sales projected to exceed $600M; 3X aggressive projections*
- Eligible to receive up to $40M sales milestones

*https://www.fiercepharma.com/vaccines/glaxosmithkline-s-shingrix-should-chip-about-600m-sales-year-execs-say

**Includes equity investments of $35M in February 2015 and $60M in February 2017



Multiple combination Ph2s ongoing:

- INCAGN1876 (GITR)
- INCAGN1949 (OX-40)
- Dose escalation complete; combinations underway

New candidates expected in clinic in 2018:

- INCAGN2390 (TIM-3) and INCAGN2385 (LAG-3)

Initial and Milestones:

- $140M received**
- Up to $510M receivable



1 undisclosed target

- Lead selection completed
- Initial milestone received; up to $99M receiveable

agenus

Jennifer Buell, PhD

Chief External Affairs and Communications Officer

- Foundational checkpoint antibodies
- Novel discoveries
- Neoantigen vaccines
- AgenTus, cell therapy subsidiary

Foundational Checkpoint Antibodies

Critical enablers of I-O combination therapy

agenus

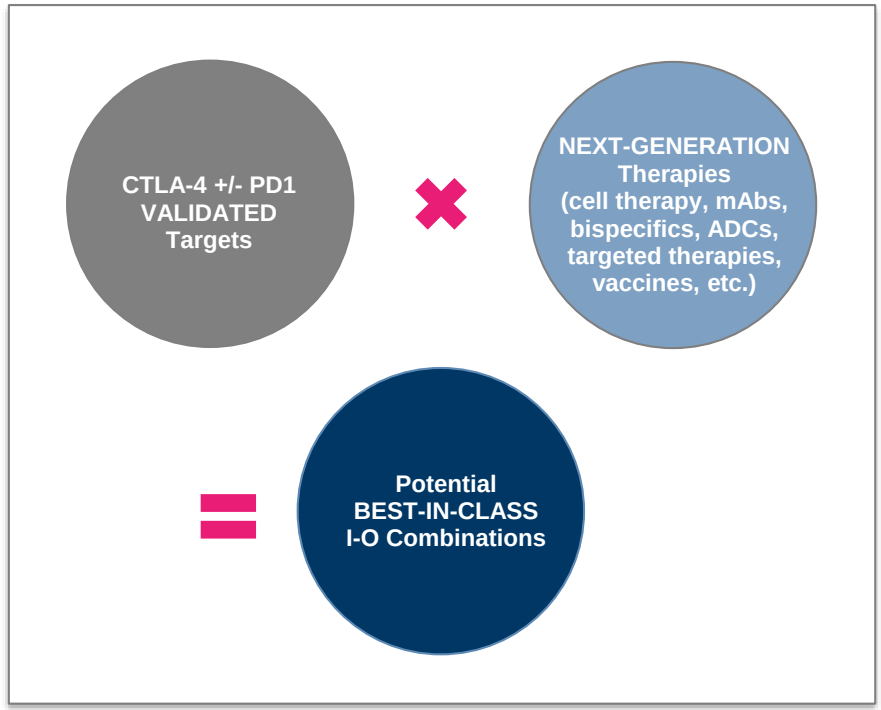
PD-1 and CTLA-4 Required as Backbone of Innovative Combos

PD-1 / CTLA-4 is only validated I-O/I-O antibody combination

AGEN2034[1]:
Anti-**PD-1** mAb –
Phase 2 ongoing

+

AGEN1884[1]:
Anti-**CTLA-4** mAb –
Phase 2 ongoing[2]



Recent posters on AGEN2034 and AGEN1884 available:
http://agenusbio.com/technology/publications/

1. AGEN2034 and AGEN1884 are partnered with Recepta for certain South American territories
2. Phase 2 recruiting in Australia

Where PD-1 works, CTLA-4 Improves Responses and Durability

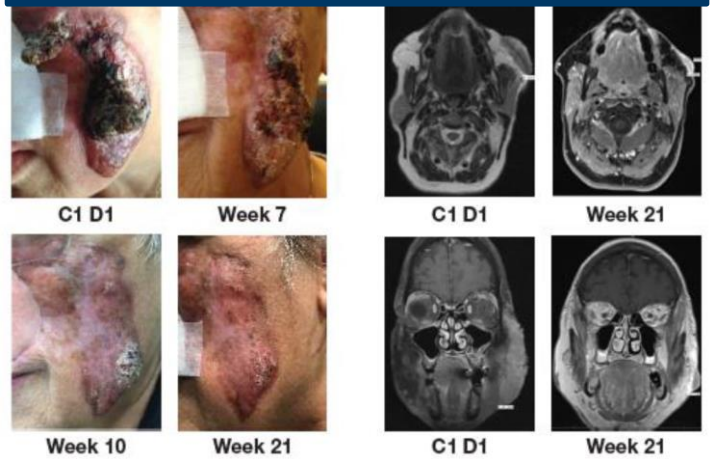
Trial Name	Indication	Treatment(s)	Objective Response Rate (ORR)
CheckMate 037	Melanoma	Nivolumab	32%
CheckMate 069	Melanoma	**Nivo + Ipi**	**61%**
KEYNOTE 016	MSI-H CRC	Pembrolizumab	40%
CheckMate 142	MSI-H CRC	**Nivo + Ipi**	**81%**

Presented by Steven Leach at 2018 Gastrointestinal Cancers Symposium

AGEN1884 (CTLA-4) and AGEN2034 (PD-1) – Clinically Active

- >100 patients treated; clinical responses observed
- Pharmacology/pharmacodynamic characterization

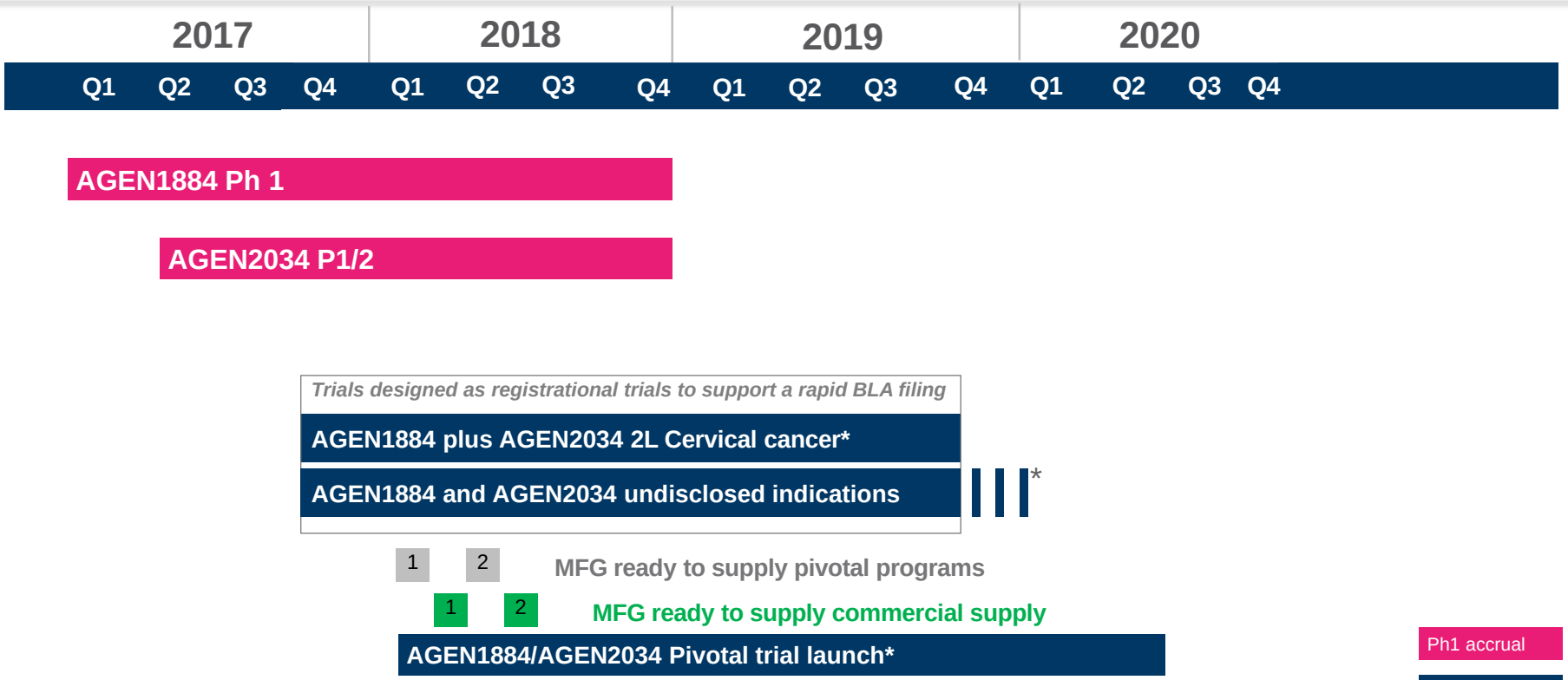
Patient with advanced cancer; complete responder post AGEN1884 treatment



CTLA-4 (AGEN1884)	Dose	Frequency
AGEN1884	0.1, 0.3, 1, 3, 6 mg/kg	Q3W
Keytruda + AGEN1884	200 mg 1 mg/kg	Q3W; Q6W
PD-1 (AGEN2034)	**Dose**	**Frequency**
AGEN2034	1, 3, 6, 10mg/kg;	Q2W; Q3W
Combination	**Dose**	**Frequency**
AGEN2034 + AGEN1884	1mg/kg 1mg/kg	Q2W Q6W
AGEN2034 + AGEN1884 **Ongoing**	3mg/kg 1mg/kg	Q2W Q6W

Gombos SITC poster presentation 2017

Planned Path to BLA: AGEN2034 (PD-1) & AGEN1884 (CTLA-4)



*Projections timelines and indications undisclosed
^Designed as potential pivotal trials
1=AGEN1884; 2=AGEN2034

Ph1 accrual

Pivotal design

agenus

Novel Immunomodulatory Antibodies & Bispecifics

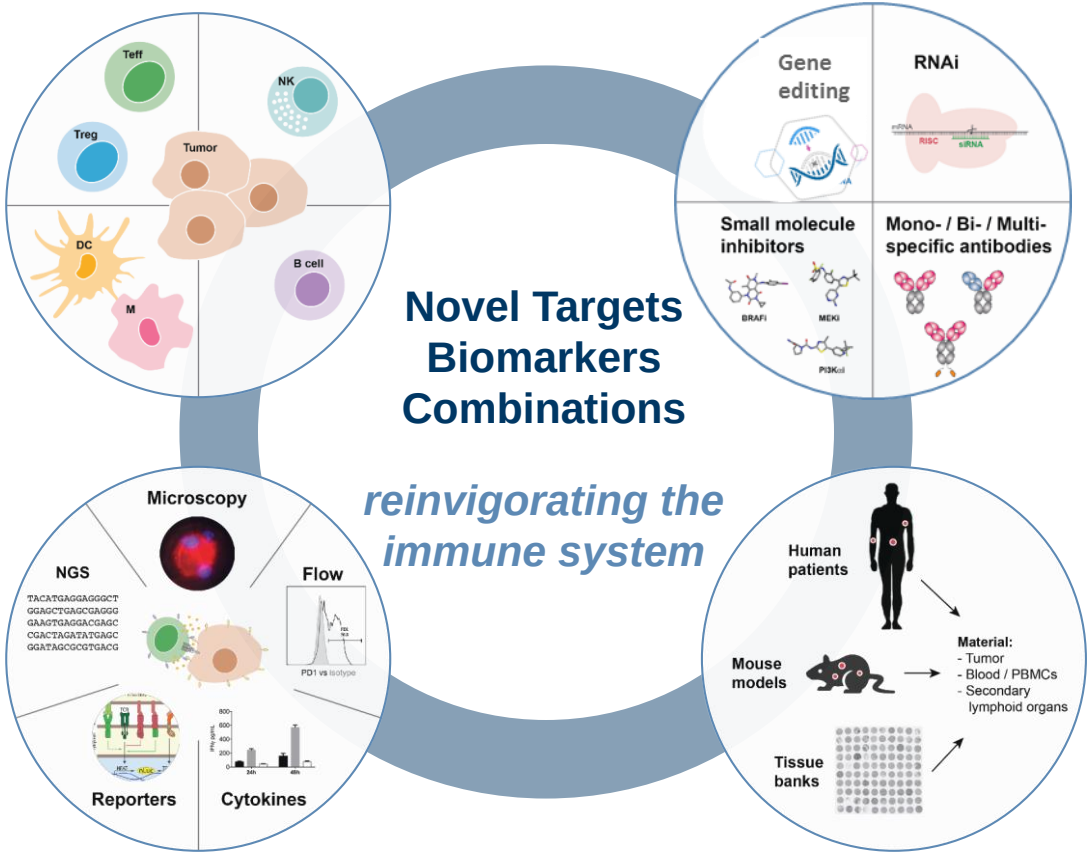
Enabling cancer immune modulation beyond the T cell

agenus

An Integrated Approach to Target Discovery in Immuno-Oncology

Physiological assays

Perturbation libraries



Readout / analysis platforms

In vivo material and data

High Throughput Discoveries; 6 New Clinical Programs in ~2yrs*

Target ID/Validation	Functional genomics Immuno-Biology
Antibody Platforms	Phage Display Yeast Display (SECANT®) Mammalian Display (Retrocyte Display™) Immunization/Phage
Optimization Technologies	Fc-engineering Bioinformatics Computational/Structural Structural biology
Product Capabilities	Cell line development Manufacturing

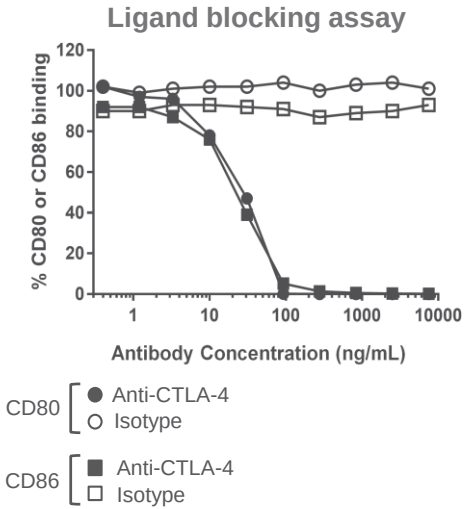
ASSET	HIT DISCOVERY	HIT OPTIMIZATION	LEAD OPTIMIZATION	CELL LINE DEVELOPMENT
Undisclosed bispecific #1 *Treg depletion, agonist costimulation*			*First-in-class Opportunity*	
Undisclosed bispecific #2 *TME conditioning, myeloid modulating*			*First-in-class Opportunity*	
CTLA-4 next generation *Fc engineered*			*Potential Best-in-class*	
TIGIT antagonist *Fc engineered*			*Potential Best-in-class*	
CD137 agonist *Conditionally active in TME*			*Potential Best-in-class*	
Undisclosed antagonist			*First-in-class Opportunity*	
Novel Bispecifics				

*anticipated

Next-Generation CTLA-4 with Novel Mechanisms – Planned IND 2018

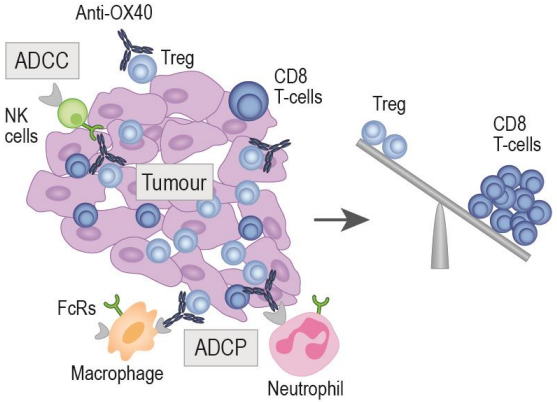
Mechanism #1

Blockade of CD80 & CD86 binding to CTLA-4



Mechanism #2

Depletion of intratumoral Tregs *via* co-engagement of FcγRs

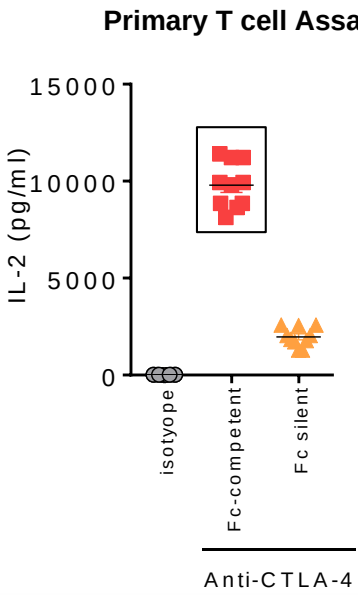


Smyth M. et al., *ICB* 2014
Bulliard Y. et al., *ICB* 2014
Bulliard Y. et al., *JEM* 2013
Simpson et al., *JEM* 2013
Shelby et al., *Can. Immunol. Res.* 2013

Mechanism #3

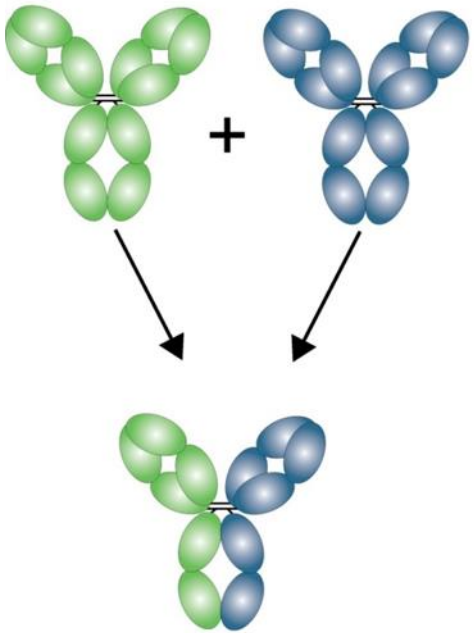
Agenus discovery

Enhanced T cell priming



Agenus Data

Best in Class & First in Class Bispecifics – Planned for IND in 2018



- **Regulatory T cells impair productive anti-tumor immune responses with multiple mechanisms of suppression**
- **Targeted elimination of regulatory T cells within the TME would address multiple suppressive mechanisms (*i.e.* in a single therapy)**
- **Agenus' novel bispecifics target elimination of regulatory T cells within the TME to address multiple suppressive mechanisms**
  - Selectively deplete intratumoral regulatory T cells as well as condition the tumor microenvironment.
  - May address tumor escape mechanisms in solid tumors as well as hematologic tumors, like B cell lymphoma.

Meng et al. Nat Rev Car. 2016
Liu et al. FEBS. 2016
Shang et al. Sci Rep. 2015

Neoantigen Vaccine Platform

Enabling differentiated personalized and warehouse vaccine offerings

agenus

ASV™ Clinically Validated* Neoantigen Vaccine Platform

ASV™

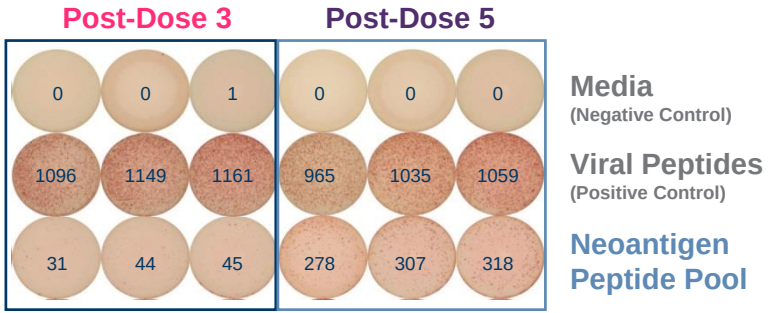


- **Potential best-in-class vaccine blueprint with QS-21 Stimulon® adjuvant for efficacy and manufacturing**
- Clinically validated in viral setting*
- Long-term memory response (preclinical)
- MHC class I and II presentation
- Optimized delivery and peptide sparing
- End-to-end logistics: 20 years operational & FDA audited

Clinical Status

- Clinical safety & immunogenicity with ASV™ neoantigen vaccine platform demonstrated*
- **Combo with CPMs planned for 2018**

ASV™ promotes *de novo* immune recognition in clinic*



Uduman et al. 2017 *AACR*

*Clinically validated in viral dx setting and oncology compassionate use setting


AgenTus
THERAPEUTICS
www.agentustherapeutics.com
agenus
www.agenusbio.com

Agenus and AgenTus Designed to Expand Response Rates and Durability

Innovation & Speed Next generation agents → **Cancer Cures**

agenus + AgenTus THERAPEUTICS

Differentiated Cancer Cell Therapy

Precision Receptors

- **T-Rx Mammalian Display - Direct selection for function**
- **Targets optimal balance between activity and specificity**

Novel Targets

- **Proprietary target discovery and validation platforms**
- **Proprietary Phosphopeptide Tumor Targets**

Allogeneic Format

- **Allogeneic approach; “Off-the-shelf”**
- **Scalable, shorter diagnosis to treatment interval**

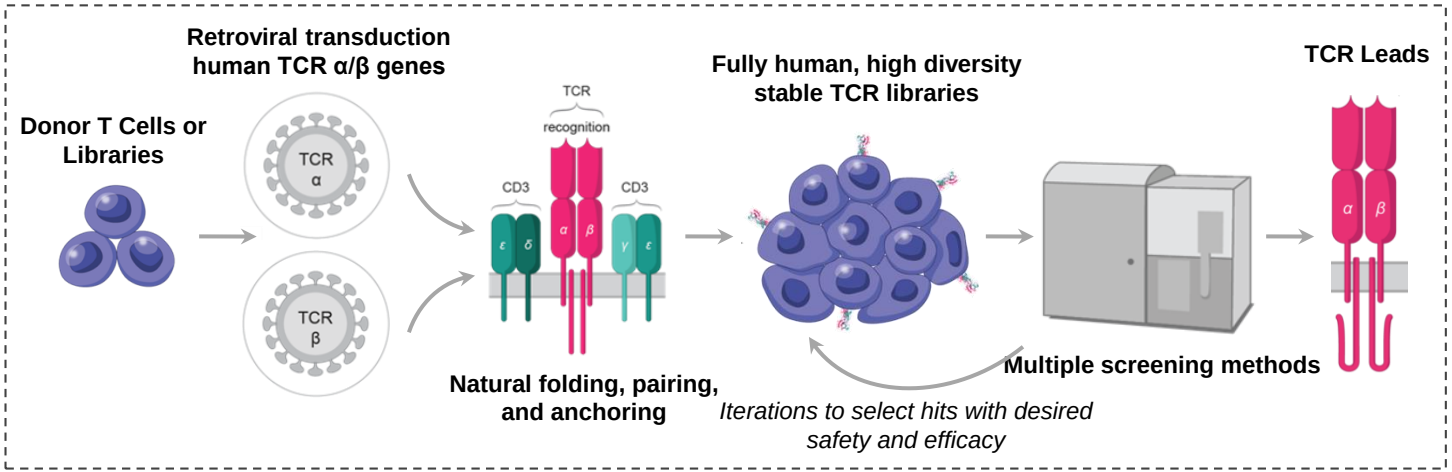
Precision Receptors

Superior Receptor Discovery Through T-Rx™ Platform

A powerful engine for delivering efficient and specific TCRs

Agenus Mammalian Display: Retrocyte Display™ and T-Rx™

Agenus mammalian display platform has delivered clinical antibodies currently in Ph1/2 clinical programs*



Applications

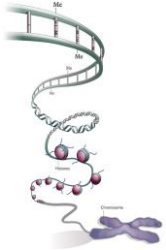
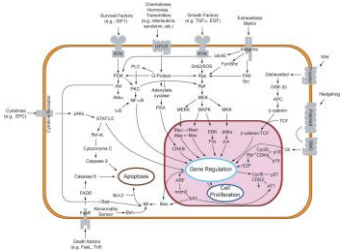
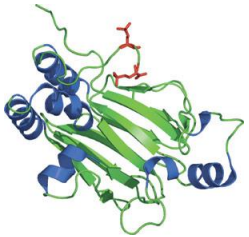
- Isolate natural TCRs
- Generate *de novo* TCRs
- Optimize natural or *de novo* TCRs

*Additional antibodies advancing to IND

Novel Targets

Agenus is Industry Leader in Discovery of Novel Proprietary Phosphopeptide Tumor Targets (PTTs)

Cancer Neo-Antigens

Nature of change	Mutations	Deregulated Expression	Deregulated Signaling
			 
Consequence for Proteins	**Mutation** *EML4-ALK Bcr-Abl KRAS*	**Over-expression** *WT-1 Telomerase Survivin*	**Ectopic Expression** *Cancer-Testis Antigens Embryonic Antigens*

Post-Translational Modifications (phosphorylation, glycosylation, etc.)

- ✓ **Neo-epitopes that trigger immunity**
- ✓ **Shared epitopes**
- ✓ **Not represented by mutations**
- ✓ **Not captured by live vector or mRNA vaccines**

AgenTus Emerged from Agenus – A Differentiated Cell Therapy Company

AgenTus THERAPEUTICS

Adoptive Cell Therapy

Direct attack

Synergies

Combinations

agenus

Checkpoint antibodies
Antibodies

Improve response

Cancer vaccines

Improve recognition

Adjuvants

Boost recognition


agenus
www.agenusbio.com
AgenTus
THERAPEUTICS
www.agentustherapeutics.com