agenus

August 2020

This version of the presentation includes corrections to an error in the original presentation contained on slide 10.

Forward-Looking Statements

This presentation contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding clinical development and regulatory plans and timelines and anticipated corporate milestones. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially. These risks and uncertainties include, among others, the factors described under the Risk Factors section of our most recent Quarterly Report on Form 10-Q or Annual Report on Form 10-K filed with the Securities and Exchange Commission. Agenus cautions investors not to place considerable reliance on the forward-looking statements contained in this presentation. These statements speak only as of the date of this presentation, and Agenus undertakes no obligation to update or revise the statements, other than to the extent required by law. All forward-looking statements are expressly qualified in their entirety by this cautionary statement.

Key Achievements in Advancing Innovative I-O Therapies

- **Delivered 15 INDs (2016 - Present)**
- **Produced 11 clinical batches GMP mAbs**
- **Positive clinical data released:**
  - *26% ORR in 2L cervical cancer ("Bali" + "Zali")*
  - *14.3% ORR in 2L cervical cancer ("Bali" mono)*
  - *Early responses in AGEN1181 Ph1 (1 CR, 1 CR by PET)*
- **"Bali" BLA submission to be initiated 3Q 2020**
- **Generated $575M (2014 - Present)**
  - *Corporate collaborations*
  - *Monetization of royalties*
- **Delivered on commitments to partners**
  - *GSK, Merck, Incyte, Gilead*

Agenus Owned Pipeline Highlights

Mechanism/Target	Product	Preclinical	Ph1	Ph2	Ph3	Filed	Approved
CTLA-4	**Zalifrelimab** AGEN1884						*BLA filing preparations underway for Bali + Zali*
PD-1	**Balstilimab** AGEN2034						*BLA filing preparations underway*
Multipurpose 2nd Gen CTLA-4	AGEN1181						
TIGIT	AGEN1327						
TIGIT (Bispecific)	AGEN1777						
Tumor Associated Macrophage	AGEN1531						
CD137	AGEN2373			OPTION			
Regulatory T cell depletion (Bispecific)	AGEN1223			OPTION			
Cancers	AGENT-797 (Unmodified iNKT Cell Therapy)						
COVID-19	AGENT-797 (Unmodified iNKT Cell Therapy)						

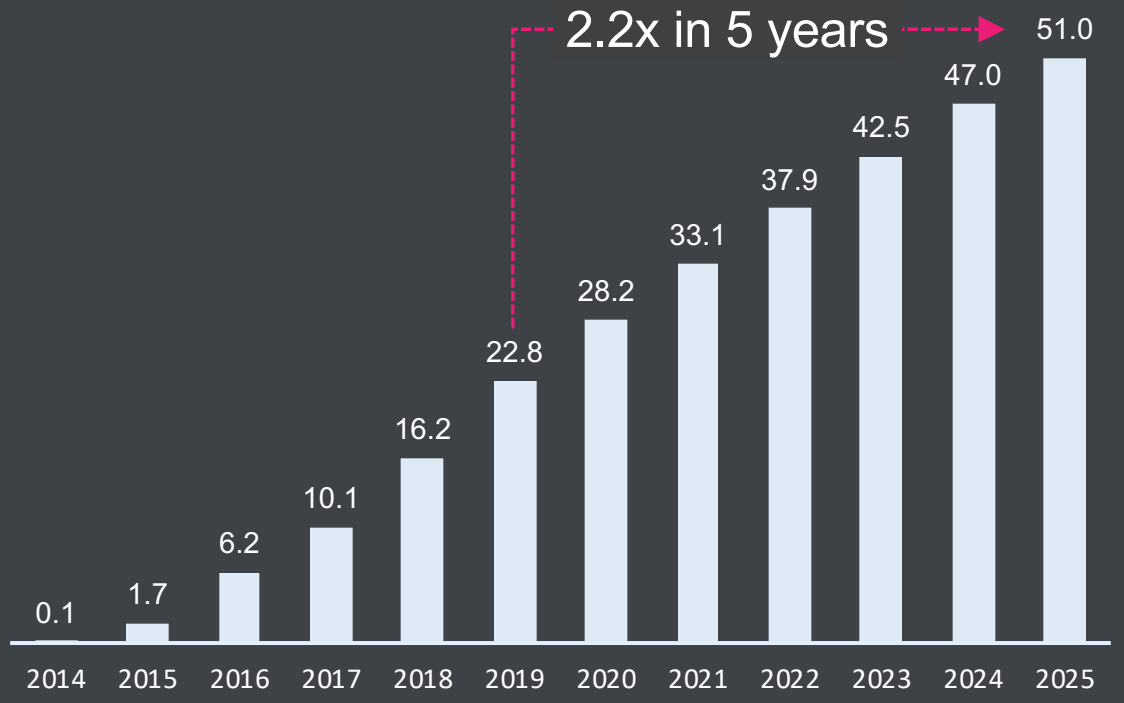
Notes: AGEN1884 and AGEN2034 are being evaluated in 2L cervical cancer and undisclosed tumors. Betta Pharmaceuticals has exclusive rights to AGEN1884 and AGEN2034 in Greater China. Recepta Biopharma S.A. has exclusive rights to AGEN1884 and AGEN2034 in Brazil and five other South American countries.
*Gilead has an exclusive option to license AGEN2373 and AGEN1223.
To view Agenus' full pipeline, please visit https://agenusbio.com/pipeline/

agenus

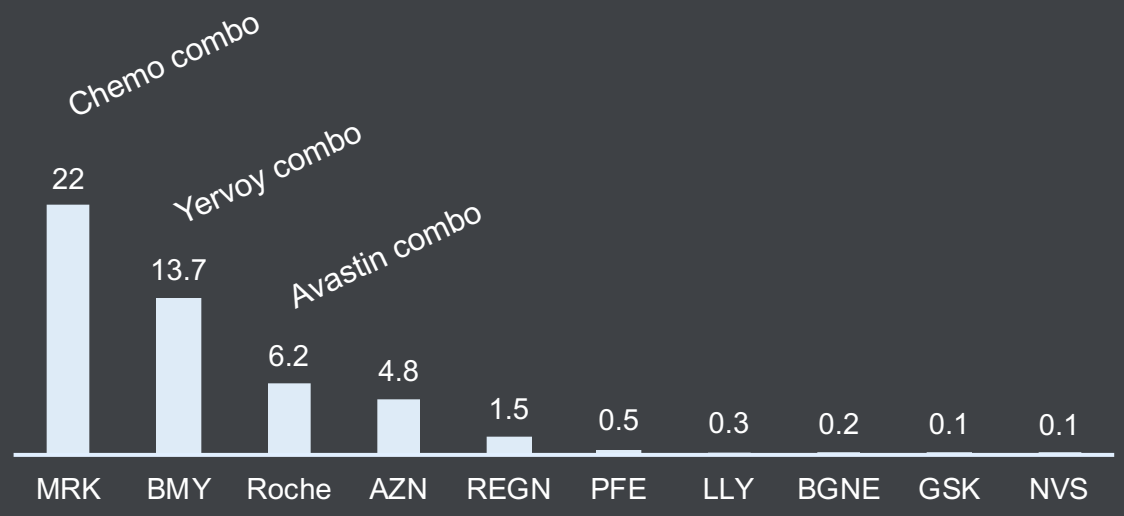
PD-1 Market is Large with Ample Room for New Entrants

Top selling PD-(L)1 agents have a combination strategy

WW PD-(L)1 Sales ($B)



2025E PD-(L)1 Sales ($B): Top Sellers are Driven by Combos



Source: Evaluate Pharma and Cowen Equity Research

agenus

Cervical Cancer: Substantial Need for More Effective Treatments

ADVANCED CERVICAL CANCER

1st LINE TREATMENT	2nd LINE TREATMENT
~22,000 eligible patients	**~9,600 eligible patients**

AGENUS OPPORTUNITY

- Best available therapy (Pembro) has 14% ORR in PD-L1+ patients
- ***AGEN combo is 26% ORR in all comers***
- Could be used as 2L treatment in high percentage of patients regardless of PD-L1 status

ORR – Objective Response Rate; 2L – Second Line

*Source: Epiphany Partners Inc. Includes US, EU5, JP

Agenus' Balstilimab (anti-PD-1) +/- Zalifrelimab (anti-CTLA-4)

Potential Best-in-class treatment for second-line cervical cancer

Fast Track Designation received for Balstilimab +/- Zalifrelimab

Evolution of cancer therapies

	Chemotherapy Topotecan[1] n=40	Roche Bevacizumab[2] n=46	Merck Pembrolizumab[3] n=77 (PD-L1 positive only)	AGEN PD-1 Balstilimab n=42*	AGEN PD-1 + CTLA-4 Bali/Zali n=55**
Response rate	**12.5%**	**10.9%**	**14.3%**	**14.3%**	**~26%**
Complete response	2.5%	0%	2.6%	2.4%	7.3%
Partial response	10%	10.9%	11.7%	11.9%	18.2%
Treatment related discontinuation (%)	N/A	8.7%	4.1%	4.5%	7.8%

~2X more patients than previously reported

~2x more active than available treatments

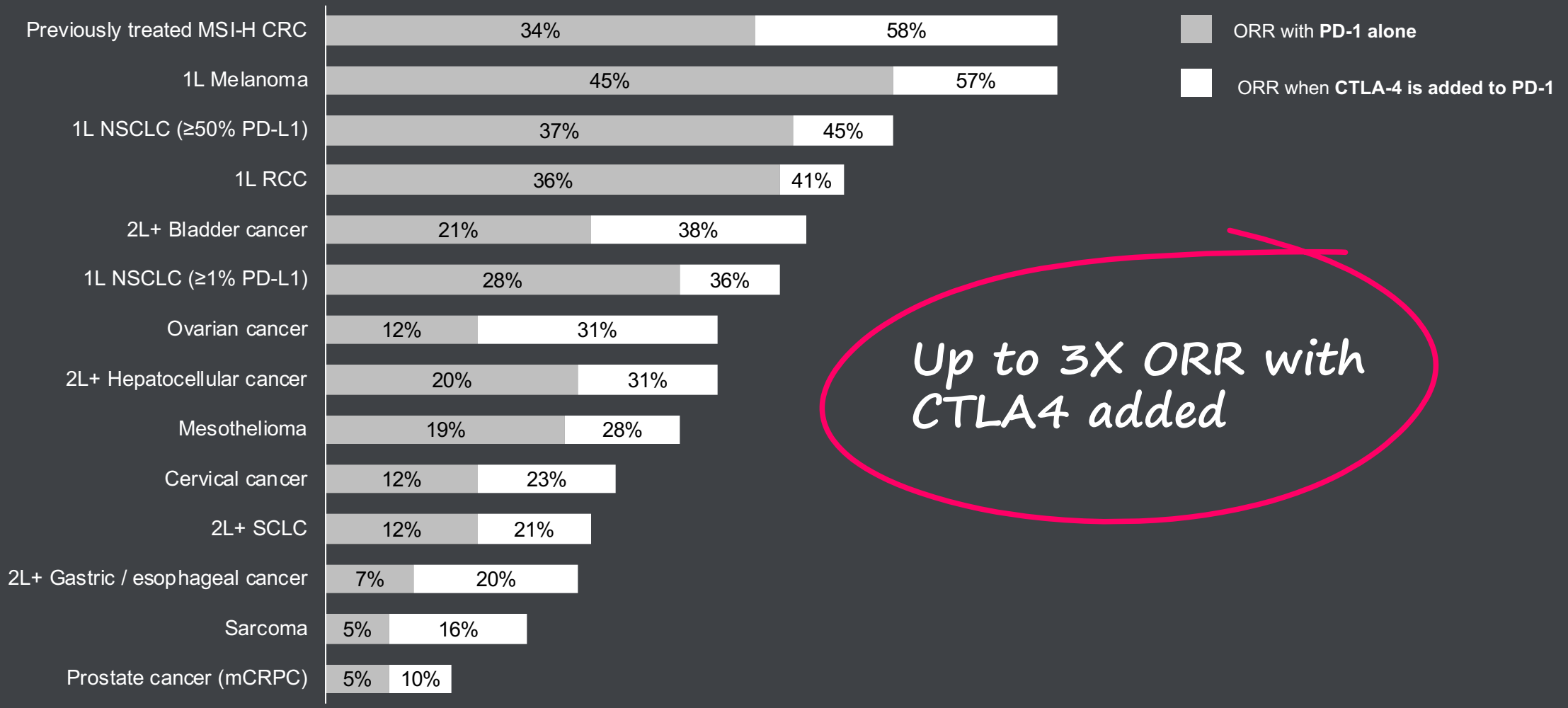
References:
1 Bookman et al., Gynecol Oncol. 2000 Jun;77(3):446-9
2 Monk et al., J Clin Oncol. 2009 Mar 1;27(7):1069-74
3 Chung HC et al., J Clin Oncol. 2019 Jun 10;37(17):1470-1478

* Data from evaluable patients enrolled as of July 15, 2019 (updated interim analysis)
** Data from evaluable patients enrolled as of May 31, 2019

agenus

Targeting CTLA-4: Best PD-1 Combination Partner

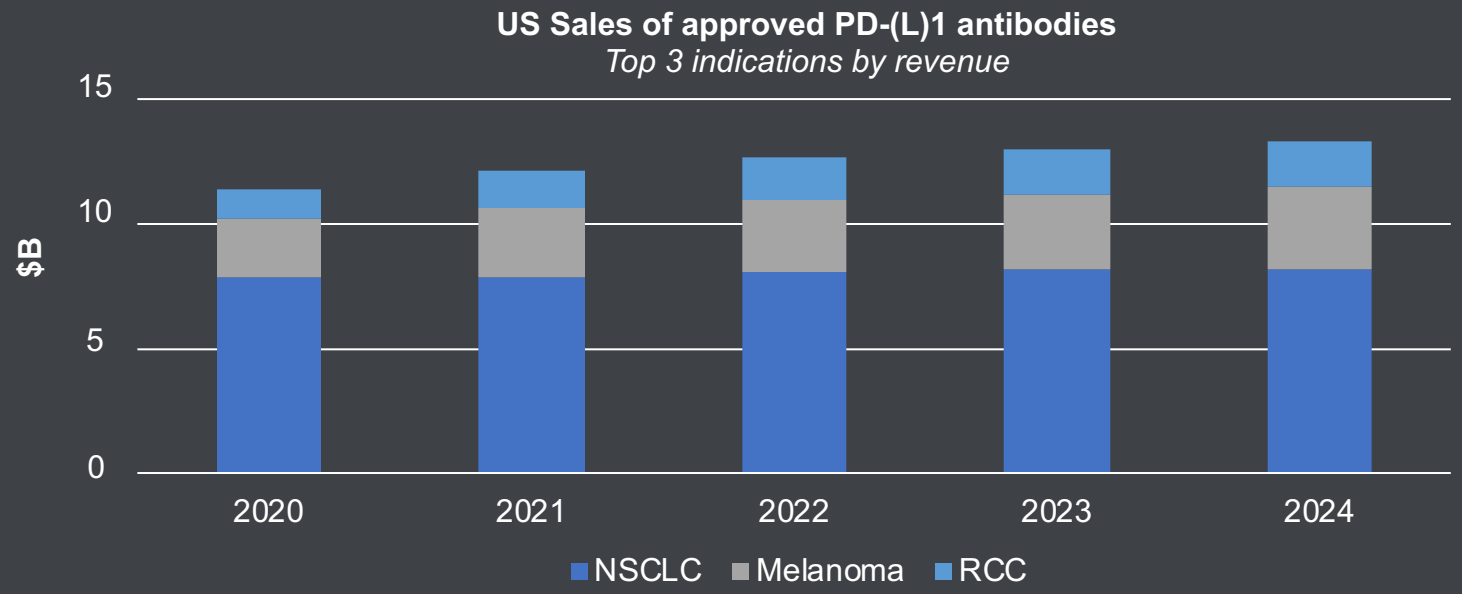
Improves Responses & Durability of responses in solid Tumor cancers



Source: Agenus analysis of published data

agenus

Balstilimab (anti-PD-1) +/- Zalifrelimab (anti-CTLA-4): $1B+ Potential with Expanded use*



Indication	2024 US Sales Estimate	5% Share	10% Share
Non-small cell lung cancer (NSCLC)	$8.2B	$410M	$820M
Melanoma	$3.2B	$160M	$320M
Renal cell carcinoma (RCC)	$1.9B	$95M	$190M
Total	**$13.3B**	**$0.7B**	**$1.3B**

Source: Evaluate Pharma, based on projected sales of Keytruda®, Opdivo®, Tecentriq®, Imfinzi®, Libtayo®
*Broader use in multiple indications driven by inclusion in NCCN guidelines

agenus

Zalifrelimab (anti-CTLA-4) Generates Complete Responses Alone and in PD-1 Refractory Patients

Phase I Overview

- Phase 1 data demonstrated 1 CR; 4 SD
- Phase 2: monotherapy in PD-1 refractory patients
  - Preliminary data: 3 PRs & 40% clinical benefit rate

Phase	Overall Response	Cancer Type
Ph1 (solid tumors)	1 CR; 4SDs	All solid tumors
Ph2 (PD-1 refractory)	3 PRs; 13SD	Angiosarcoma, SCCHN, Neuroendocrine

- Zalifrelimab demonstrated a curative CR & durable PR in refractory angiosarcoma
- Ph2 Bali +/- Zali trial in angiosarcoma to launch 3Q2020
- **Complete Response – Durable beyond 3yrs and ongoing**

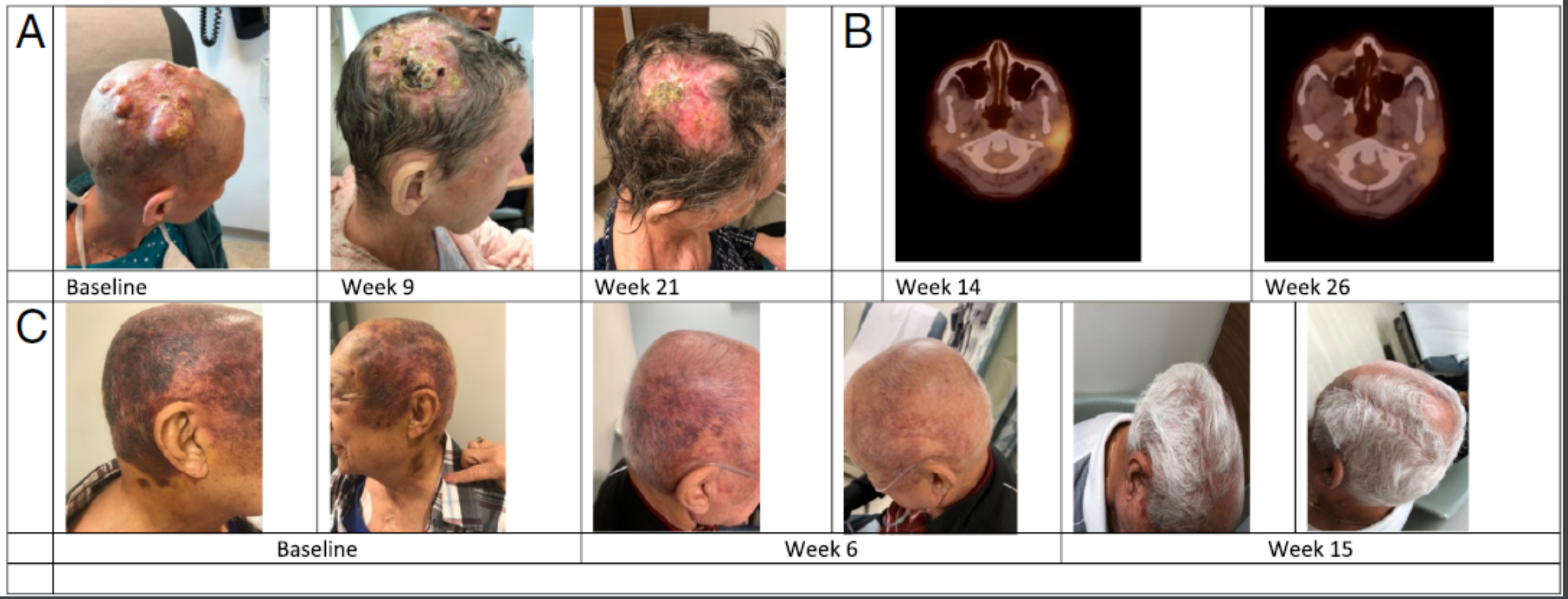




Zalifrelimab is in a pivotal trial in combination with balstilimab in refractory cervical cancer

CORRECTED SLIDE

Anti-CTLA-4 +/- Anti-PD-1 Demonstrated Clinical Benefit in Patients with Cutaneous Angiosarcoma



Florou, Wilky et al. Journal for ImmunoTherapy of Cancer (2019) 7:213

agenus

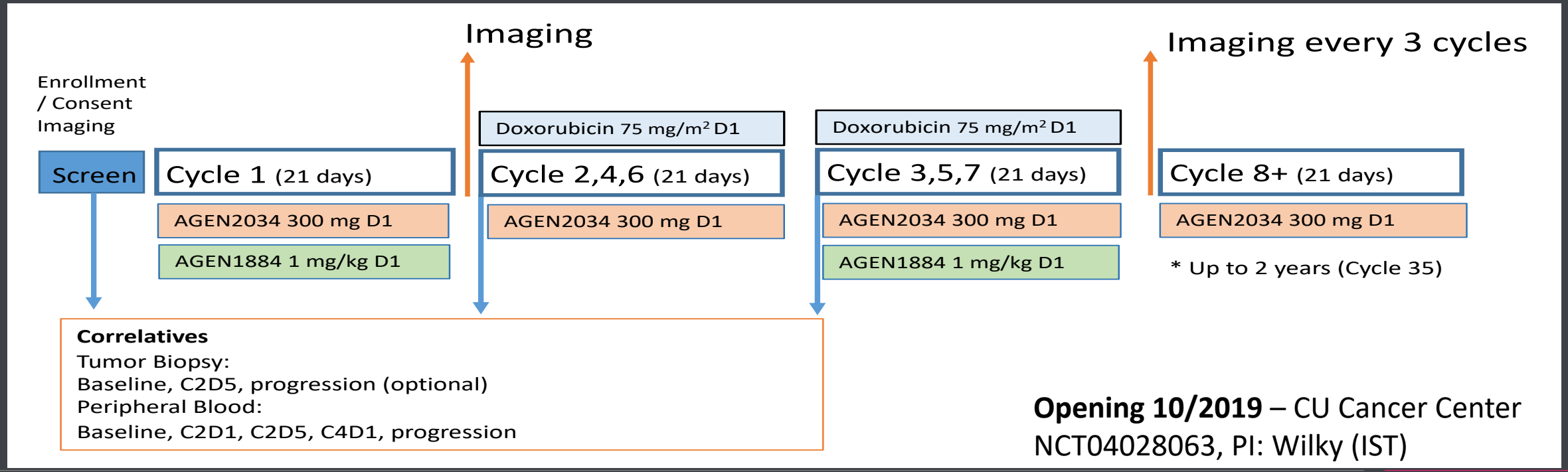
Doxorubicin + AGEN2034/1884 (anti-PD1/CTLA-4)

Hypothesis: Doxorubicin will increase antigen presentation/T cell expansion in combination with checkpoint blockade

Design: Open Label, single arm, single center, Phase II for up to 28 evaluable patients with advanced/metastatic STS, anthracycline naïve, max of 1 prior therapy

Primary: PFS rate at 6 months

Secondary: ORR, CBR, OS, duration of response, toxicity profile



Opening 10/2019 – CU Cancer Center
NCT04028063, PI: Wilky (IST)

agenus

Agenus has Generated $575M from Strategic and Financial Transactions (2014 – Present)

GILEAD

$172.5M

BETTA PHARMACEUTICALS

$35M

UroGen Pharma

$10M

Incyte

$145M

MERCK

$9M

gsk

$205M

Agenus' next Generation I-O Innovations

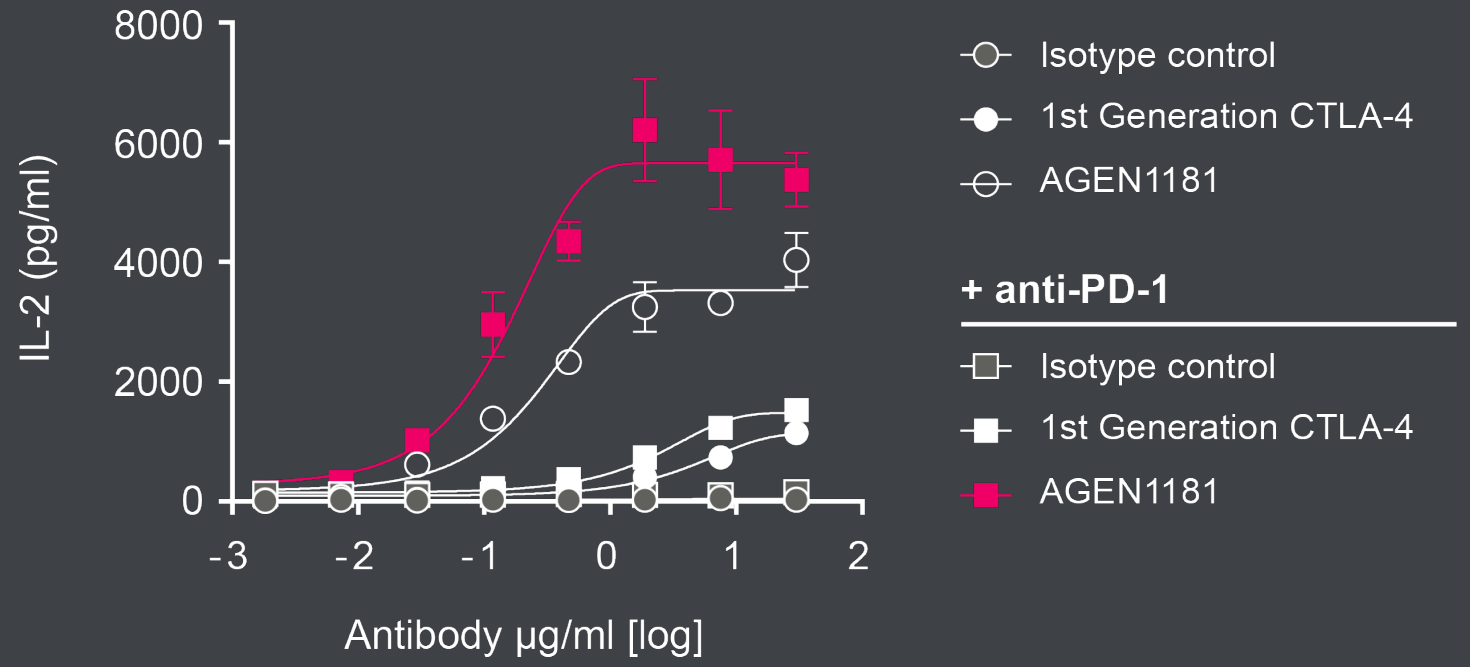
AGEN1181: Multi Functional CTLA-4
AGEN1777: First-in-class TIGIT bispecific
AGEN1327: Fc-enhanced TIGIT monospecific
AGENT-797: Allogeneic iNKT cell therapy

agenus

AGEN1181: Multifunctional anti-CTLA-4

AGEN1181 is Fc enhanced

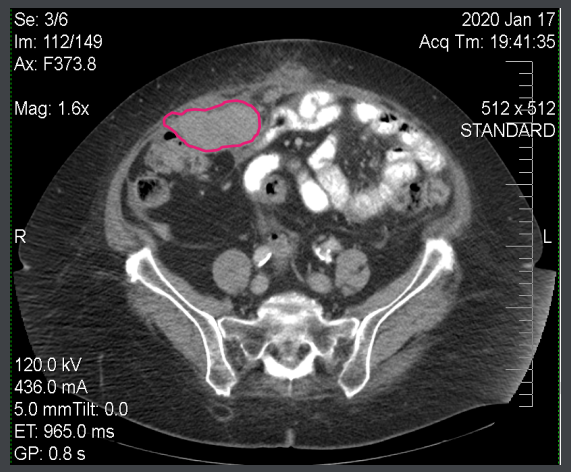
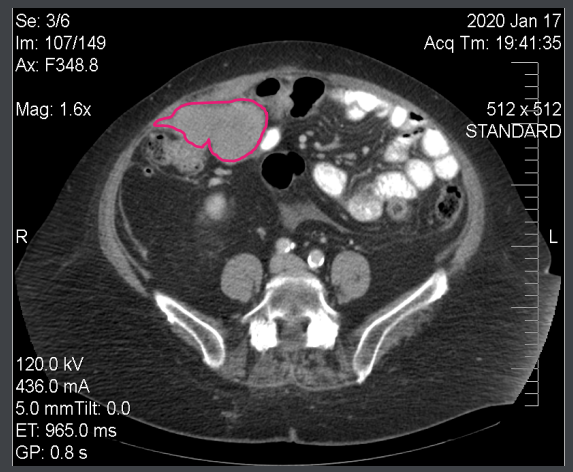
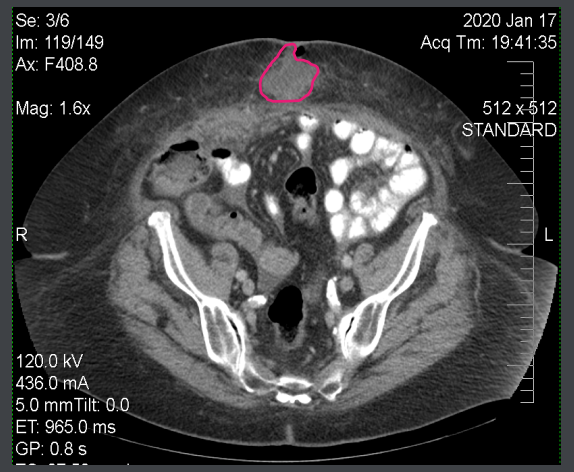
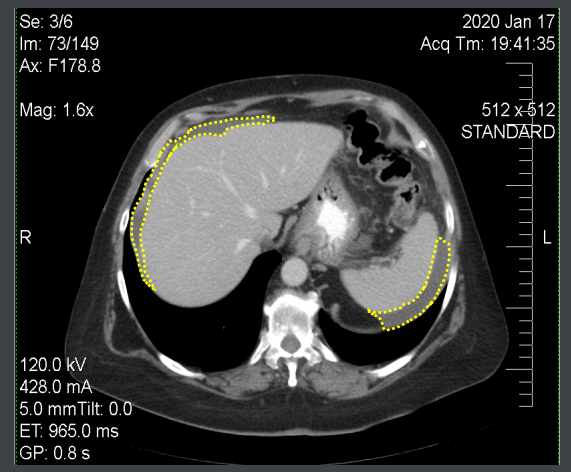
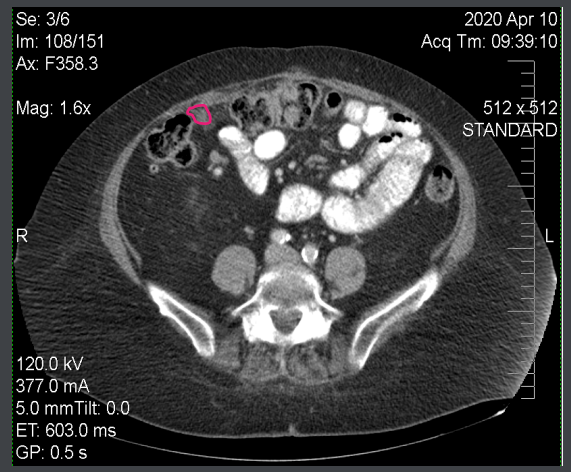
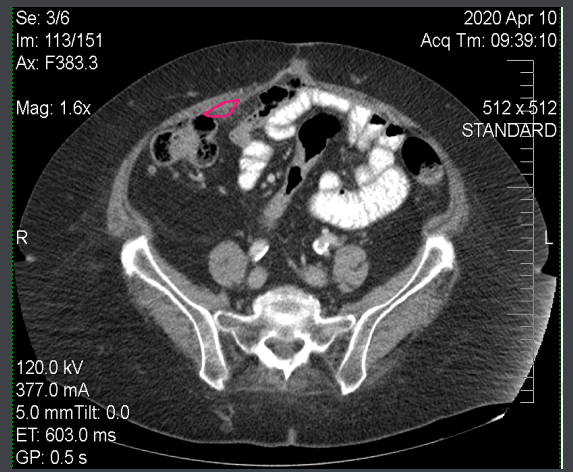
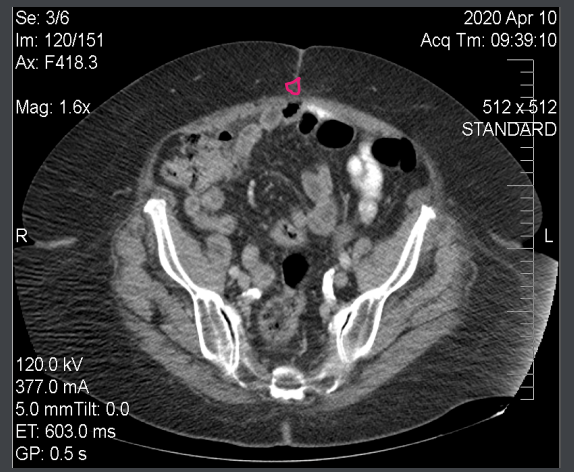
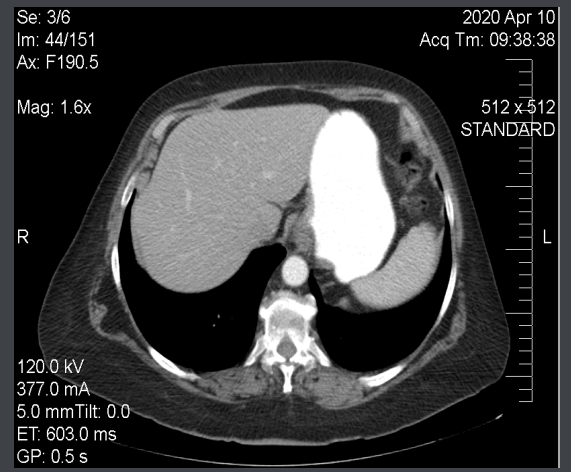
- ✓ **To expand benefit to 3X more patients than first gen anti CTLA-4**
- ✓ **To deliver superior performance alone and in combination with anti-PD-1**
- ✓ **To improve safety**



Source: Agenus data
Waight et al., Cancer Cell 2018

agenus

AGEN1181 + Balstilimab (anti-PD-1): Endometrial Cancer Patient Shows **Partial Response** in **Three** Target Lesions and **Complete Response** in Non-Target Lesion

	Target Lesion 1	Target Lesion 2	Target Lesion 3	Non-Target Lesion
Baseline				
12 weeks				

Source: Agenus data

Aug 2020 Update: Patient achieved Complete Response per PET scan

agenus

AGEN1181/Balstilimab Combination has Blockbuster Revenue Potential

Fast to market strategy via accelerated pathways in indications with large market and no active treatments

Targeting cancer patients who have failed previous standard therapies for:	US Population (2020E)
Non-small cell lung cancer (NSCLC)	~31,000
MSS tumors (ie CRC, endometrial, etc)	>6,000
Melanoma	~6,000

Source: GlobalData

TIGIT: Highly Promising Novel Target for Immuno-Oncology

What is TIGIT? (aka T cell immunoreceptor with Ig and ITIM domains)

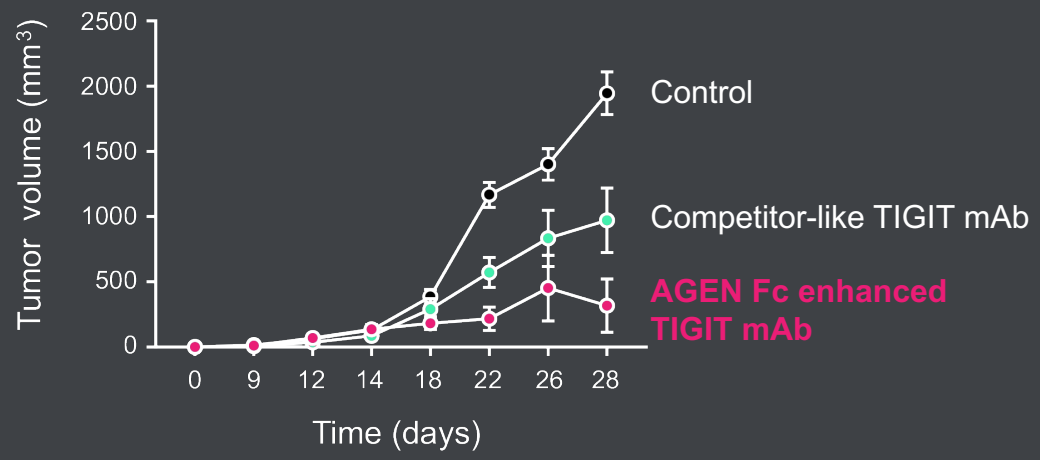
- A critical regulator of innate and adaptive immune response
- A key synergistic mechanism to anti PD-1 therapy
- Hence, a natural partner for PD-1 combination therapy – particularly active in TIGIT-expressing tumors
- Target of high interest, externally validated by late-stage Roche and Merck TIGIT programs

Agenus' TIGIT programs have unique properties to optimize anti-tumor activity

- **TIGIT Monospecific - AGEN1327**:
  - TIGIT antibody differentiated via "Fc enhanced" backbone for superior tumor killing as monotherapy or in combination with PD-1
- **TIGIT Bispecific - AGEN1777**:
  - TIGIT bispecific which also inhibits an undisclosed receptor expressed on T and NK cells

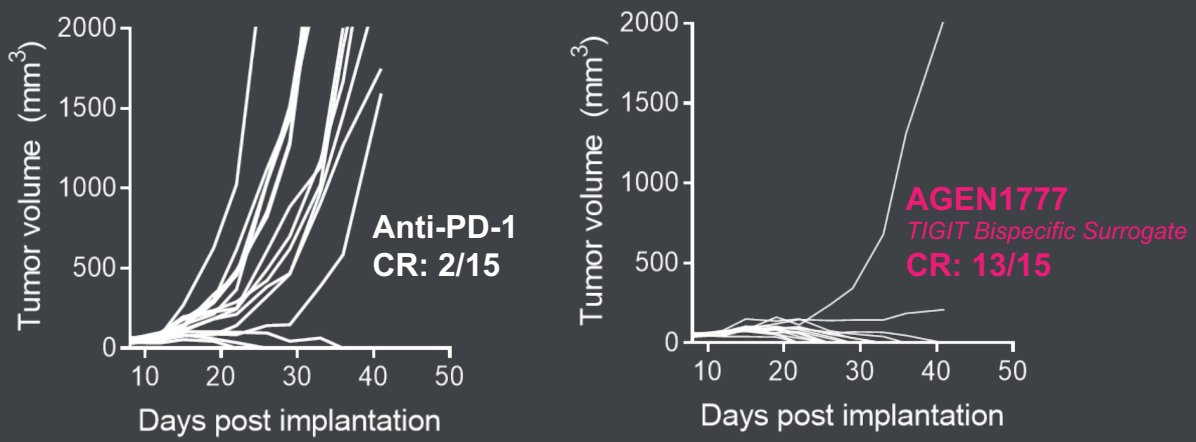
AGEN1327 (TIGIT monospecific) as Optimal PD-1 Partner
AGEN1777 (TIGIT bispecific) for PD-1 Refractory Tumors

AGEN's Fc-enhanced TIGIT monospecific offers superior tumor control



IND H1 2021

AGEN1777 shows effective tumor control in PD-1 refractory colon cancer model

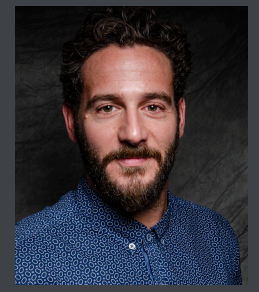


IND Target 2020

Source: Agenus data in mouse models

agenus

Rationale Combination Therapy with AGEN1181 Expands Therapeutic Reach and Enables Curative Responses



AACR ANNUAL MEETING 2020
June 22 - 24, 2020
Virtual Meeting II, Sessions Available Online

Expanding the therapeutic potential of anti-PD-1 and anti-CTLA-4 therapy with innovative Fc engineering and rationale combinations for the treatment of solid tumors.

Antoine J. Tanne, Sylvia Vincent, Elena Paltrinieri, Sudesh Pawaria, Vidur Patel, Margaret Wilkens, Shalu Kharkwal, Daniel Levey, David Savitsky, Jennifer Buell, Dhan Chand[1]
[1]Agenus Inc. or subsidiary thereof (current or former employee), Lexington, MA

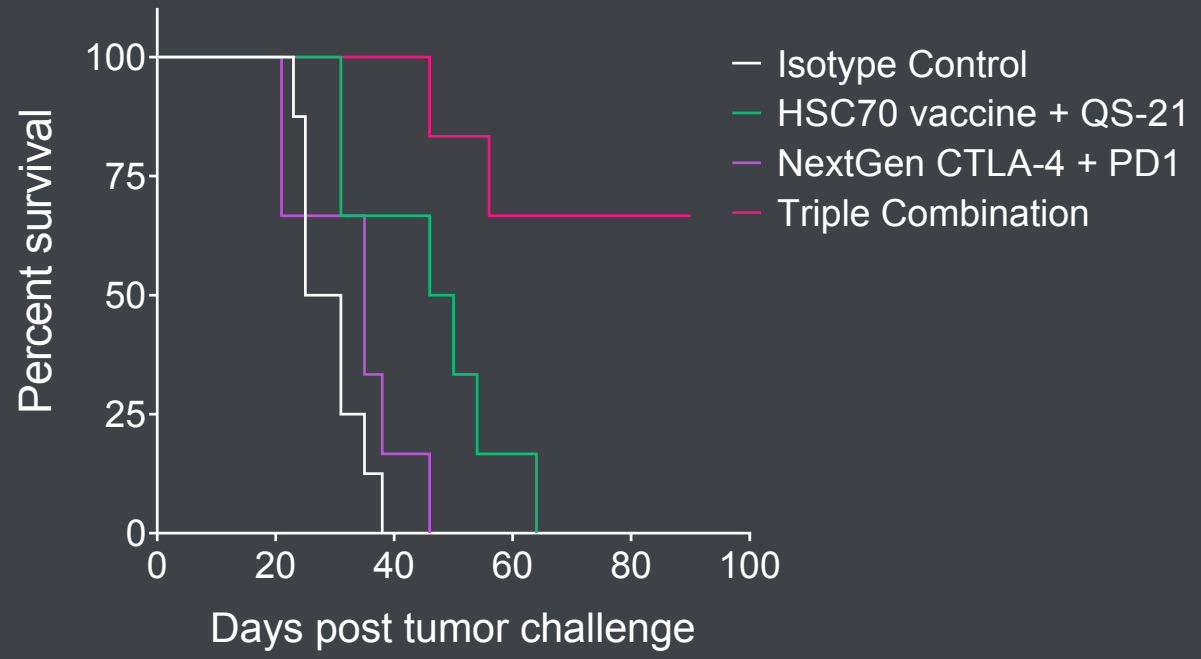
Agenus at AACR 2020:

- Fc-enhanced anti-CTLA-4 (AGEN1181) engages multiple mechanisms of action to promote optimal anti-tumor immunity
- Demonstrates superior tumor control than conventional anti-CTLA-4 (e.g. Yervoy)
- Promotes curative responses in checkpoint resistant preclinical cancer models in combination with anti-PD-1 and:
  - ✓ Vaccine + QS-21
  - ✓ Adoptive T cell therapy
  - ✓ iNKT activating Alpha-GalCer adjuvant therapy
  - ✓ Radiation therapy
- Enhances T cell responsiveness in combination with anti-PD-1 or anti-TIGIT mAbs
- Combination of AGEN1181 with Agenus's balstilimab (anti-PD-1) is advancing in the clinic

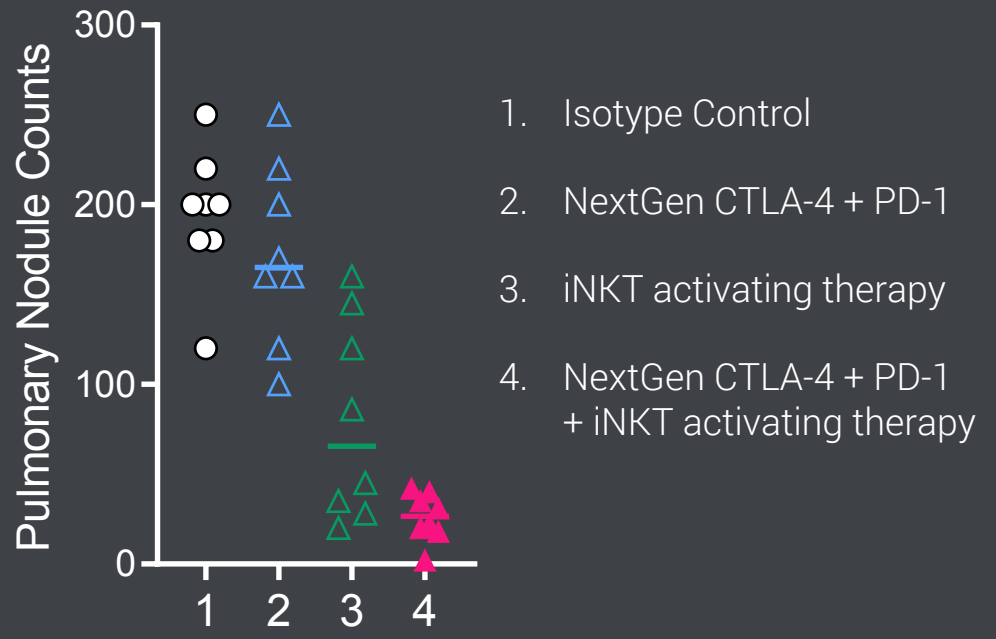
agenus

AGEN1181:
Identifying effective combinations across our pipeline

AGEN1181 synergizes + HSC70 Vaccine and PD-1 to promote anti-tumor immunity



AGEN1181* + iNKT activating therapy clear lung metastases

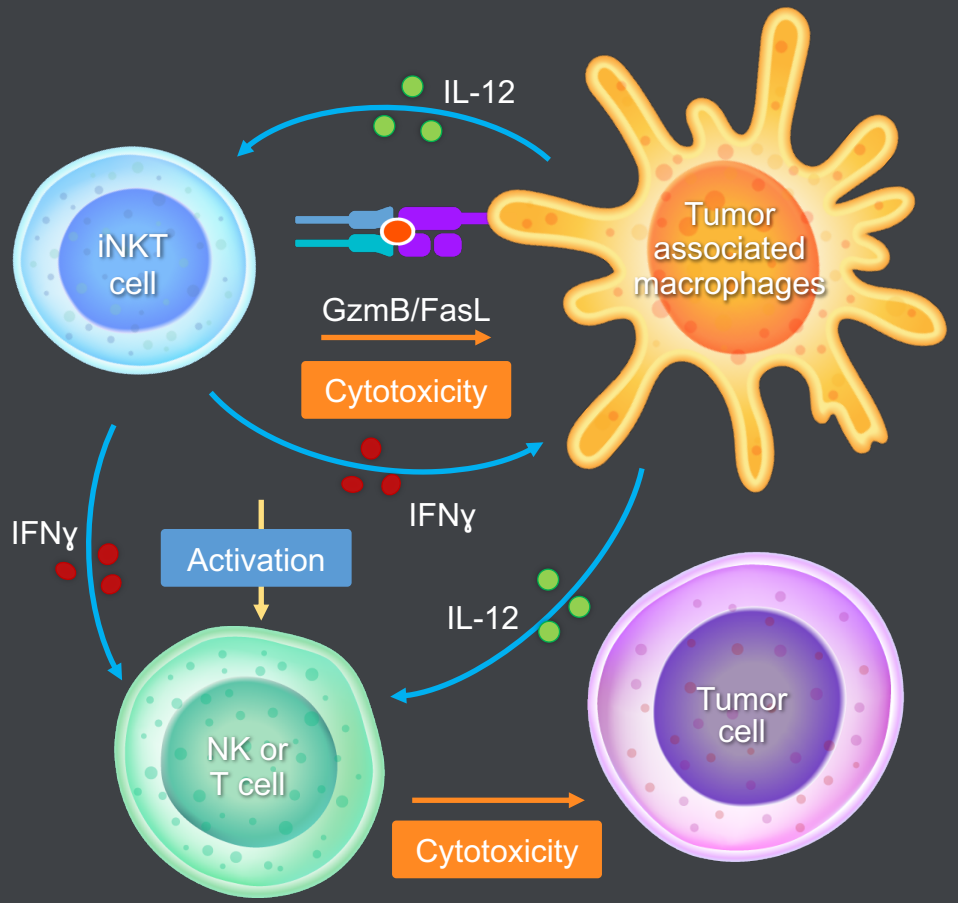


** Experiments conducted with a mouse surrogate of AGEN1181*

agenus

iNKTs - Invariant Natural Killer T Cells

Unmodified allogeneic cell therapy to treat solid tumors and COVID-19



AgenTus iNKTs:

- ✓ Require no genetic manipulation
- ✓ Have potential to treat both solid and liquid tumors
- ✓ Diminish the risk of graft vs. host disease (GvHD)
- ✓ Can be manufactured to treat large numbers of patients from a single batch
- ✓ Are synergistic with Agenus' pipeline for combination treatment
- ✓ Can be available at substantially lower costs vs. today's cell therapies

IND Cleared

agenus

agenus