

July 2022

ADAGENE

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Investment Rationale

- ✓ Robust pipeline of 3 wholly-owned clinical assets and 5 IND-enabling programs leveraging SAFEbody® precision masking technology
- ✓ Anticipated clinical milestones drive significant pipeline value
 - ✓ Anti-CTLA-4 combination results of dose escalation with PD-1 therapy in H2 2022
- ✓ Global network of collaborations
 - SAFEbody validated in technology licensing with Sanofi (\$2.5B) and Exelixis
 - Clinical collaborations (e.g., Merck) pave way for future partnerships
 - IIT clinical partnerships reduce burn and explore biomarkers in targeted indications



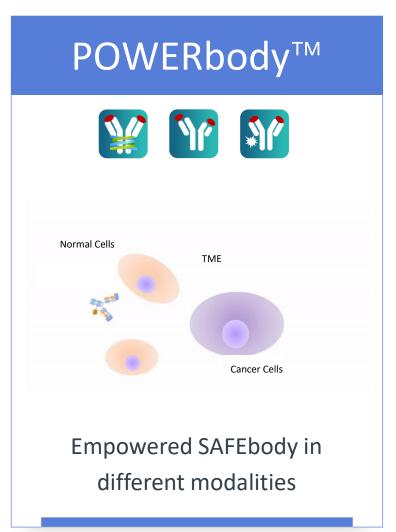
- \$174M cash position as of December 31, 2021 (audited)
- Received \$17.5M Sanofi upfront payment and \$3M Exelixis milestone in early 2022



Disruptive Technologies For Tailor-Made Antibody Therapeutics

NEObody™ Adaptive Binding between CD137 and ADG106





Global Partnerships and Collaborations Validate Our Platform

SAFEbody Development - \$17.5M upfront (2 targets), up to \$2.5B in milestones, plus royalties



- \$11M upfront (2 targets), plus royalties; \$3M milestone achieved*



Licensing fee, up to \$166M milestones, plus royalties and certain right to Greater China

ADC THE PARELLY INC.

Development of an ADC against a solid tumor target

TANABE RESEARCH

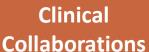
DPL Discovery

- Antibodies targeting HERV associated with RCC



Bristol Myers Squibb®

- Generate antibodies targeting novel antigens
- Antibodies against multi-transmembrane targets



- Ph 1b/2 trials with pembrolizumab



- Ph 1b/2 trial of ADG106 and nivolumab in advanced NSCLC in Singapore







Validation by Other Entities

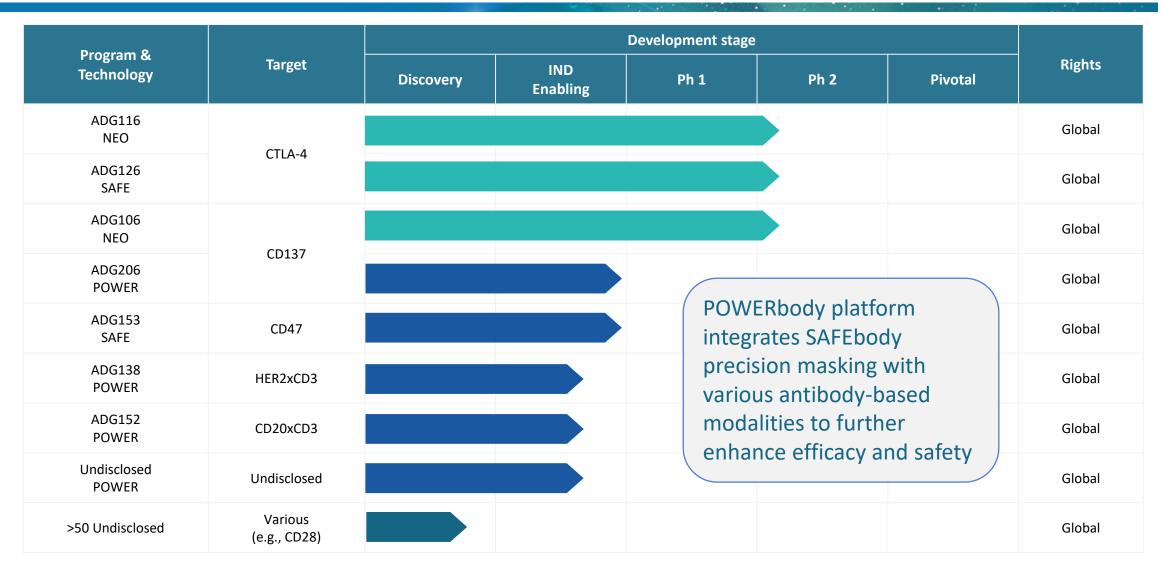
- Two programs: an anti-PD-L1 (ADG104), and a novel anti-CSF-1R (ADG125 / BC006)



- Discovered cross-reactive agonistic antibody for IO



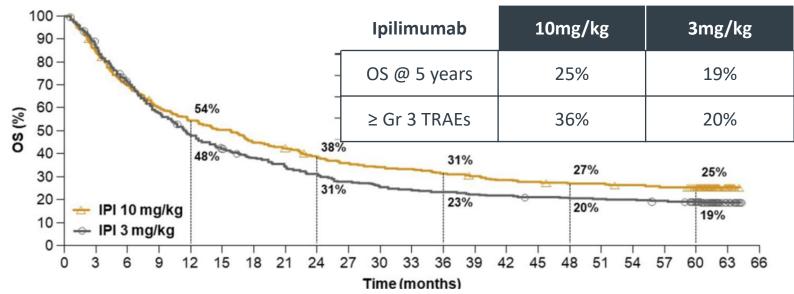
A Robust, Transformative Pipeline of Wholly-Owned Assets



Clinical Pipeline

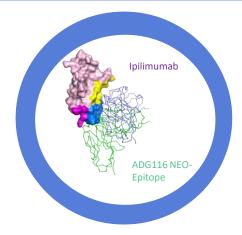
Ipilimumab is the Only Approved Anti-CTLA-4, but Clinical Utilization is Limited by Toxicity

- CTLA-4 is the first FDA approved immune checkpoint target with established clinical benefit
 - Clinically validated, strong survival benefit in a subset of patients
 - Monotherapy approved in melanoma
 - Combination with PD-1 approved in melanoma, NSCLC, RCC, MSI-H CRC, HCC, mesothelioma and ESCC
- Therapeutic potential of CTLA-4 monotherapy or in combination with anti-PD-1 has been curtailed by dose-limiting toxicity
 - Dose-dependent efficacy associated with severe toxicity
 - A low dose of ipilimumab (1 mg/kg) required in combo with nivolumab



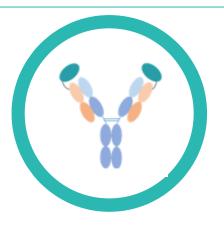
Two Wholly-Owned Potential Best-in-Class Anti-CTLA-4 Antibodies in Clinic

ADG116: anti-CTLA-4 NEObody



✓ Unique epitope triggers a softer ligand blocking and stronger regulatory T-cell depletion in TME

ADG126: anti-CTLA-4 SAFEbody



✓ Applies SAFEbody precision masking to same ADG116 binding site to enhance safety

ADG126: Interim Monotherapy Dose Escalation Data Show Compelling Profile with Repeat Dosing Across Dose Levels*

Dosing every 3 weeks up to 10 mg/kg in heavily pretreated patients (n=16) with advanced metastatic solid tumors

Safety: Only Grade 1 TRAEs across All Dose Levels

- No DLTs at doses up to 10 mg/kg
- Only Grade 1 TRAEs reported across dose levels
- Most common were fatigue (19%) and pruritis (13%)

PK: Prolonged Exposure with Steady Accumulation

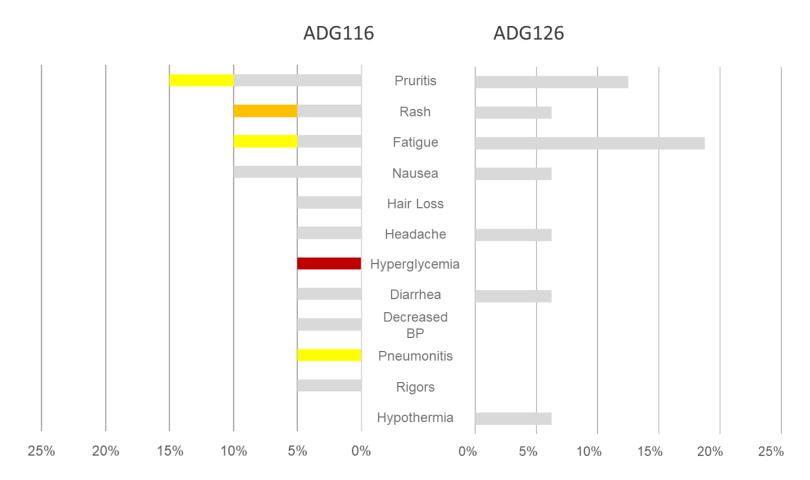
- Plasma PK ~linear with ~1.7-fold increase in half-life of total ADG126
- Activated ADG126 accumulated steadily during repeat dosing
- Indicative of prolonged exposure of activated ADG126 in the TME

Antitumor Activity in Cold Tumors

- Ovarian cancer patient showed
 >20% tumor reduction and a 77%
 reduction in CA-125 levels after 7th
 cycle at 1 mg/kg
- Uveal melanoma patient showed
 >20% tumor reduction after
 progressing on nivo + ipi
- Stable disease in 5/16 patients

Next Milestone: Data from dose escalation in combination with anti-PD-1 therapy

Snapshot of ADG116 (Parental) and ADG126 (SAFEbody) Safety





	ADG116	ADG126
N	20	16
G1	11 (55%)	10 (63%)
G2	3 (15%)	0 (0%)
G3	1 (5%)	0 (0%)
G4	1 (5%)	0 (0%)

^{*} Data plotted in this graph include: ADG116 monotherapy evaluated in 20 patients at 0.1mg/kg (n = 3), 0.3mg/kg (n = 3), 1mg/kg (n = 3), 3mg/kg (n = 4) and 10mg/kg (n = 7), as of datacut on December 20, 2021; ADG126 monotherapy evaluated in 16 patients at 0.1mg/kg (n = 3), 0.3mg/kg (n = 3), 1mg/kg (n = 4), 3mg/kg (n = 3) and 10mg/kg (n = 3), as of datacut on November 21, 2021. Percentage of TRAE was calculated by the number of TRAE divided by the number of patients. BP = blood pressure.

Ipilimumab Monotherapy Safety Summary

Trial	Tumor Type	Patient Population	Dosing Level	Dosing Frequency	AEs Lead to Discontinuation	TRAE >=G3		
NCT01515189	-	unresectable or metastatic (1L) Melanoma Adjuvant (stage III complete resection)		q3w for 4 doses	19%	20% (71/362)		
NCT00094653					NR	23% (30/131)		
NCT01844504					15%	27% (85/311)		
NCT01515189	Melanoma			10mg/kg	10mg/kg	q3w for 4 doses	34%	36% (132/364)
NCT01274338			3mg/kg	q3w for 4 doses	35%	38% (197/516)		
NCT01274338	•		10mg/kg	followed by q12w up to 4 doses	54%	57% (285/503)		
NCT00636168			10mg/kg	q3w for 4 doses followed by q12w up to 3 years	40%	*56%(262/471) 43%(201/471)-irAE		

^{*}all cause

Source: Data from published literature. Publications list on file.

ADG116 and 126: Global Clinical Programs in Advanced Solid Tumors

Next Milestone

	ADG116-1002	ADG116-1003			ADG116-P001
Regimen	ADG116 Monotherapy	ADG116 Monotherapy	ADG116 + ADG106	ADG116 + Toripalimab	ADG116 + Pembrolizumab
Location	China	U.S. & APAC	U.S. & APAC	APAC	U.S.
Status	Dose escalation	Dose escalation and expansion	Dose escalation	Dose escalation	Dose escalation

	ADG126-1002	ADG126-1001			ADG126-P001
Regimen	ADG126 Monotherapy	ADG126 Monotherapy*	ADG126 + ADG106	ADG126 + Toripalimab	ADG126 + Pembrolizumab
Location	China	U.S. & APAC	U.S. & APAC	APAC	U.S. & APAC
Status	Dose escalation	Dose escalation and expansion	Dose escalation	Dose escalation	Dose escalation

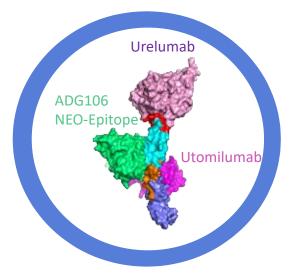
^{*} Data published in an abstract at ASCO 2022 and summarized in press release issued May 26, 2022; data cut off 2/15/22

Ipilimumab Combo Safety Summary

Trial	Tumor Type	Patient Population	Combo Agent	Dosing Level	Dosing Frequency	AEs Lead to Discontinuation	TRAE >=G3						
NCT02231749	RCC	intermediate or poor risk advanced (1L)				22%	46% (250/547)						
NCT02060188	CRC	MSI-H or dMMR metastatic progressed on chemo (2L)	nivolumab 3mg/kg		q3w for 4 doses	13%	32% (38/119)						
NCT01658878	НСС	Previously treated with sorafenib (2L)				6%	29% (14/49)						
NCT02477826	NSCLC	metastatic expressing PD-L1 (≥1%) (1L)									q6w up to 2 years	18%	33% (189/576)
NCT02899299	Pleural Mesothelioma	unresectable malignant (1L)	4			23%	30% (91/300)						
NCT03215706	NSCLC	metastatic with no EGFR or ALK mutation(1L)	nivolumab 360mg +2 cycles chemo	1mg/kg	q6w up to 2 years	19%	47% (168/358)						
NCT01844505	Melanoma	unresectable or metastatic (1L)	nivolumab	3mg/kg	q3w for 4 doses	36%	55% (172/313)						
NCT01658878	нсс	Previously treated with sorafenib (2L)	1mg/kg			18%	53%(26/49)						

Two Potential First & Best in Class Anti-CD137 Antibodies

ADG106: anti-CD137 NEObody



- ✓ Unique epitope to balance safety and efficacy
- ✓ Completed Ph1 monotherapy in >100 patients
- ✓ Ph1b/2 combos with toripalimab, nivolumab or pembrolizumab
- ✓ Ph1b/2 novel combo with ADG116 or 126

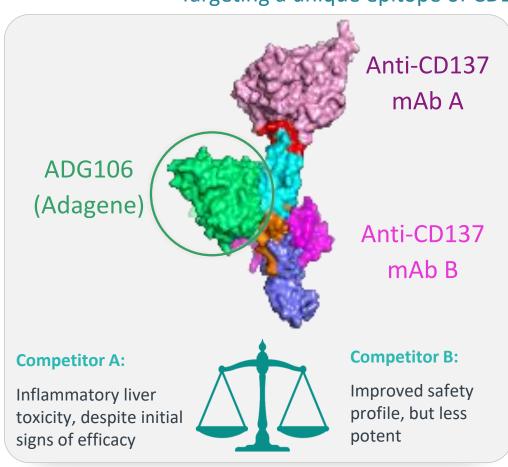
ADG206: anti-CD137 POWERbody



- ✓ Fc-engineered IgG1 antibody designed for empowered potency
- √ 4x stronger Fc crosslinking than urelumab analog
- ✓ Applies SAFEbody precision masking to same binding site as ADG106
- ✓ IND or equivalent planned in 2022

ADG106: Anti-CD137 NEObody Program

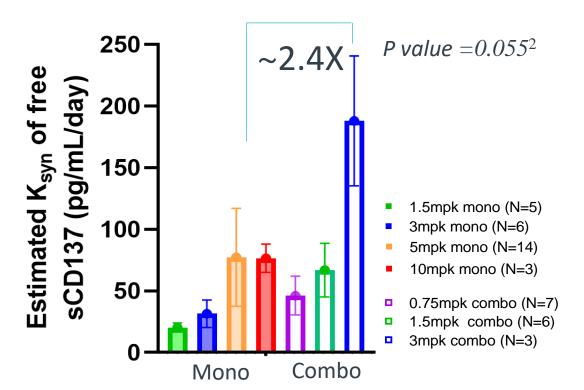
Targeting a unique epitope of CD137/4-1BB pathway validated by CAR-T



- ✓ Well-tolerated with cohort expansion at 3 & 5mg/kg and at 300mg and 400mg flat doses in US and China
- ✓ Single agent clinical efficacy with 56% disease control rate, including PR for a solid tumor patient R/R to PD-L1 therapy
- ✓ Proprietary biomarker identified with tumor shrinkage in 75% of biomarker positive patients
- ✓ Combination trials with anti-PD-1 ramping up targeting biomarker-enriched indications

ADG106 Showed 2-Fold Synergistic Effect with Toripalimab for Immune Activation in Clinical PD Biomarker Analysis*

Assessment of Biomarker Kinetics for ADG106 alone and in combination¹



- Demonstrated synergistic effect of ADG106 with anti-PD-1 toripalimab, compared to ADG106 monotherapy
- Synergy observed in patients who failed prior anti-PD-1 and CTLA-4 therapies
- Informed RP2D dose in ongoing trial, enabling dose expansion in biomarker enriched tumor types

^{*} Data presented at ESMO-IO 2021 and summarized in press release issued December 6, 2021

 $^{^{1}}$ Mean \pm standard error of the mean (SEM) is shown

² P value shown for 3mpk combo vs. 5 and 10mpk mono combined, 1-sided T test

ADG106: Global Clinical Trials Explore Multiple Novel Combinations in Biomarker Enriched Tumors

	ADG106-1008	ADG106-T6001	ADG116-1003	
Patient Population*	 Dose escalation in advanced solid tumors Dose expansion in select tumors 	Advanced NSCLC	 Dose escalation in advanced solid tumors Dose expansion in select tumors 	
Combination	ADG106 + Toripalimab	ADG106 + Nivolumab	ADG106 + ADG116	
Location	China	Singapore	U.S. & APAC	
Status	Dose expansion	Dose escalation	Dose escalation	

Planning additional novel combinations via both sponsored trials and IITs to efficiently explore pathway potential in targeted tumors

^{*} Program targets biomarker-enriched tumors

Preclinical Pipeline

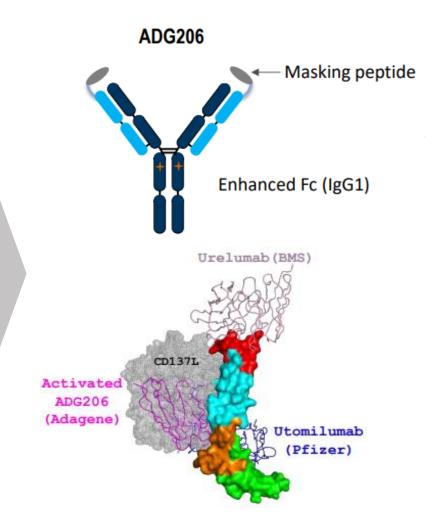
AACR and ASH Posters Demonstrate Build-Out of Deep, Broad & Differentiated Pipeline of Antibody-Based Therapeutics

	Target	Approach	Status	Next Steps
ADG206 (AACR)	CD137 POWERbody	 Enhanced crosslinking with engineered Fc and SAFEbody masking 	IND-enabling	Submit IND or equivalent in 2022
ADG153 (AACR & ASH)	CD47 SAFEbody	- IgG1 antibody with SAFEbody masking	IND-enabling	Submit IND or equivalent in 2022
ADG138 (AACR)	HER2xCD3 POWERbody	- Bispecific TCE with SAFEbody masking on <i>both</i> arms	IND-enabling	IND-enabling studies
ADG152 (ASH)	CD20xCD3 POWERbody	- Bispecific TCE with SAFEbody masking on tailor-made CD3 arm	IND-enabling	IND-enabling studies
CD28 TCE (AACR)	Various TAAx CD28 POWERbody	 Broadens TCE platform with CD28 Multiple potential TAA targets, including B7-H3, HER2 	Discovery	Finalize lead selection

ADG206: Masked, Fc Engineered Anti-CD137 Agonistic POWERbody™

- Masked, anti-CD137 conditionally activated in TME with strong agonistic activity through heightened Fc γ R-mediated crosslinking for enhanced therapeutic potential
- ✓ Potency: 4-fold stronger activity than benchmark antibody in development (analog of urelumab) for T cell co-activation
 - ✓ Enhanced anti-tumor activity: as a *single agent* in multiple preclinical tumor models and *in combination* with checkpoint inhibitors, including anti-PD-1 or anti-CTLA-4 therapy
- ✓ **Safety:** Well-tolerated in rats and cynomologus monkeys
- ✓ **PK**: Normal properties and minimal activation in circulation

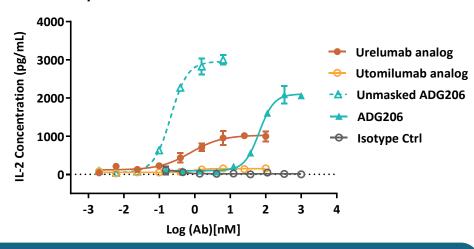
Next step: Submit an IND or equivalent filing in 2022



ADG206, Strong Crosslinking and Tumor Selective Activation for Tailor-Made Efficacy, Safety and Single Agent and Combinational Cancer Immunotherapy

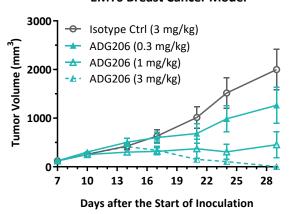
Potent co-stimulation of human T cells by unmasked ADG206 in vitro

IL-2 secretion by human T cells stimulated with anti-CD137 and SEA

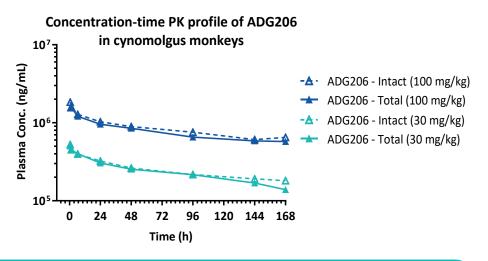


ADG206 exhibits robust anti-tumor activity in mouse tumor models

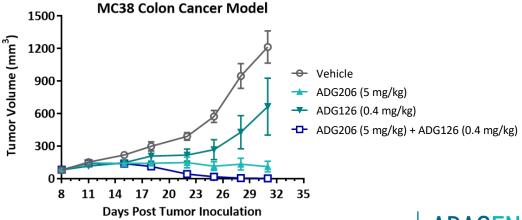
EMT6 Breast Cancer Model



ADG206 demonstrates normal systemic PK properties and minimal accumulation after repeat dosing in cynomolgus monkeys



Combination of ADG206 with checkpoint inhibitors shows enhanced in vivo antitumor activity

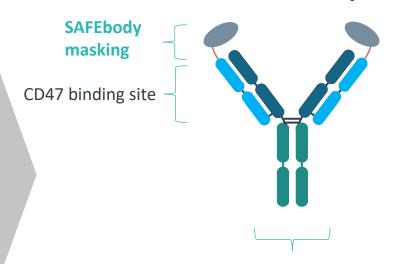


ADG153: A Highly Differentiated IgG1 Anti-CD47 SAFEbody®

- Anti-CD47 antibody with IgG1-mediated strong effector functions for potent tumor killing, while minimizing antigen sink and red blood cell (RBC) depletion
- Integrates safety and efficacy into one single modality
- ✓ Potency: Maximize tumor killing via IgG1-mediated ADCC and ADCP unlike other anti-CD47 antibodies in clinic
- ✓ **Safety**: Reduced RBC-related and antigen sink liabilities
 - ✓ Well-tolerated at 10 mg/kg in monkeys, with an 8% decrease in RBCs, vs a 49% decrease for Hu5F9 analog in IgG4
- ✓ PK: ~8-fold prolonged half-life for convenient dosing and administration

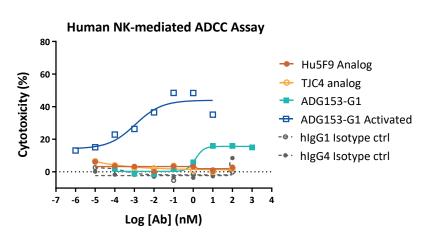
Next step: Submit an IND or equivalent filing in 2022

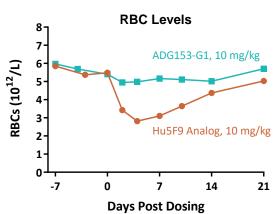
ADG153 SAFEbody - G1

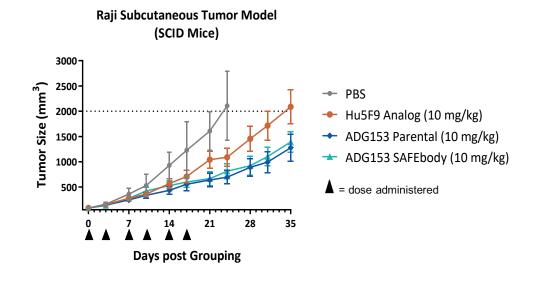


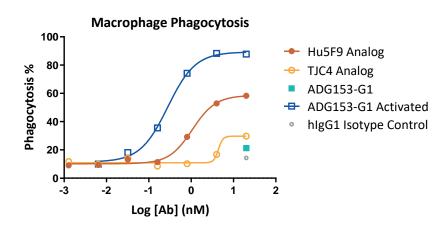
IgG1 isotype introduces potent antibody-dependent cellular cytotoxicity (ADCC), and antibody-dependent cellular phagocytosis (ADCP) effector function

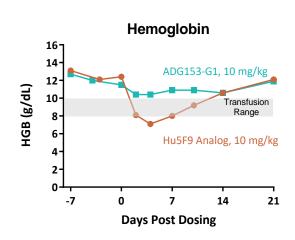
ADG153-IgG1 SAFEbody: Potency, Safety Profile, and PK Offers Best-in-Class Profile as Potential Treatment for Liquid and Solid Tumors

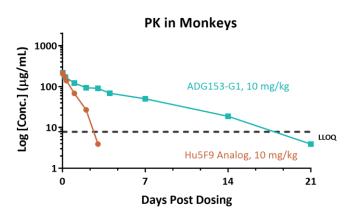










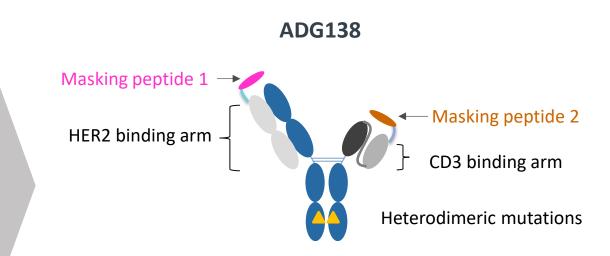


The 1st conc. point below LLOQ was shown as half of LLOQ

ADG138: Novel, Double Masked HER2xCD3, Bispecific POWERbody™

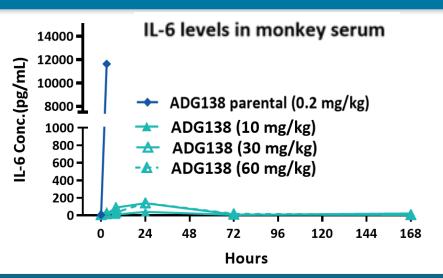
- ADG138 integrates bispecific TCE (T cell engager) with precision masking on both arms to control cytokine release syndrome and on-target off-tumor toxicity for single agent and combination therapies in HER2expressing solid tumors
- ✓ Potency: Anti-tumor activity in HER2 high and low expressing tumors, as well as resistant refractory tumors, relative to DS-8201
- ✓ **Safety:** 100-fold greater reduction in cytokine release syndrome compared to its parental TCE
- ✓ **Synergistic anti-tumor activity** when combined with anti-CD137 or anti-PD-1 therapy in HER2 positive tumors

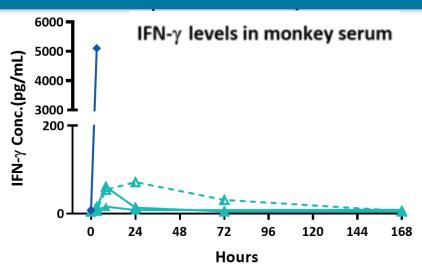
Next step: IND-enabling studies ongoing



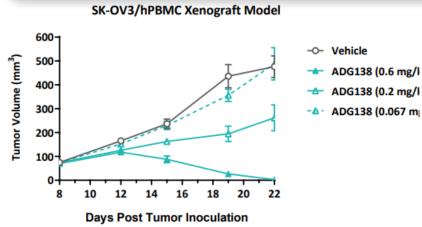
ADG138 Controls Cytokine Release Syndrome Leveraging SAFEbody Masking

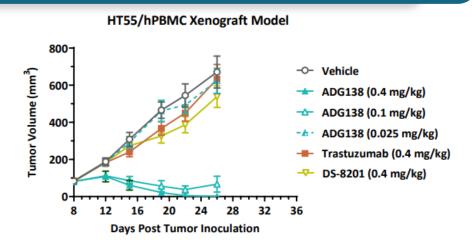
ADG138 caused ~100-fold reduced cytokine release compared with parental TCE in cynomolgus monkeys





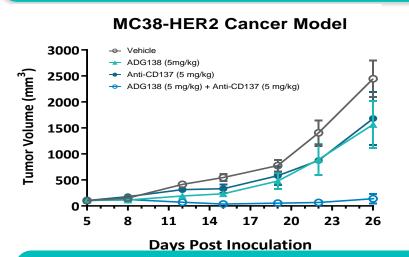
Potent in vivo anti-tumor activity by ADG138 POWERbody in HER2-high, -low, and resistant/refractory tumor models

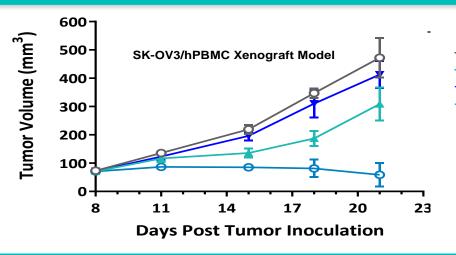




ADG138 Shows Potent Activity Compared to Benchmarks, and Can be Combined with Anti-CD137 & Anti-PD-1 & TAAxCD28 Therapy

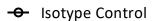
Combinations of ADG138 with I-O agents exhibited synergistic anti-tumor activities in mouse tumor models



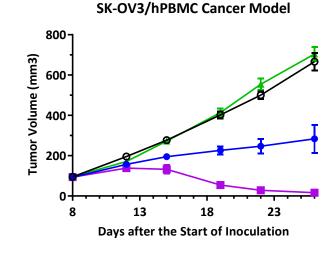


- -o- Isotype Ctrl (5 mg/kg)
- ADG138 (0.2 mg/kg) + Isotype Ctrl (5 mg/kg)
- Anti-PD-1 (5 mg/kg)
- ADG138 (0.2 mg/kg) + Anti-PD-1 (5 mg/kg)

Combination of TAA*CD3 TCE with TAA*CD28 demonstrates enhanced in vivo antitumor effect



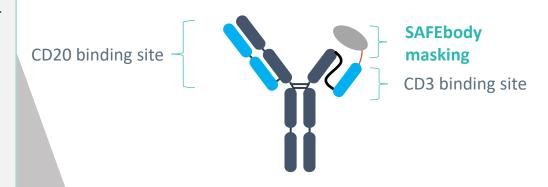
- **→** ADG138
- → B7H3×CD28
- ADG138 + B7H3×CD28



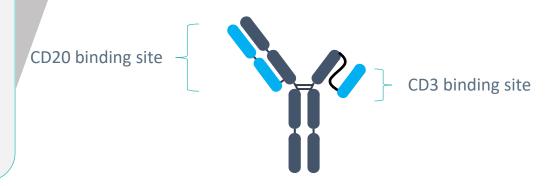
ADG152: Anti-CD20xCD3 is First Bispecific T-cell engager from POWERbody™ Platform

- Integrates SAFEbody precision masking technology to minimize cytokine release syndrome (CRS) and on-target/offtumor toxicities for an increased therapeutic index (~10-fold higher)
- Enhanced binding to CD20; anti-CD3 arm has tailor-made affinity for CD3 with SAFEbody technology
- ✓ Potency: Antitumor activity as a single agent in the mouse xenograft tumor model
- ✓ Safety: ~100-fold less CRS than a plamotamab analog in monkeys
- ✓ PK: Improved half-life and area under the curve than a plamotamab analog in monkeys

ADG152 POWERbody

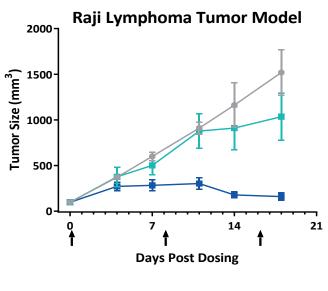


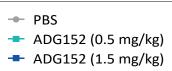
ADG152 Parental Antibody



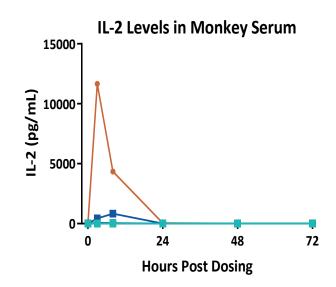
ADG152: Strong Efficacy, Improved Safety and PK Compared to a Plamotamab Analog

Strong anti-tumor activity in the mouse xenograft tumor model

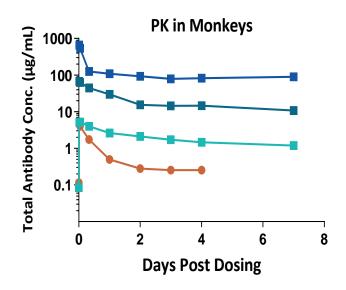




Less CRS at ADG152 30 mg/kg vs. plamotamab analog at 0.3 mg/kg (>100-fold safety margin)



2-fold longer half-life (7-13 days) and ~8-fold higher AUC



- plamotamab analog (0.3 mg/kg)
- ADG152 (0.3 mg/kg)
- → ADG152 (3 mg/kg)
- → ADG152 (30 mg/kg)

Collaborations & Outlook

Current Collaborations Pave Way for Long Term Partnerships



Discovery

 Leverage SAFEbody precision masking technology Validates technology across multiple modalities









Preclinical

 Leverage efficiency of discovery engine Accelerate path to clinic via partnership







Clinical

- Advance assets to clinical POC
- Collaborate for clinical development and commercialization

Drive global commercialization, while retaining optionality (i.e., codevelopment, geographic rights)

Product supply:









Sanofi Technology Licensing Collaboration Valued at \$2.5 Billion Shows Broad Potential of SAFEbody® Across Modalities

- Multi-target collaboration for SAFEbody, novel masked immuno-oncology antibody candidates:
 - 2 initial candidates; option with fee for 2 additional
 - Includes monoclonal and bispecific antibodies
- Adagene responsible for early-stage research to develop masked versions of Sanofi candidate antibodies, using SAFEbody technology
- Sanofi solely responsible for later stage research & all clinical, product development and commercialization



Total Potential Transaction > \$2.5B*

- \$17.5M upfront (2 programs); option exercise fee for 2 additional
- \$2.5B in development, regulatory & commercial milestones
- Tiered royalties

"Adagene's antibody platform should help us to precisely target established, but poorly addressed oncology mechanisms with **best-in-class medicines**." *Valeria Fantin, Global Head of Oncology, Sanofi*

Building a Global Pipeline of Antibody-Based Products Through Partnerships



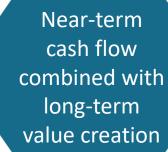
Discovery

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Preclinical

 Leverage efficiency of discovery engine Accelerate path to clinic via partnership







 Collaborate for clinical development and commercialization Drive global commercialization, while retaining optionality (i.e., codevelopment, geographic rights)

2022 Outlook

✓ Completed a major collaboration – partnering activities continue

- Demonstrate safety and single-agent activity for anti-CTLA-4 programs (ADG116/126) in warm and cold tumors in heavily pre-treated patients
- Demonstrate safety and preliminary efficacy profile for anti-CTLA-4 programs with anti-PD-1 therapy
- Evaluate profile for novel combination of wholly-owned anti-CTLA-4 and anti-CD137 (ADG106)
- Show synergistic effect of anti-CD137 with anti-PD-1 therapy in biomarker-enriched tumors
- Submit filings to advance two more candidates to clinic, and expand programs into IND-enabling phase
- Continue efficient discovery operations, with >50 projects underway

Financial Summary

	As of June 30, 2021	As of December 31, 2021
Cash and cash equivalents	US\$208 million (unaudited)	US\$174 million (audited)

\$3M Exelixis milestone and \$17.5M Sanofi upfront payment received in 2022

ADAGENE

Thank you