

OUR VISION: COMBINING TO CURE WITH BEST-IN-CLASS CANCER THERAPIES

NYSE: RCUS

AUGUST 2020

Forward-looking Statements/Safe Harbor

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RCUS Investment Thesis

- **Advanced pipeline of products that target 3 of the most highly pursued IO pathways: TIGIT, Adenosine, and PD-1**
  - Well-understood science; Relevant in many tumor types; Potential biomarkers for patient selection
  - Multiple product candidates for major pathways (e.g., TIGIT, adenosine) increases probability of success in such pathways
- **Early signs of clinical activity from our ongoing trials will be followed by preliminary randomized data in multiple settings/combinations in 2H2020**
- **Unique intra-portfolio combinations not available to any other company**
- **Well-positioned to fully unlock the value of our pipeline**
  - > $825M cash*
  - Gilead collaboration provides resources and expertise to efficiently and more fully exploit multiple intra-portfolio opportunities

* Cash, cash equivalents and investments as of June 30, 2020 adjusted to reflect $375M from Gilead upfront and equity investment on July 13, 2020

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Strategic in Our Choices of Targets and Combinations; Purposeful in Our Decisions and Investments

- **Critical pathways and targets**
  - **Essential Backbones:**
    - **AB154 (Domvanalimab)**: anti-TIGIT mAb – rapidly advancing in randomized combinations
    - **Zimberelimab**: anti-PD-1 mAb with clear line-of-sight to commercialization, enables portfolio combination strategies
  - **Adenosine Axis:**
    - **AB928 (Etrumadenant)**: $A_{2a}R$ / $A_{2b}R$ antagonist – first and only dual antagonist in the clinic
    - **AB680**: CD73 inhibitor – first small-molecule in the clinic; exceptional potency
- **Targeting best-in-class molecules: modality, biology and properties**
- **Critical aspect of discovery strategy, focus and investment: enabling long-term success**
- **New programs likely to have synergistic activity with other molecules in the Arcus portfolio**
  - **HIF-2α, PI3K-γ and Axl**

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Essential Backbone Agents

- **PD-1/PD-L1 Axis**
  - Essential to fully leverage other programs and enable development and commercialization opportunities
  - Zimberelimab has profile similar to that of pembrolizumab: preclinically and clinically
  - Path to zimberelimab single-agent approval to be disclosed in 2H 2020
- **TIGIT/CD155 Axis: Arcus early investment/commitment to success**
  - AB154 (Ph2): FcR-silent; potential advantages in solid tumors
  - AB308 (IND 4Q20): FcR-capable; potential advantages in hematology
  - Arcus is well positioned: only company known to have both types of antibodies

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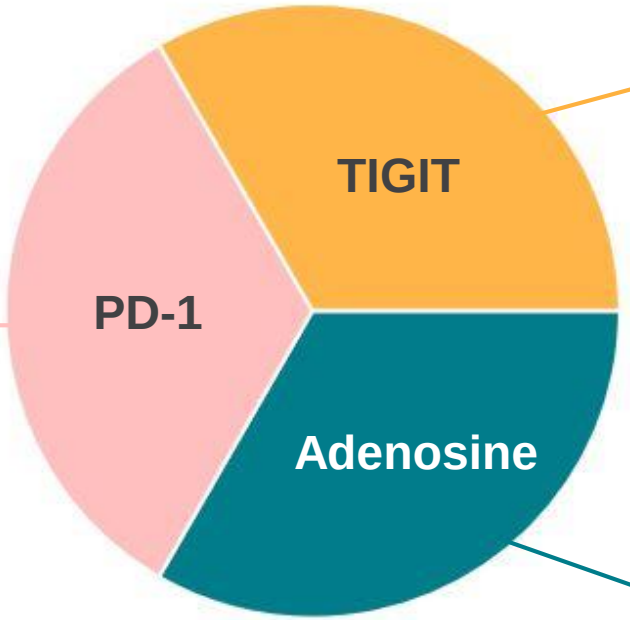
ATP/Adenosine Axis: One of the Most Ubiquitous Pathways Associated with Immunosuppressive Tumor Microenvironment

- **Arcus's early and broad investment in modulating the pathway**
- **Potential best-in-class adenosine receptor antagonists designed and optimized for oncology setting**
- **AB928 (Ph2): first & only clinical agent that blocks A_{2a} and A_{2b} receptors**
  - Multiple potential biological advantages relative to selective A_{2a} receptor blockers
  - Growing evidence of A_{2b} role in both TME immunosuppression and cancer cell-intrinsic biology
- **AB680: first and most advanced small-molecule CD73 inhibitor in the clinic**
  - Small molecule best modality for tumor-associated enzyme inhibitor (e.g., better tumor penetration)
  - AB680 capable of complete inhibition of both membrane bound *and* soluble forms of CD73; the most advanced antibodies are not capable of fully inhibiting the enzymatic activity of CD73
  - IV and oral formulations in development

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Advanced Pipeline of Products Against 3 of the Most Important IO pathways

- PD-1 inhibition reactivates exhausted intra-tumoral T cells
- Well-established backbone therapy

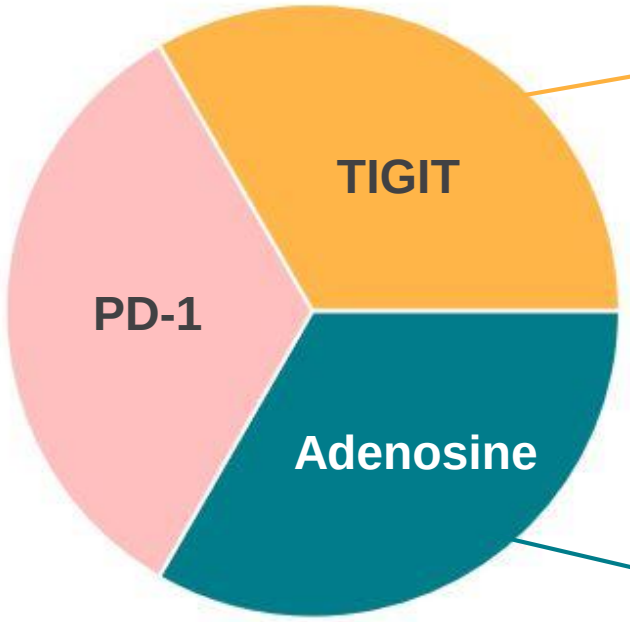


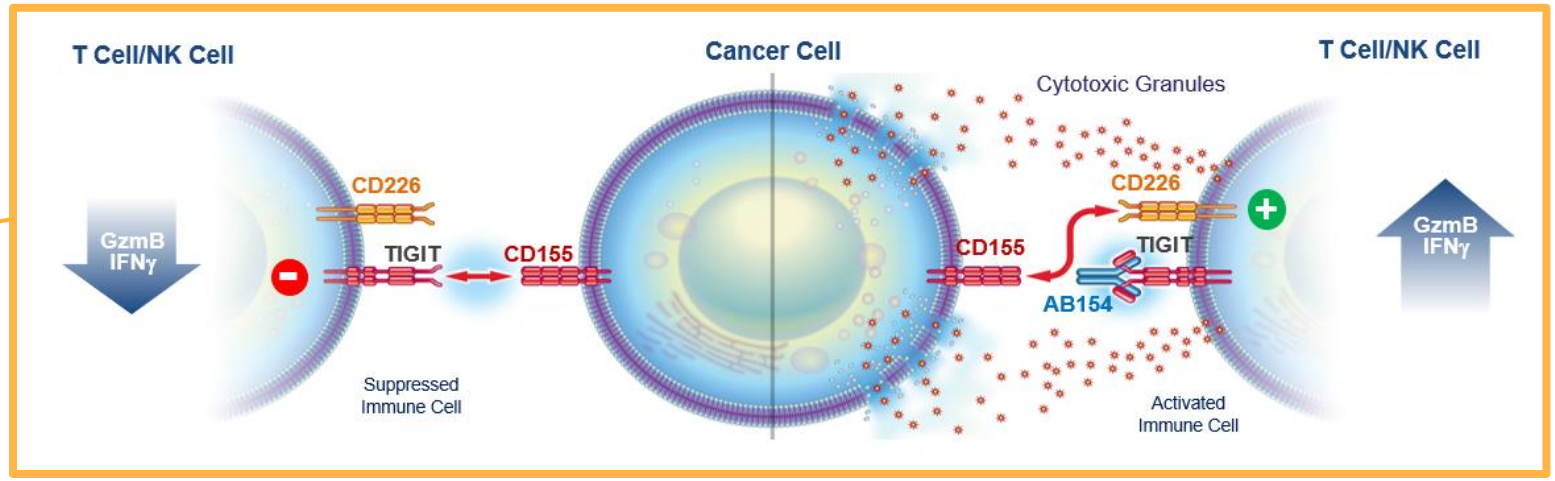
- TIGIT inhibition provides selective reactivation of exhausted T cells
- The “other” real immune checkpoint
- Complementary to PD-(L)1 inhibition

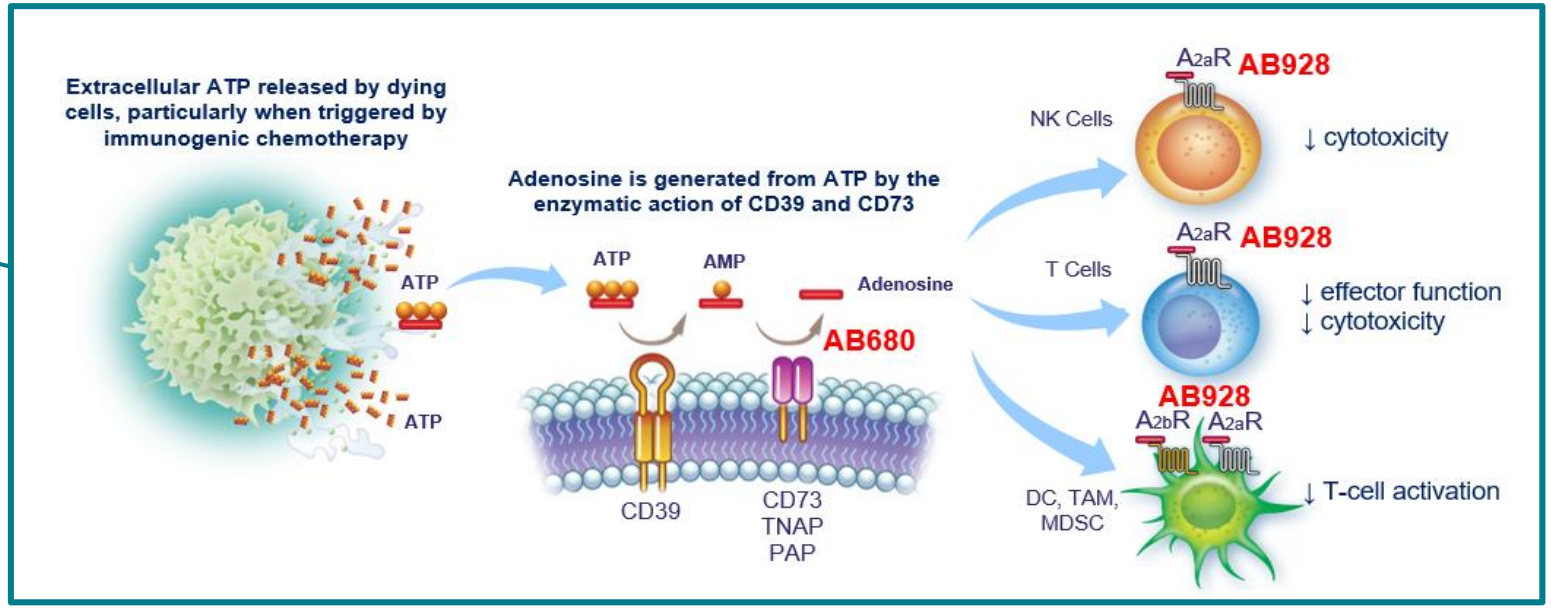
- High adenosine levels in tumors prevent activation of T cells and NK cells
  - Direct effects mediated by A_{2a} receptor
  - Indirect effects mediated by A_{2b} receptor on dendritic/myeloid cells
- Adenosine inhibition allows maximal T & NK cell activation

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Advanced Pipeline of Products Against 3 of the Most Important IO pathways





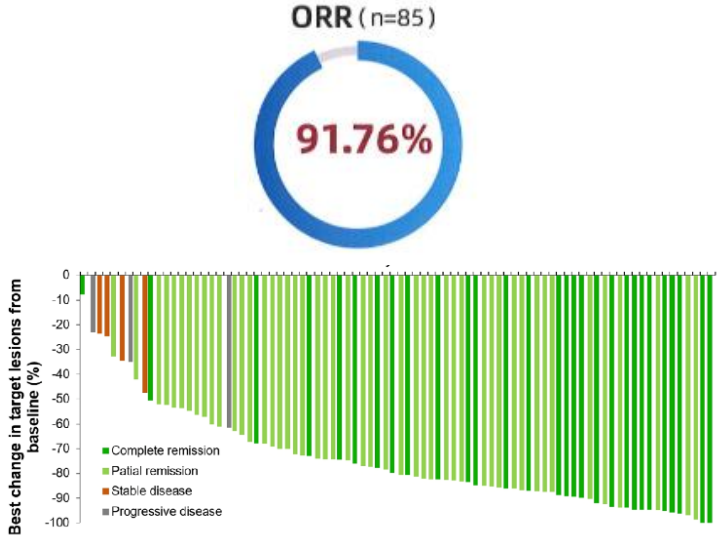


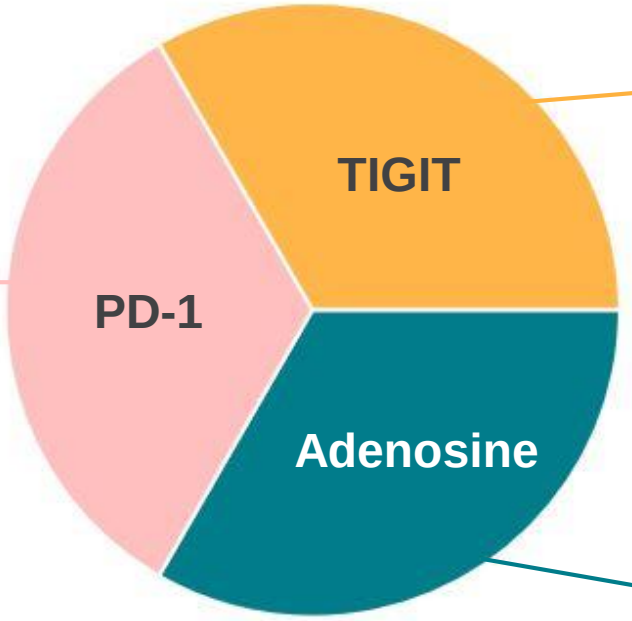
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Pathways Significantly De-risked Based on the Totality of Available Internal and External Clinical Data

As presented by Gloria Biosciences at ASCO (2020)

Ph2 (GLS-010/Zim) in r/r cHL

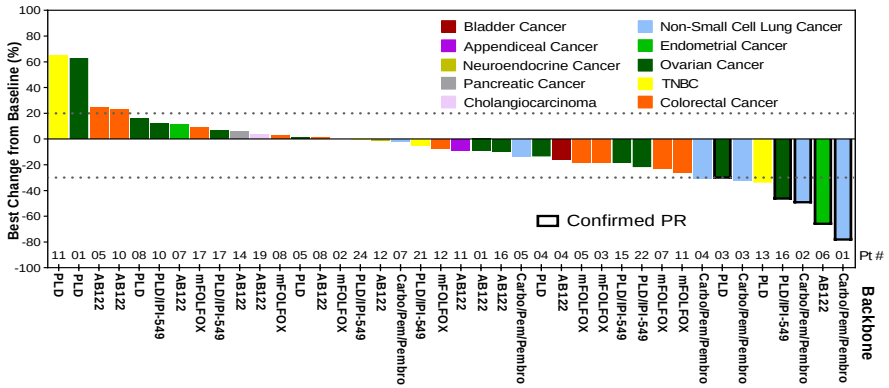




Genentech/Roche CITYSCAPE Presentation – ASCO (2020)

NSCLC - PD-L1-high (TPS ≥ 50%)		
	Tirago + Atezo (n=29)	Atezo (n=29)
ORR (95%CI)	55.2% (35.3, 75.0)	17.2% (1.8, 32.7)
Odds Ratio	5.91 (95%CI: 1.76, 19.81)	
mPFS (95%CI)	NE (5.3, NE)	3.9 (2.1, 4.7)

Combined Dose Escalation Studies with AB928 (DCO of 31Jan2020)



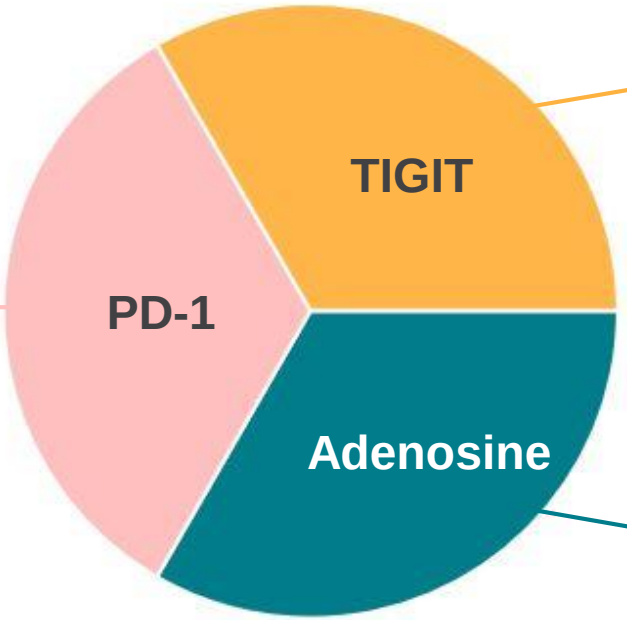
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Multiple Product Candidates Provide Optionality and Increase Probability of Maximal Clinical Benefit

-- Product Portfolio Addresses Open Scientific Questions Unlike Any Other Pipeline --

Proprietary anti-PD-1 backbone

- AB122 (Zim): anti-PD-1 awaiting regulatory approval in China[1]; Ph2



Various FcR binding modes

- AB154: FcR-silent mAb; Optimized for use in solid tumors; Ph2
- AB308 : FcR-capable mAb; Optimized for use in hematology; IND 4Q20

Multiple modes of adenosine pathway inhibition

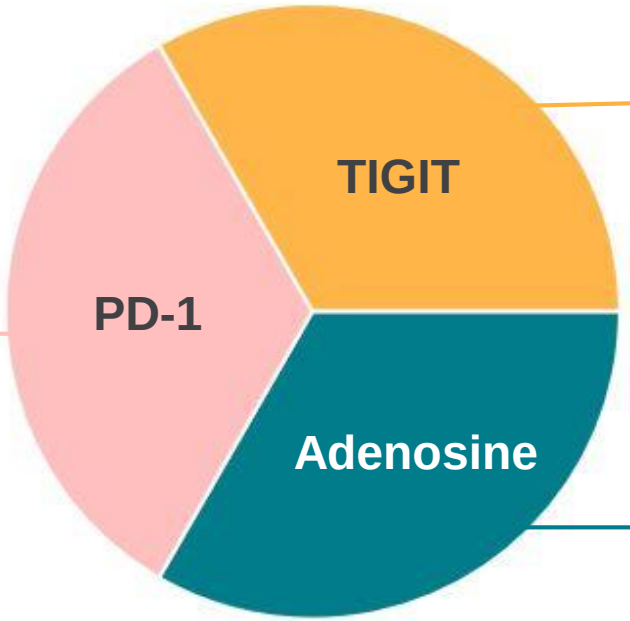
- AB928: Dual $A_{2a}R/A_{2b}R$ antagonist; Ph2
- AB745: Select $A_{2a}R$ ant.; Preclin. Parked
- AB680: CD73 inhibitor; Ph1b

[1]Regulatory filing in China made by Gloria Biosciences, Gloria's activities are independent of Arcus.

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Our 3 Advanced Clinical Programs Lend Themselves to Biomarker-based Patient Selection

-- Major biomarker-data collection effort ongoing in all of our trials --



Novel IHC assays developed to quantify TIGIT and CD155 expression as potential biomarkers for anti-TIGIT efficacy

In certain tumor types, PD-L1 levels correlate with response to anti-PD-(L)1 antibodies

Novel CD73 IHC assay and adenosine fingerprint (gene expression profile) developed as potential biomarkers for anti-adenosine efficacy

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Expanding on Proven Clinical Roles of These Pathways: Combinations Address Major Areas of Medical Need and Are Uniquely Enabled by Arcus Pipeline

-- Illustrative Major Tumor Types Associated with Each Pathway –
-- See Next Slide for Our Complete Clinical Development Plan --

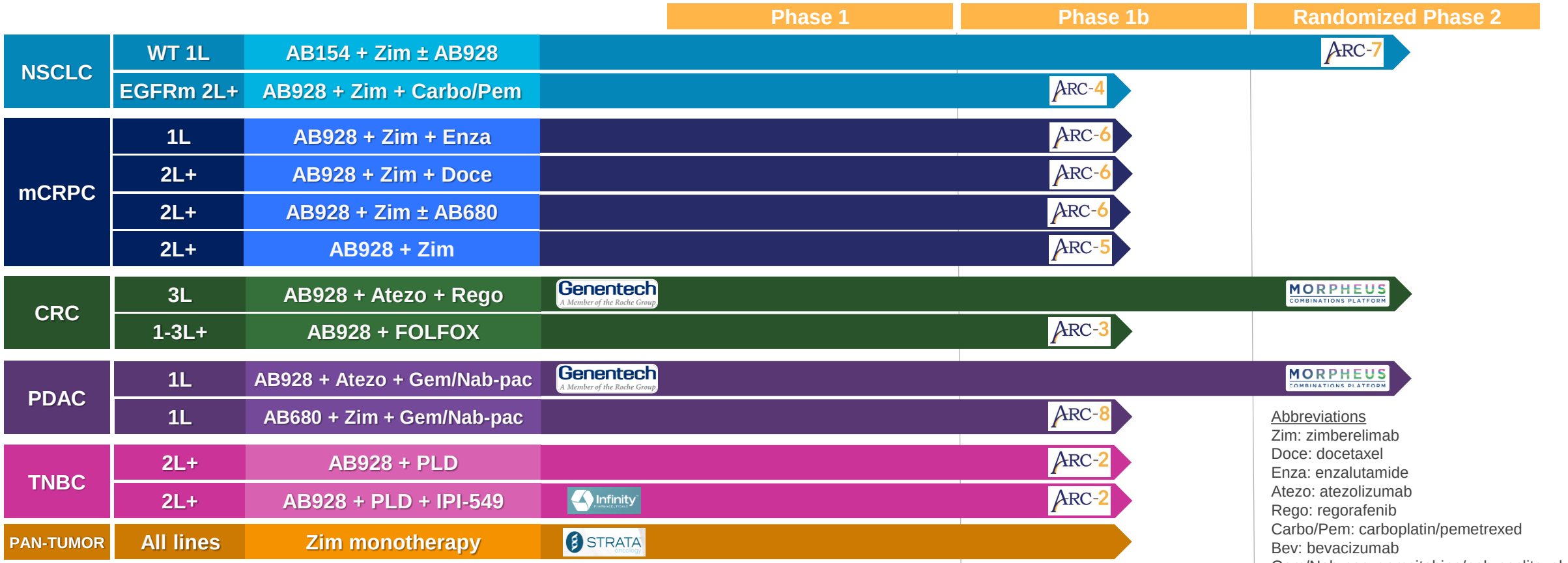
	NSCLC	CRC	PDAC	CRPC	TNBC
Adenosine	✓	✓	✓	✓	✓
TIGIT	✓	✓	✓		✓
PD-1	✓	✓	✓	✓	✓

- ARC-4 Zim + Carbo/Pem ± AB928
- ARC-7 Zim ± AB154 ± AB928
- ARC-3 AB928 + FOLFOX
- MORPHEUS COMBINATIONS PLATFORM AB928 + Rego + Atezo
- ARC-5 ARC-6 AB928 + Zim ± SOC
- ARC-2 AB928 + PLD
- MORPHEUS COMBINATIONS PLATFORM AB928 + Atezo + Gem/Nab-pac
- ARC-8 AB680 + Zim + Gem/Nab-pac

✓ Strong scientific rationale; current RCUS study
✓ Strong scientific rationale; potential future RCUS study

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Broad Clinical Program to Compete Aggressively in Settings with Significant Therapeutic and Commercial Potential



Abbreviations
Zim: zimberelimab
Doce: docetaxel
Enza: enzalutamide
Atezo: atezolizumab
Rego: regorafenib
Carbo/Pem: carboplatin/pemetrexed
Bev: bevacizumab
Gem/Nab-pac: gemcitabine/nab-paclitaxel
PLD: pegylated liposomal doxorubicin
SOC: standard of care

ONGOING
PLANNED

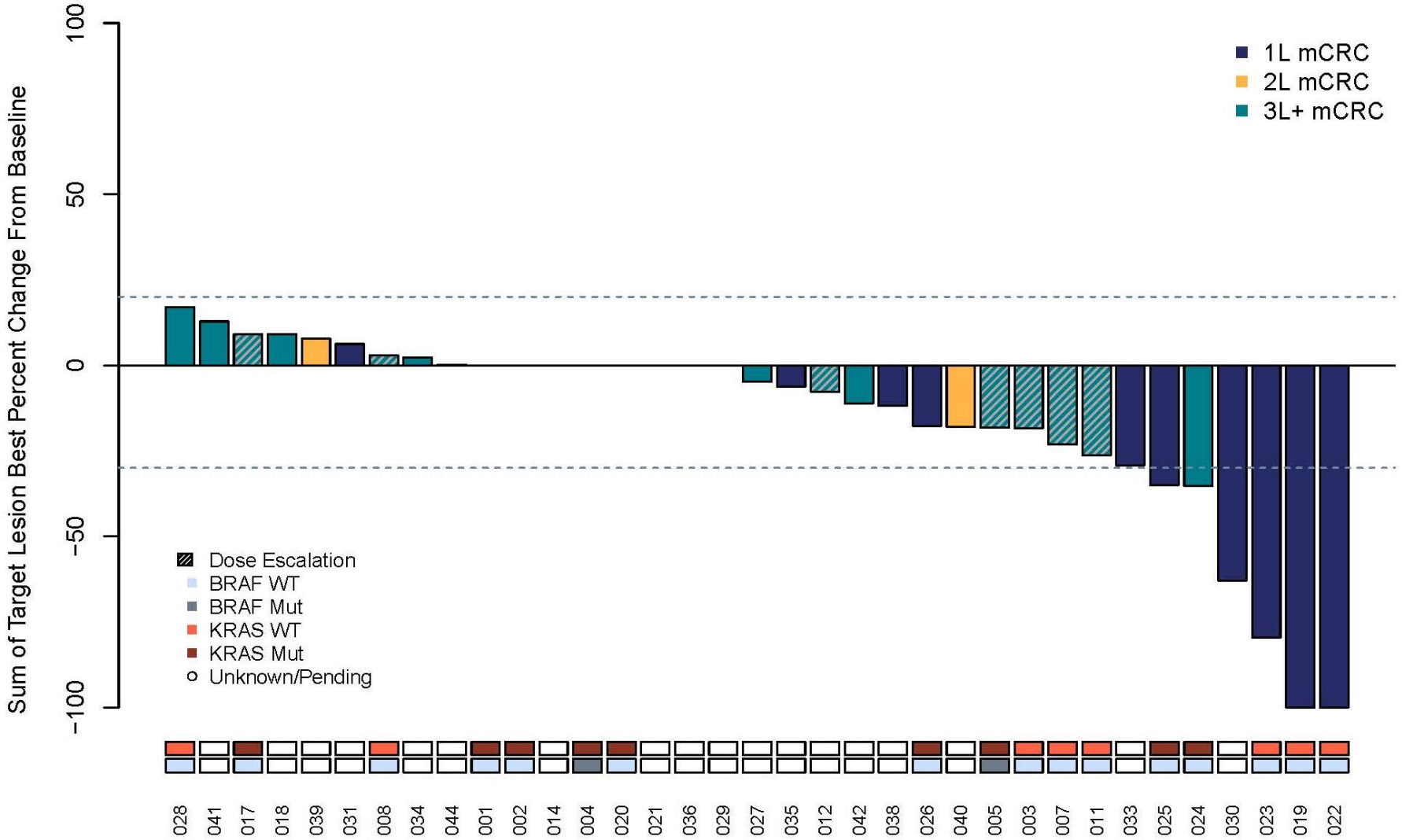
AB680: CD73 inhibitor
Zim: PD-1 mAb
AB928: Dual $A_{2a}R/A_{2b}R$ antagonist
AB154: TIGIT mAb

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Preliminary Evidence of Clinical Activity in Metastatic CRC with AB928 + FOLFOX

Cecchini et al., AACR (2020); abstract no. 9953; clinicaltrials.gov NCT03720678

- **Investigator-assessed DCR was 76% with 6 PRs and 10 SD for ≥ 2 disease assessments**
- **For 11 patients treated with ≥ 2 prior lines of therapy for metastatic disease (3L+), DCR was 64% with 1 PR and 6 SD for ≥ 2 disease assessments**

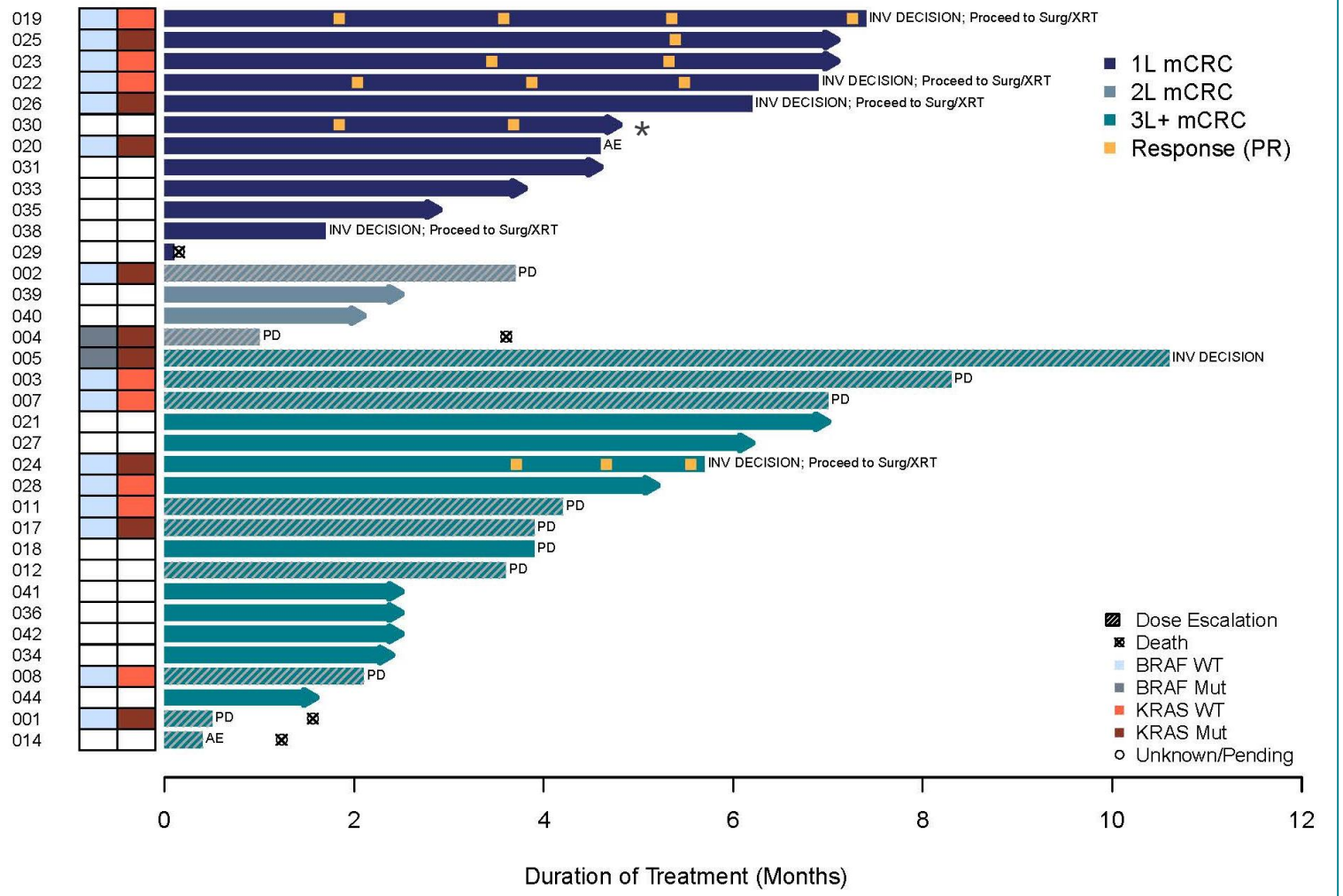


DCO: 5May2020

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Preliminary Evidence of Activity Seen with AB928 in Late-Line Metastatic CRC (ARC-3)

Time on Treatment



- Two patients had CRs of target lesions; both received AB928 + mFOLFOX-6 as 1L mCRC treatment, then discontinued the study at the investigator's discretion to undergo surgical resection of remaining non-target lesions:
  - Patient 019: 2 target lesions (60 mm) at baseline; PR at Days 56, 109, and 163; CR on Day 221
  - Patient 022: 4 target lesions (64 mm) at baseline; PR at Day 62; CR on Days 118 and 167
- After the DCO*, a third 1L patient (Patient 030) deepened their response to a CR at Day 162
- Given deep responses and the potential for definitive cure, 3 additional patients (including a 3L+ patient) proceeded to surgical resection (+/- chemo/radiotherapy) at the investigator's recommendation.
- 16 subjects were still on study, as of 5May2020

Cecchini et al.; AACR2020; Abstract # LB-387; Data Cut Off 05MAY20

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AB928 in Metastatic CRC: Conclusions from ARC-3 Trial & Next Steps

- AB928 with mFOLFOX-6 has been well tolerated without significant evidence of additive toxicity in subjects with mCRC
- Combination treatment was associated with disease control in all evaluable patients, including those with microsatellite stable and RAS/BRAF mutated mCRC
- Patients with 3L+ disease previously treated with FOLFOX and/or FOLFIRI have shown encouraging clinical benefit (PR and/or SD >4 mo) with AB928 combination
- Encouraging deep responses across 1L-3L+ patients, with several patients being taken to definitive cure with surgical resection/XRT of remnant lesions
- Preliminary biomarker data to be presented at scientific conference later this year
- Ongoing randomized Ph2 study in 3L mCRC in clinical collaboration with Genentech (Morpheus platform) in combination with atezolizumab and regorafenib
- Plans for additional evaluation of AB928 in mCRC to be announced later this year

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Important Clinical Milestones over the Course of Next Year

	Mid-2020	EOY 2020	1H 2021
AB154 (TIGIT mod.IgG1)	Ph2 in 1L NSCLC (ARC-7) enrolling	Prelim. randomized data in 1L NSCLC (ARC-7)	Planned start of pivotal trial(s); mature Ph2 data
AB928 ($A_{2a}R/A_{2b}R$)	Prelim. data from Ph1b expansion cohorts	Prelim. randomized data; multiple studies (NSCLC, CRC, PDAC)	Maturing randomized data in multiple studies (NSCLC, CRC, CRPC, PDAC)
AB680 (CD73)	Ph1 in 1L PDAC (ARC-8) enrolling	Prelim. Ph1/1b data in 1L PDAC (ARC-8)	Maturing data in multiple studies (PDAC, CRPC)
Zimberelimab (PD-1)	Ph2 in 1L NSCLC (ARC-7) enrolling	Prelim. randomized data in 1L NSCLC (ARC-7)	Planned start of pivotal trial(s); mature Ph2 data

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Gilead Collaboration Positions Arcus to Unlock the Value of Arcus's Pipeline

- 10-year "all-in" collaboration brings a well-aligned partner with the financial and operational resources, scientific expertise and long-term vision required to capitalize on the promise of the Arcus pipeline
- Preserves Arcus's independence and provides strategic flexibility, while accelerating its path towards becoming a fully-integrated commercial biopharmaceutical company
- Allows Arcus to maintain substantial commercial rights over its entire pipeline while also accelerating the associated opportunities
- Provides a mechanism for Arcus to fund its portion of co-development costs through ongoing R&D support and opt-in/milestone payments

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Summary of Gilead Collaboration Terms

($ in millions)

Upfront	• Arcus received **$375M** upon closing on 7/13/20, consisting of a **$175M** upfront payment and a **$200M** equity investment from Gilead
Commercial Rights	• Companies to **Co-commercialize** Gilead-Optioned Programs in the U.S. with **Equal Profit Share**
Clinical Opt-in/ Milestones	• Gilead gained rights to zimberelimab, and has the right to opt-in to all other current Arcus clinical candidates, including AB154, AB928, and AB680, upon payment of an opt-in fee that ranges from **$200M** to **$275M** per program, after delivery of a qualifying data package • If Gilead opts-in to the AB154 program, Arcus is eligible to receive up to **$500M** in potential future U.S. regulatory approval milestones for AB154
Additional Portfolio Opt-in	• Gilead has the right to opt-in to all other programs that emerge from Arcus's research portfolio over the next 10 years, upon payment of an opt-in fee of **$150M** per program after Arcus's delivery of a qualifying data package
Ex-U.S. Royalties	• Tiered royalties ranging from **high-teens to low twenties**
Ongoing R&D Support	• Gilead will further provide ongoing research and development support of up to **$400M** over the collaboration term
Additional Equity	• Gilead has the right to purchase additional shares from Arcus, up to a maximum of 35% of Arcus's then outstanding common stock over the course of the next five years, at a 20% premium at the time Gilead exercises such option, or, if greater, at the initial per share purchase price

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AB928 & AB680

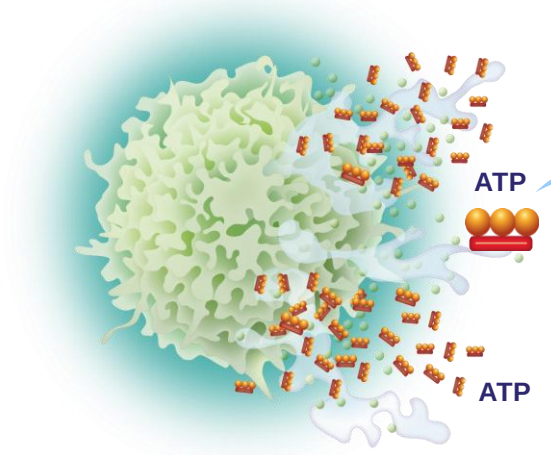
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Arcus is a Leader in the Development of Therapeutics that Target the Adenosine Axis

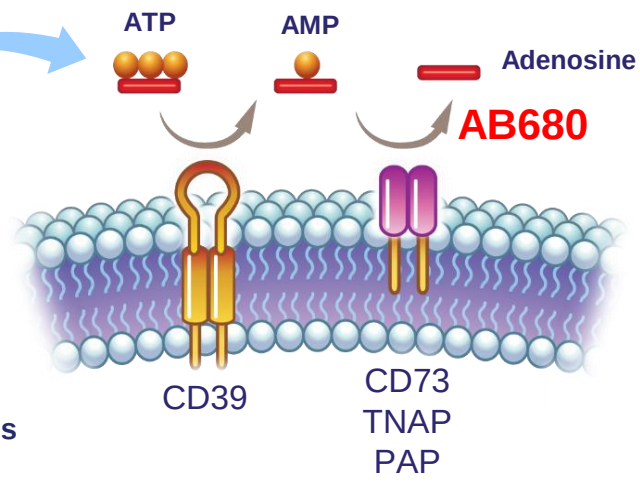
The Adenosine Axis

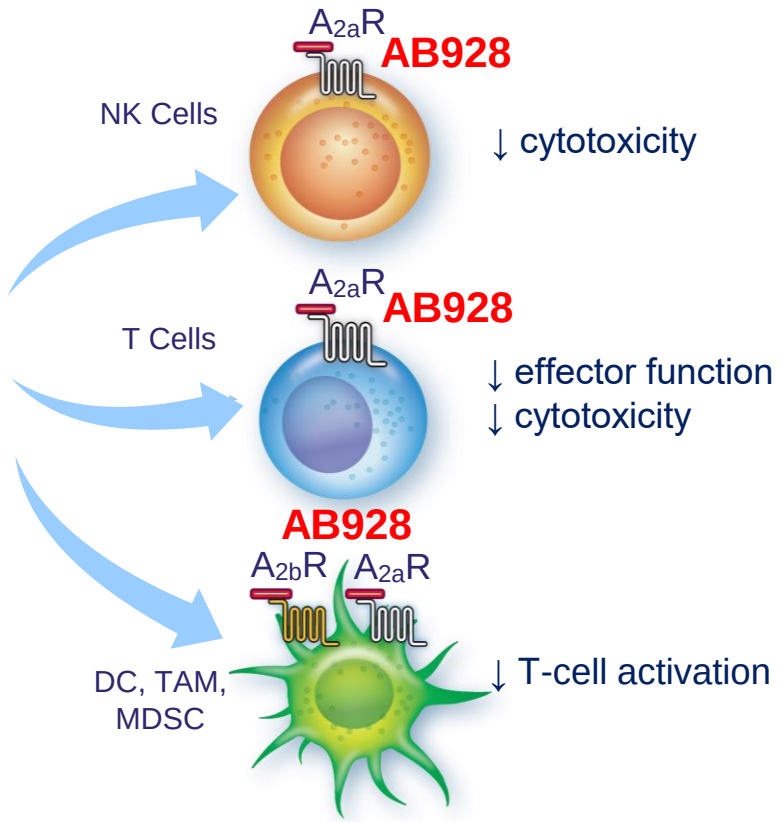
-- Well-established and Critical Role in Tumor-associated Immune Suppression --

Extracellular ATP released by dying cells, particularly when triggered by immunogenic chemotherapy



Adenosine is generated from ATP by the enzymatic action of CD39 and CD73





Adenosine is produced by enzymatic machinery found on cancer cells; this adenosine prevents (directly and indirectly) activation of effector T cells that would otherwise kill those cancer cells

This science is well studied, unequivocal and understood at a molecular level; we can block the action of adenosine on immune cells (AB928) as well as inhibit its formation (AB680)

TNAP: tissue non-specific acid phosphatase; PAP: prostatic acid phosphatase; DC: dendritic cell; TAM: tissue-associated macrophage; MDSC: myeloid-derived suppressor cell

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AB928 Represents a Potentially Best-in-Class Adenosine Receptor Antagonist

- **First A_2R antagonist to enter clinical development that:**
  - Was specifically designed for the oncology setting
  - Inhibits both $A_{2a}R$ and $A_{2b}R$ receptors
- **Multiple advantages over other A2aR antagonists in clinical development:**
  - Minimal shift in potency due to decreased non-specific protein binding
  - Excellent penetration of tumor tissue
  - Excellent drug properties (PK, etc.)
- **Differentiated, highly efficient clinical development plan ongoing:**
  - First clinical program to evaluate an A_2R antagonist with multiple different backbone therapies (e.g., anti-PD-(L)1, chemo, anti-TIGIT)

High potency against both the $A_{2a}R$ and $A_{2b}R$ receptors allows for potentially broader activity

Compound	$A_{2a}R$ Blood (IC_{50}, nM)[c]	$A_{2a}R$ (K_B, nM)[d]	$A_{2b}R$ (K_B, nM)[d]
AB928 (Arcus)	**80**	**1.4**	**2.4**
CPI-444 [a,b] (Corvus)	~10,000	5.4	493
AZD 4635 [a,b] (AstraZeneca)	2,600	1.7	64
NIR178 [a,b] (Novartis)	~10,000	58	189
Preladenant [a,b] (Merck)	785	3.3	3,121

AB928 has ideal pharmacological properties for an oncology drug

Attribute	AB928 Value
Retains potency in physiologically relevant conditions	**IC_{50} = 80 nM**
High tumor penetration	**Tumor : Plasma ratio: >60%**
Low CNS permeability (in mouse model)	**~ 1% of the concentration found in blood**
Full engagement of target across dosing time period in humans	**≥90% target inhibition at trough**

[a] Arcus data generated with compound samples synthesized or purchased by Arcus.

[b] CPI-444: Structure from AACR, April 2017 (#CT119), synthesized by Arcus; AZD4635: Structure from AACR, April 2017 (#2641), synthesized by Arcus; NIR178: Structure from WHO Drug Information, Vol. 32, No. 4, 2018; https://www.who.int/medicines/publications/druginformation/innlists/PL120.pdf?ua=1), synthesized by Arcus. Preladenant: Purchased from Ark Pharma (AK-43905).

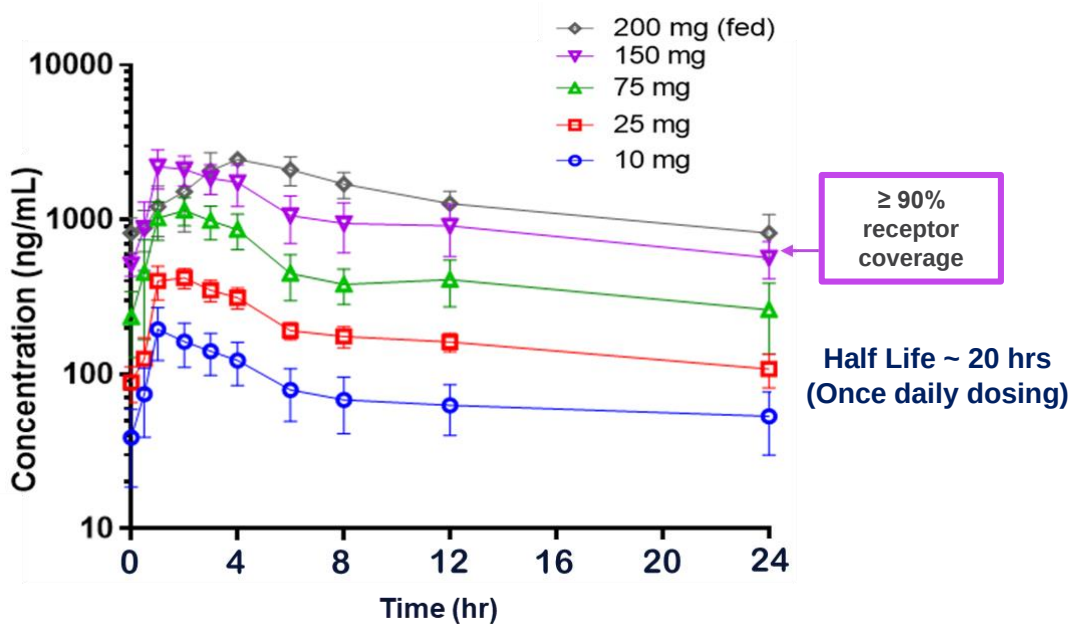
[c] Measured in human blood CD8+ T cells; CREB is a transcription factor that becomes phosphorylated when A2aR is activated; thus, the level of pCREB inhibition is a measure of the ability of an A2aR antagonist to inhibit A2aR.

[d] K_B is a measure of a compound's thermodynamic ability to bind/block its target receptor; lower K_B values reflect greater potency for a given receptor.

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AB928:
Excellent Safety, PK/PD Profile, & “24/7” Target Coverage

Excellent Human PK Profile[1]



Optimal Receptor Coverage Achieved at 150 mg QD

Dose Level	% Receptor Coverage (Inhibition of 5 µM NECA)	
	2-hr Post-Dose	24-hr Post-Dose
200 mg	≥ 90 %	≥ 90 %
150 mg [2]	**100 %**	**≥ 90 %**
75 mg	100 %	76 %
25 mg	82 %	51 %
10 mg	51 %	(12 %)

[1] PK/PD data from Phase 1 Healthy Volunteer study (Seitz et al. Invest. New Drugs. 2018); highly consistent PK/PD demonstrated in oncology patients

[2] 150 mg once daily dosing confirmed receptor coverage in oncology patients and was chosen as the dose for combinations

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Four Dose-escalation Trials Established Safety/Tolerability of AB928 with Different Combination Backbones and Provide the Foundation for Ongoing Efficacy Studies

	AB928 COMBINATION	DOSE-ESCALATION POPULATIONS
ARC-2	AB928 + PLD[1] +/- IPI-549[2]	Advanced/Late-line TNBC and Ovarian
ARC-3	AB928 + FOLFOX	Advanced/Late-line CRC
ARC-4	AB928 + anti-PD1 + Carboplatin/Pemetrexed	Advanced/Late-line NSCLC
ARC-5	AB928 + Zim (anti-PD1)	Advanced/Late-line Solid Tumors

[1] PLD = pegylated liposomal doxorubicin
[2] PI3Kγ inhibitor; clinical collaboration with Infinity Pharmaceuticals
CRC = colorectal cancer, NSCLC = non-small cell lung cancer, TNBC = triple-negative breast cancer

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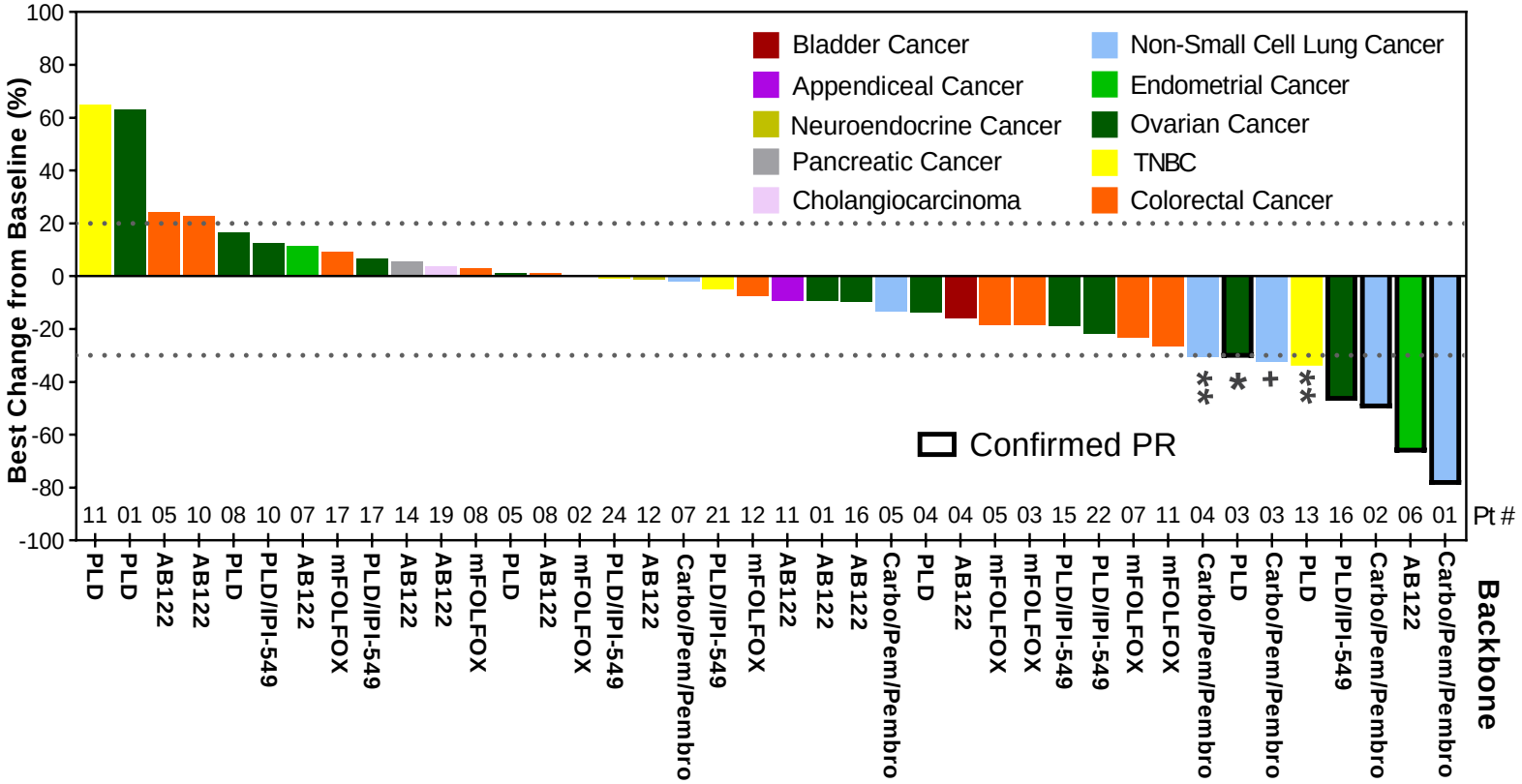
AB928 was Well Tolerated Across Four Dose-escalation Studies in Combination with Other Therapies

- **AB928 exhibited a favorable safety profile across all combination regimens**
- **The only dose-limiting toxicity (DLT) observed was due to a Grade 2 rash in ARC-5 (AB928 + Zimberelimab)**
  - Patient restarted therapy post rash resolution
- **A maximum tolerated dose (MTD) of AB928 has not been reached in any of the combinations**
- **Only one possible Grade 4 AB928-related AE (thrombocytopenia) was reported in ARC-4 dose-escalation (AB928 + pembrolizumab + chemotherapy)**
  - Patient had a reported history of chemo-related thrombocytopenia
- **No Grade 5 AB928-related AEs were reported across the AB928 dose-escalation cohorts**
- **The PK and PD profiles of AB928 in cancer patients were similar to those previously characterized in healthy volunteers**
  - Once-daily dosing demonstrated a $t_{1/2}$ = 20 hrs
  - 150 mg QD provides ≥ 90% receptor coverage at trough

Data cut-off (DCO) of 27 Dec 2019

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Phase 1 Combination Studies of Safety/Tolerability and PK/PD also Provided Early Efficacy Data Consistent with Clinical Hypotheses



***** confirmed PR post DCO
****** new lesion
+ previously reported as confirmed; open query to verify revised data entry

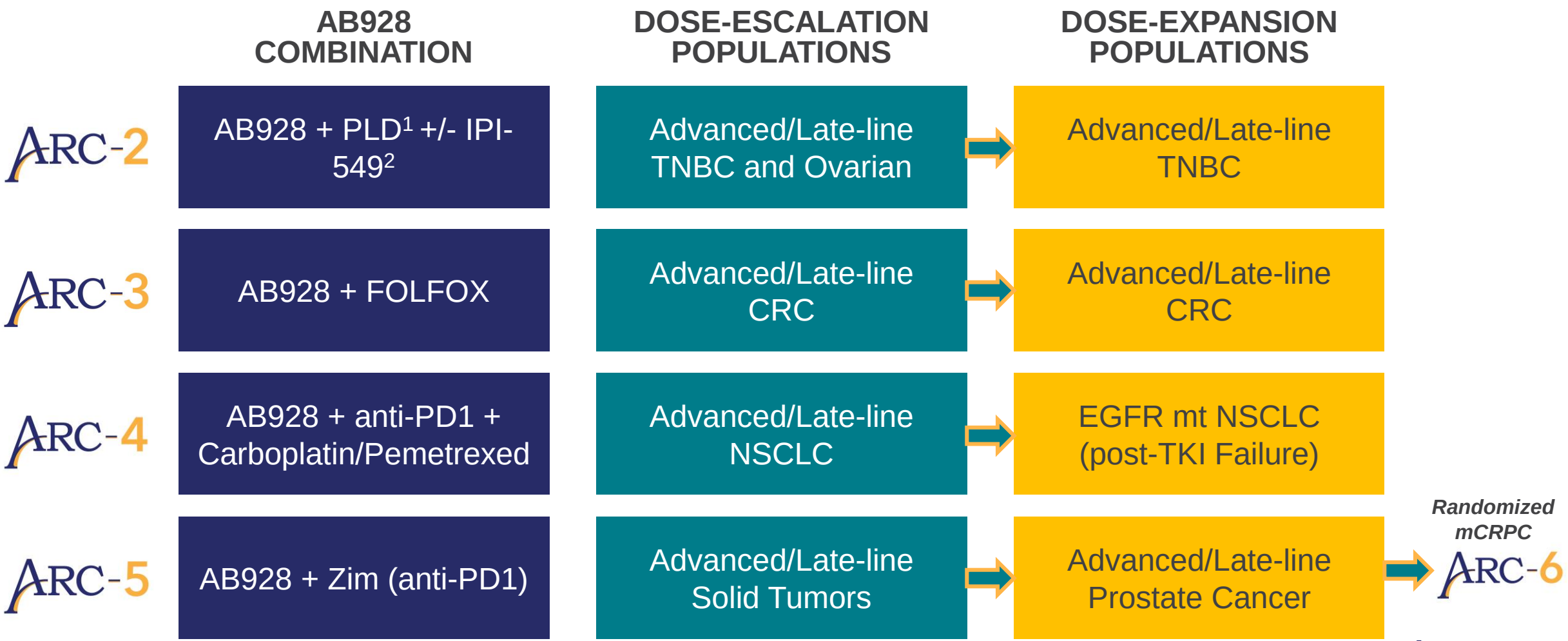
TKI = tyrosine kinase inhibitor; PLD = Pegylated liposomal doxorubicin;
CR = complete response; PR = partial response; SD = stable disease
Data cut-off (DCO) of 31 Jan 2020

Summary

- **AB928, in combination with chemotherapy and/or anti-PD-1 therapy, demonstrates tumor responses and prolonged disease stabilization in advanced tumor types (median 3-4 prior lines of therapy), supportive of continued disease-specific evaluations**
  - **Non-small Cell Lung Cancer:** partial responses observed in post-TKI and post-checkpoint failure patients
  - **Gynecological Malignancies:** partial responses observed in ovarian and endometrial carcinosarcoma patients
  - **Colorectal Cancer:** tumor shrinkage and prolonged disease stabilization >6 months were observed in heavily pre-treated patients, including patients with KRAS mutations
- **As of the data cut-off date, the Disease Control Rate (defined as CR + PR + SD ≥ 6 months) was 43% (17 out of 40 evaluable patients)**
- **Extensive biomarker characterization of tissue and blood across the AB928 studies is ongoing**

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Four Dose-escalation Trials Established Safety/Tolerability of AB928 with Different Combination Backbones and Provide the Foundation for Ongoing Efficacy Expansion Studies

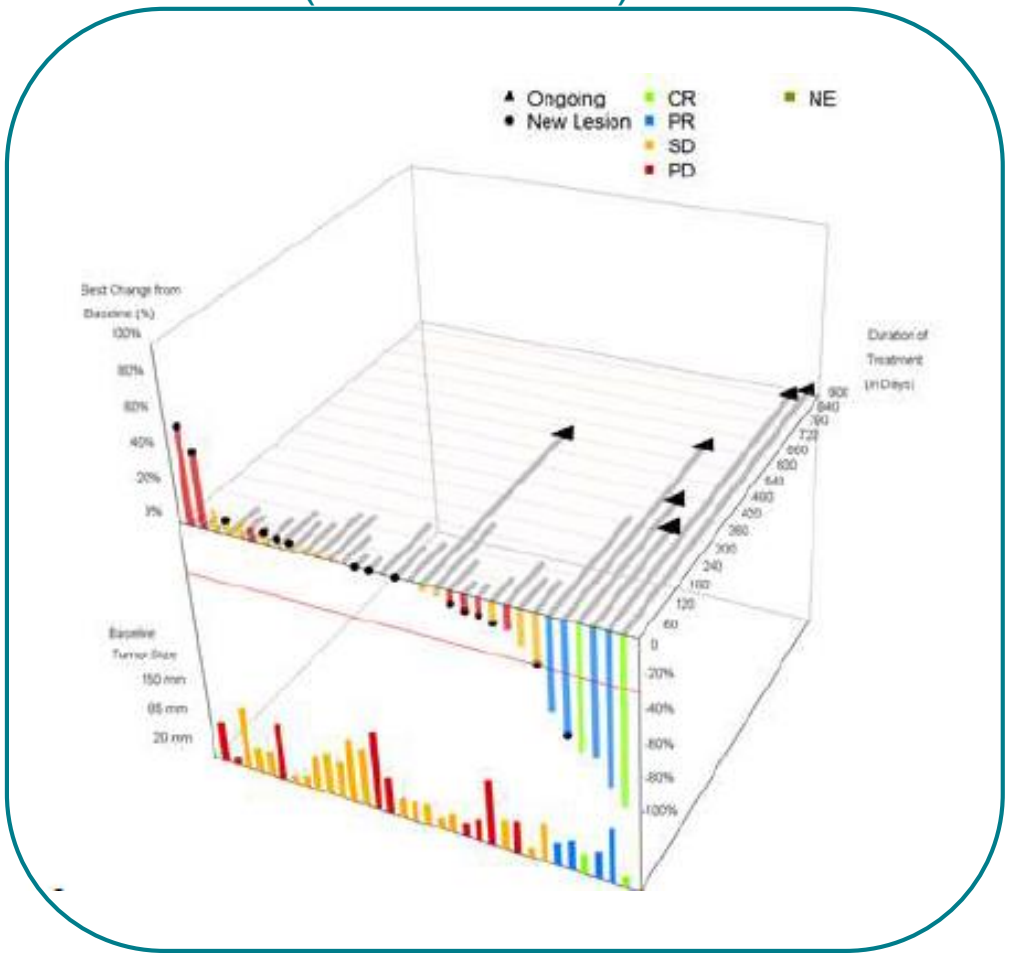


[1] PLD = pegylated liposomal doxorubicin
[2] PI3Kγ inhibitor; clinical collaboration with Infinity Pharmaceuticals
CRC = colorectal cancer, NSCLC = non-small cell lung cancer, TNBC = triple-negative breast cancer

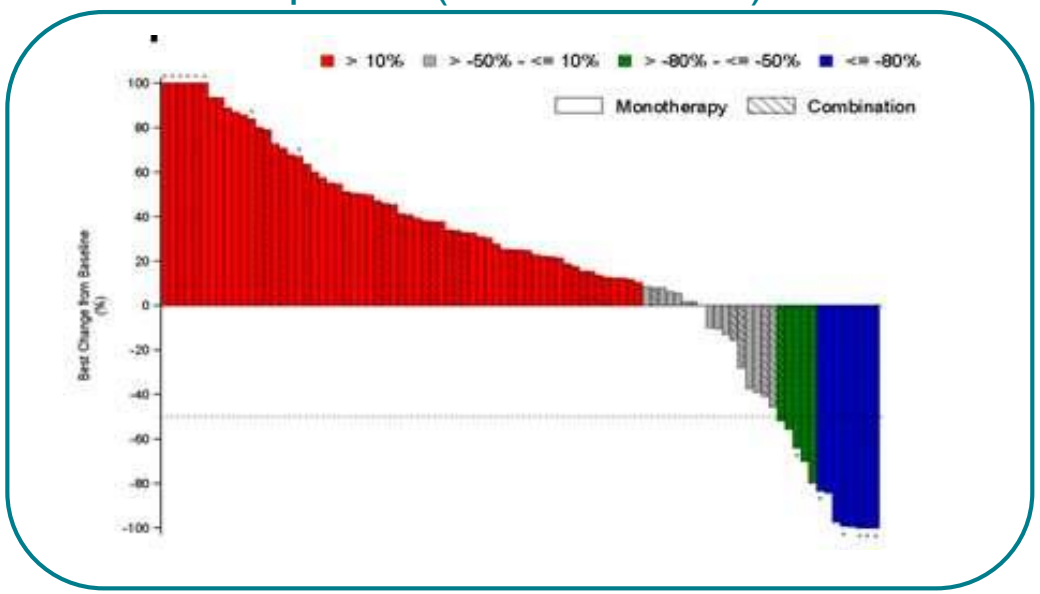
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Competitor Compound (AZD4635; $A_{2a}R$ Antagonist) Continues to Demonstrate Activity in Late Line mCRPC, in the Context of a Broadly Expanded Prostate Cancer Program

ORR (‘4635 + Durva) = 16.2%



PSA Response (‘4635 + Durva) = 22.2%



BOR[1] n(%)	Mono(N=36)	Combo (N=37)
CR/PR	2 (5.6%)	6 (16.2%)
SD	13 (36.1%)	18 (48.6%)
PD	13 (36.1%)	11 (29.7%)
NE	8 (22.2%)	2 (5.4%)
PSA response[2]	3/51 (5.9%)	10/45 (22.2%)

Median Prior Lines of Therapy for Combo Patients: 5 (1-10)

Lim et al.; ASCO2020; Abstract #1085

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We are Running Multiple Expansion and Randomized Studies with AB928 in 2020

- **Several studies with randomized cohorts to evaluate combination vs. control**
  - Opportunity for biomarker-based selection of pts at randomization stage
- **Early randomized data expected in 4Q20**
- **Settings/combinations selection criteria:**
  - Observed clinical activity
  - CD73 and/or adenosine levels
  - High unmet medical need

Indication	Line	Combination
NSCLC	EGFRm[1] 2L+	AB928 + Zim + Pem/Carbo
	WT 1L	Zim ± AB154 ± AB928
CRPC	2L+	AB928 + Zimberelimab
	2L+	AB928 + Zim + AB680
	2L	AB928 + Zim + Docetaxel
	1L	AB928 + Zim + Enzalutamide
CRC	3L	Regorafenib ± Atezo ± AB928
	1-3L	AB928 + FOLFOX
	2L	AB928 + Zim + FOLFOX/Bev
PDAC	1L	Gem/Nab-pac ± Atezo ± AB928
TNBC	2L+	AB928 + PLD ± IPI-549

Initiated | Planned | Phase 2

Abbreviations
CRPC: metastatic castration-resistant prostate cancer; CRC: colorectal cancer; NSCLC: non-small cell lung cancer; TNBC: triple-negative breast cancer; PDAC: pancreatic ductal adenocarcinoma; RCC: renal cell cancer

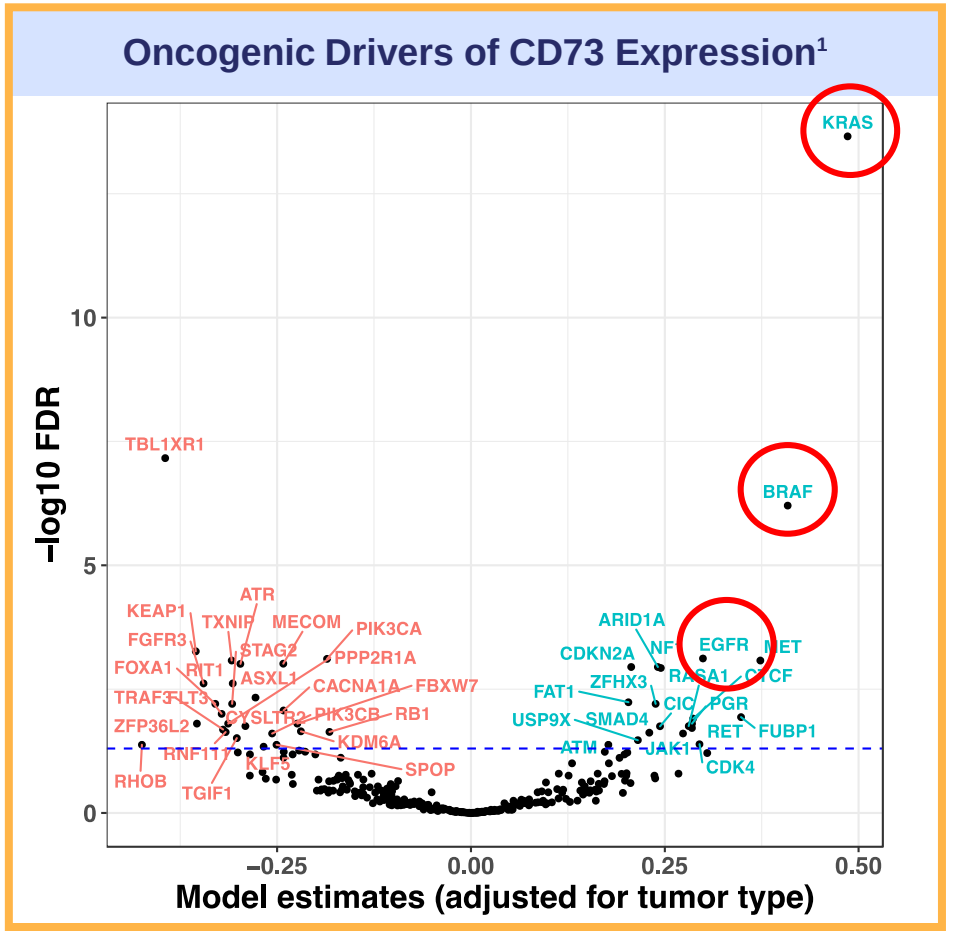
Zim: zimberelimab; Doce: docetaxel; Enza: enzalutamide; Atezo: atezolizumab; Rego: regorafenib; Carbo/Pem: carboplatin/pemetrexed; Bev: bevacizumab; Gem/Nab-pac: gemcitabine/nab-paclitaxel; PLD: pegylated liposomal doxorubicin

[1] Patients who have progressed on one or more tyrosine kinase inhibitors

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Exciting New Insights into Adenosine Biology in Oncogene-driven Tumors Suggest Important Role for $A_{2b}R$ Blockade in Combination Strategies

- **Multiple oncogene mutations (e.g., KRAS, BRAF, EGFR) strongly associated with high expression of CD73 and $A_{2b}R$**
- **$A_{2b}R$ stands out among the 4 adenosine receptors because of its ability to activate MAP kinase pathway**
  - May explain the unique importance of $A_{2b}R$ in mediating effects of adenosine on dendritic cells
  - Cancer cells carrying certain mutations (e.g., KRAS) can both make more adenosine and activate adenosine signaling pathways synergistic with the oncogenic mutation
- **AB928 is the only adenosine receptor antagonist in the clinic that potently blocks $A_{2b}R$**

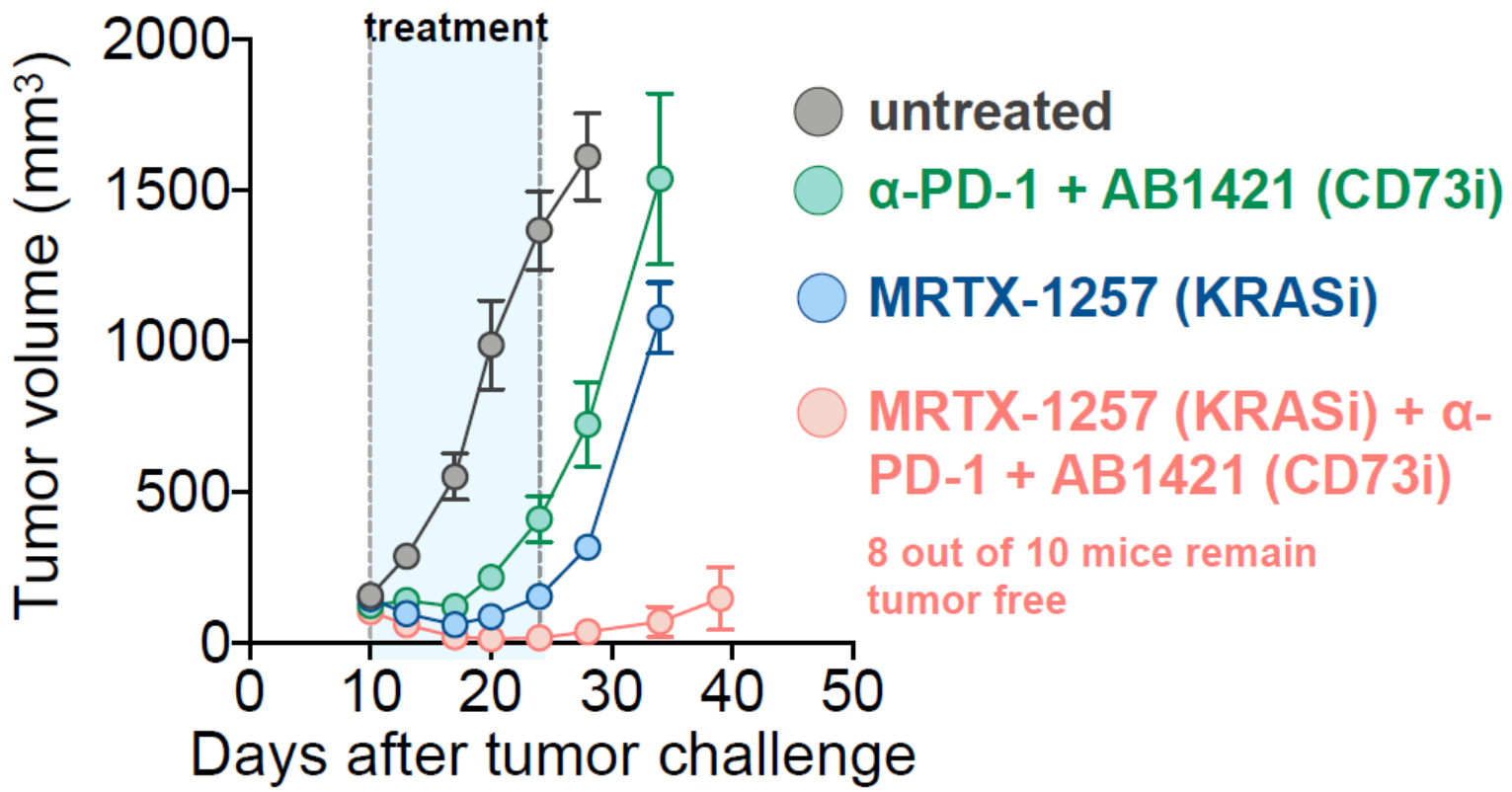


[1] Analysis of Tumor Cancer Genomic Atlas (TCGA) performed by Arcus

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Co-targeting KRAS and CD73 Enhances Efficacy in a PDAC Mouse Model

$KRAS^{G12C}/TP53^{R172H/+}$ PDAC Mouse Model[b]



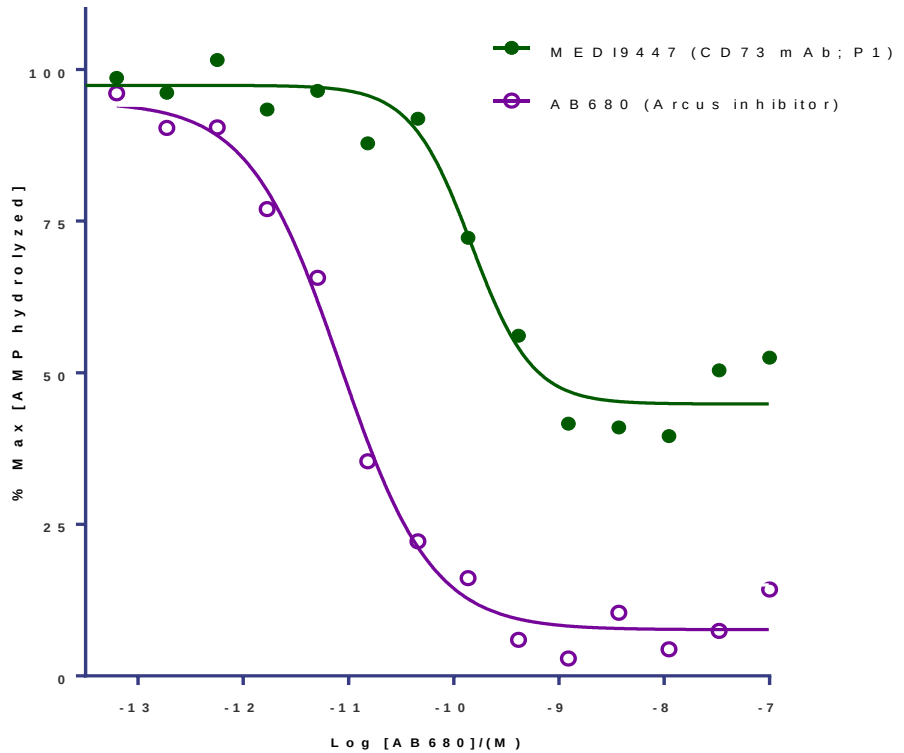
[a] Le et al., Abst. A46; Tumor Immunol. & Immunotherapy. Symposium, Boston, Nov 17-20, 2019. AB1421 is a close analogue of Arcus's clinical CD73 inhibitor (AB680)

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AB680: First Small-molecule CD73 Inhibitor to Enter Clinical Development

- **AB680 offers potential advantages over anti-CD73 antibodies in development:**
  - Greater inhibition of CD73 enzymatic activity (soluble & cell-bound)
  - Deeper tumor penetration
  - IV and oral formulations
- **Unique small-molecule properties**
  - Extraordinarily potent: IC_{50} = 0.008 nM (T cells)
  - Low clearance, long half-life molecule
- **Oral formulation completed IND-enabling studies**

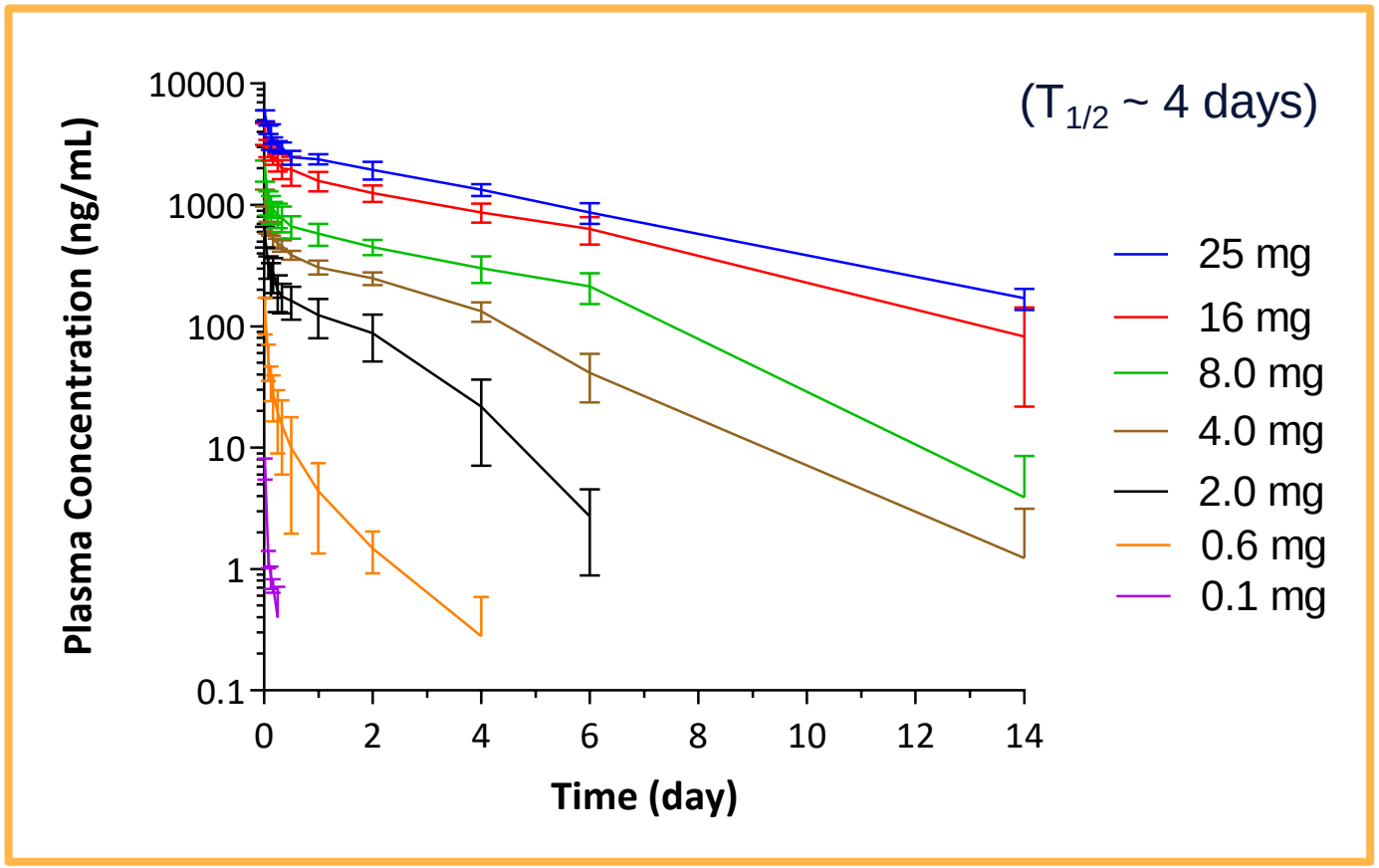
AB680 Potently Inhibits CD73 Enzymatic Activity on $CD8^+$ T Cells



[a] MEDI9447 synthesized by Arcus based on the following publication and patent application: Hay et al., OncoImmunology (2016) 5, e1208875; Patent Appl. US 2016/0129108.

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AB680 Displays Excellent PK Profile in Healthy Human Volunteers Consistent with q2w Dosing

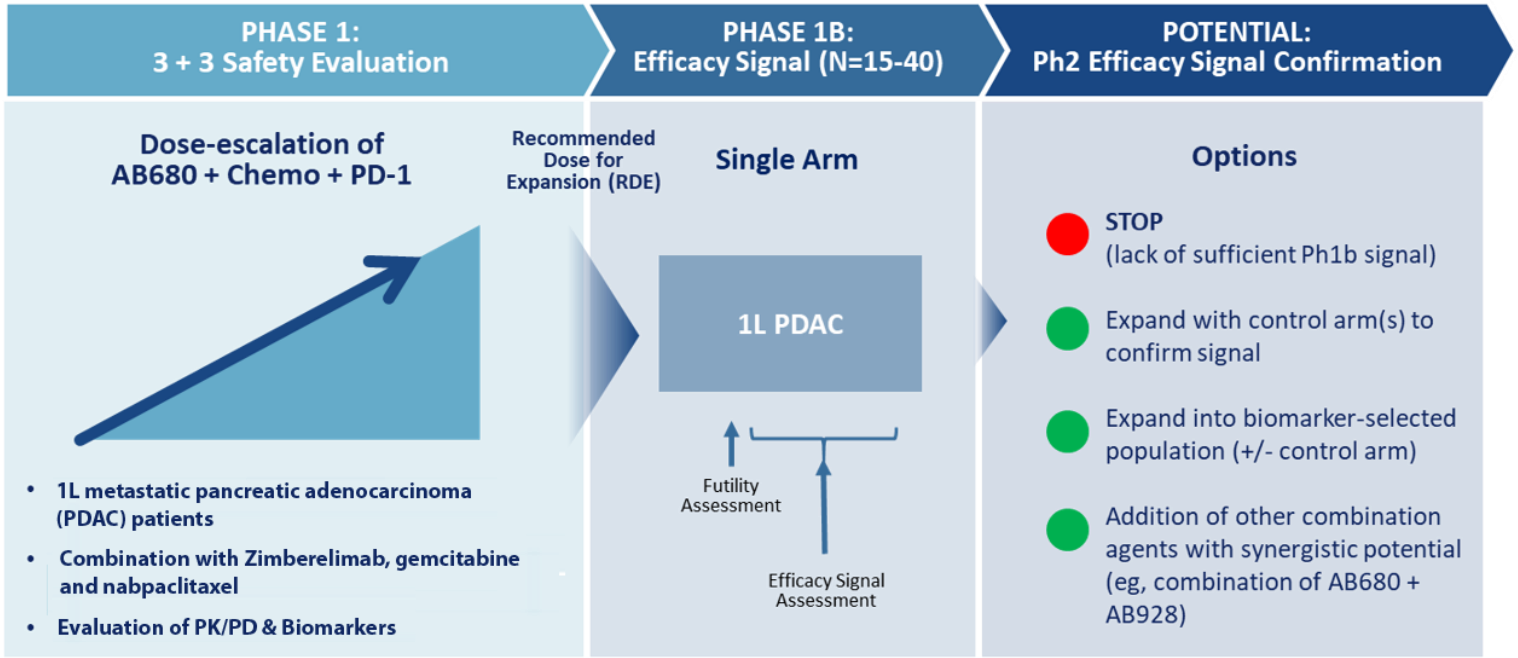


AB680 was administered (30-60 min) by i.v. infusion on day 0

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AB680 (CD73 inhibitor) Development Status

- **Evaluation in 1L pancreatic cancer in combination with zimberelimab (anti-PD-1) + gemcitabine/nab-paclitaxel**
  - Phase 1 dose-escalation ongoing (passed safety evaluation of second 50-mg cohort)
  - Phase 1b expansion anticipated to start in 2H2020
- **Plans underway to evaluate AB680 in multiple combinations and indications once RDE achieved (e.g., mCRPC)**



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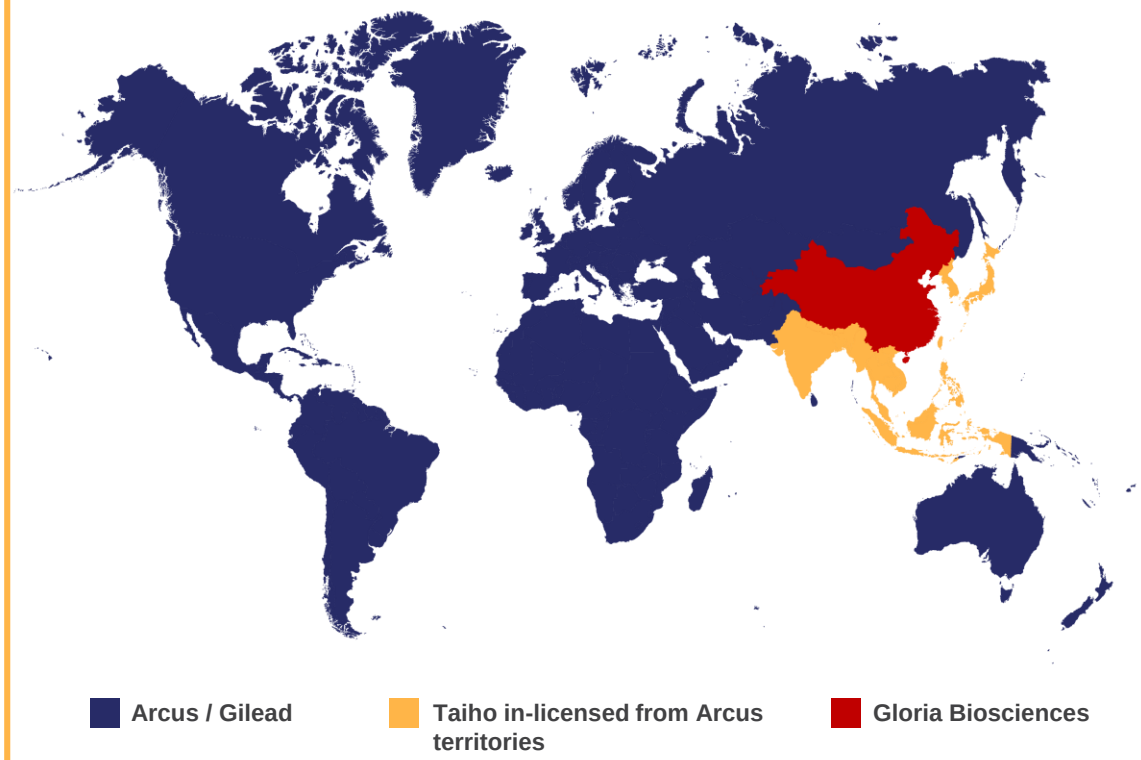
ZIMBERELIMAB & AB154 DEVELOPMENT STRATEGY

ARCUS BIOSCIENCES

Zimberelimab (anti-PD-1) Provides Flexibility & Optionality in Clinical Development

- **Zimberelimab was in-licensed by Arcus to fully enable portfolio combinations**
- **Gloria Biosciences filed an NDA for zimberelimab (GLS-010) in China in Jan. 2020 for classical Hodgkin's lymphoma; ORR similar to other checkpoint inhibitors[1]**
  - >90% ORR in late-line classic Hodgkin's lymphoma (cHL)
  - >20% ORR in late-line GI cancers (e.g., esophageal, cholangiocarcinoma and gastric)
  - Over 400 patients treated in China alone
  - Gloria Biosciences also has an ongoing Ph2 study in cervical cancer
- **Arcus currently has 7 active studies that contain zimberelimab combinations across multiple indications, targeting >700 patients**
- **Arcus developing strategic plans for gaining approvals of zimberelimab in select indications**

Global Commercialization Rights to Zimberelimab

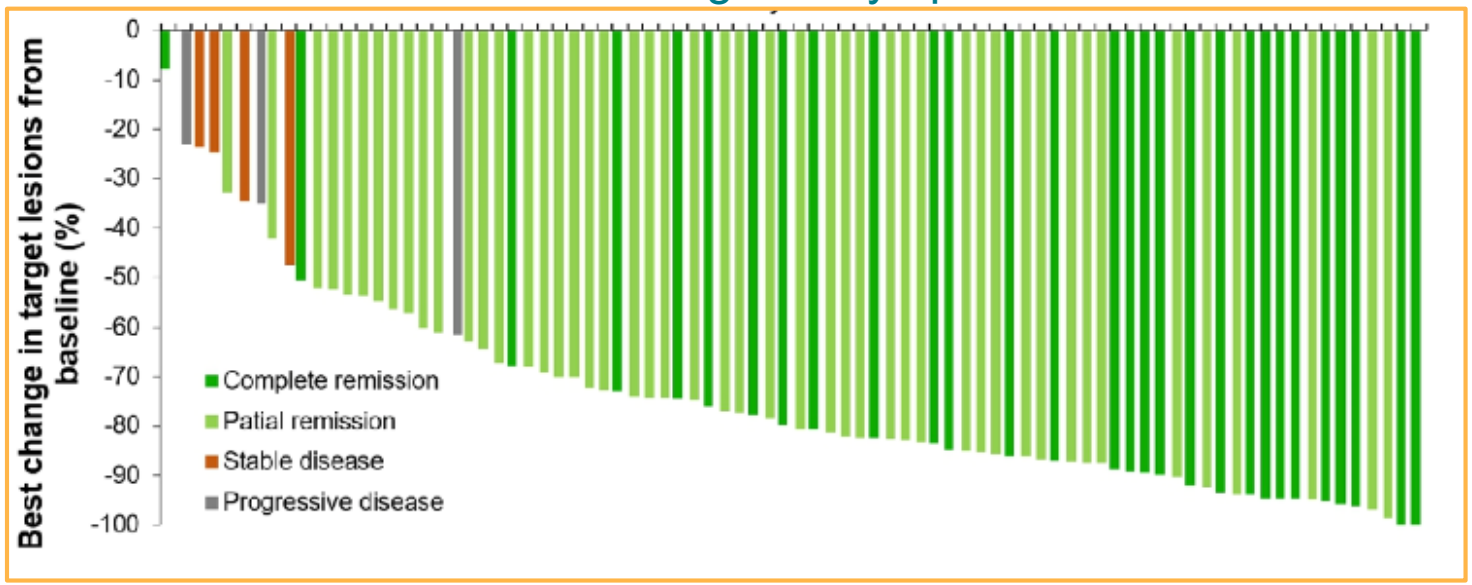


[1] Presentations by Gloria Biosciences at CSCO 2019. Gloria's studies conducted independently of Arcus.

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Zimberelimab* Demonstrates Robust anti-Tumor Activity in R/R Classical Hodgkin's Lymphoma & Cervical Cancer (Data from Gloria Biosciences)

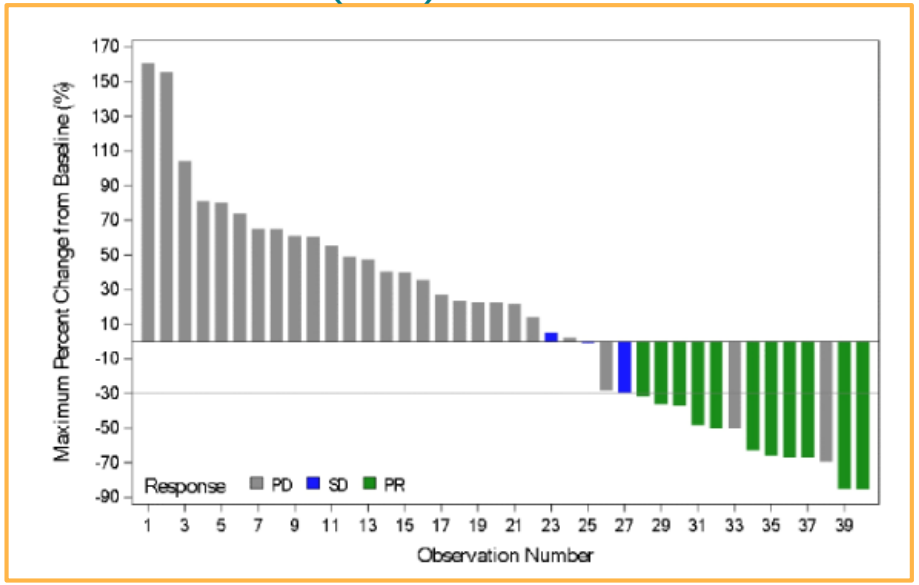
R/R Classical Hodgkin's Lymphoma



Best overall response, n (%)	
Complete response	30 (35.3)
Partial response	48 (56.5)
Stable disease	4 (4.7)
Progressive disease	3 (3.5)
Objective response rate	
% (95% CI)	**91.76** (83.77- 96.63)
Disease control rate	
% (95% CI)	**96.47** (90.03, 99.27)

Y. Song et al., ASCO (2020) Abstract #8033

Advanced (2L+) Cervical Cancer



Best overall response, n (%)	
Complete response	0
Partial response	11 (26.83, 1 unconfirmed)
Stable disease	11 (26.83)
Progressive disease	19 (46.34)
ORR, n (%)	11 (26.83)
95% CI	14.22-42.94
DCR, n (%)	22 (53.66)
95% CI	37.425-69.344

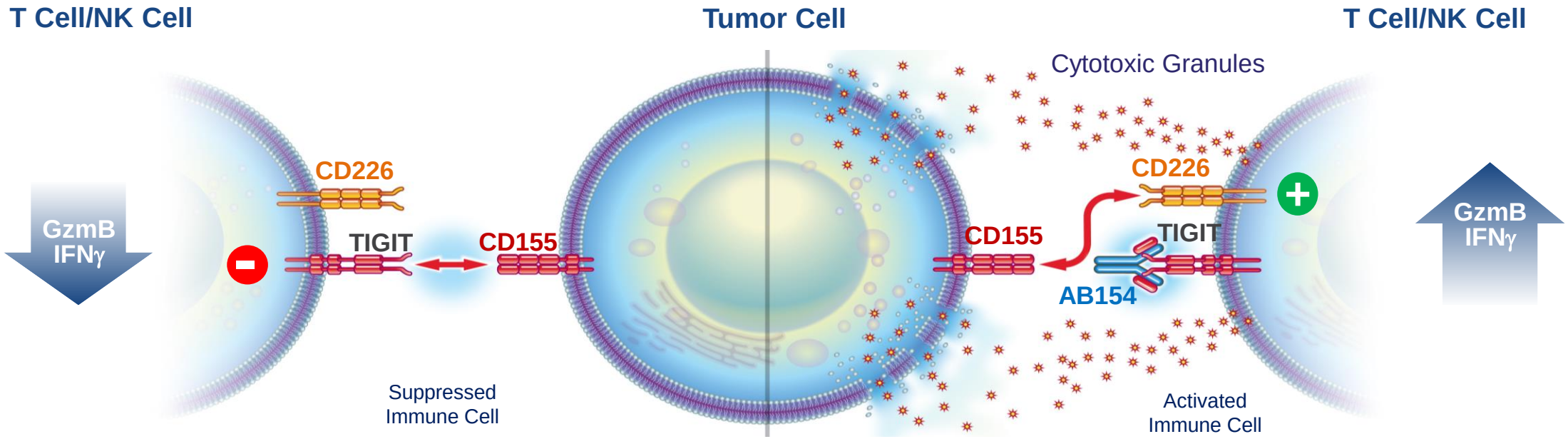
X. Wu et al., ASCO (2020) Abstract #6032

* Also known as GLS-010 in China (Gloria Biosciences)

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AB154 (anti-TIGIT): Next I-O Backbone

Dual Mechanism: blocking TIGIT inhibits a critical immuno-suppressive pathway while promoting the CD226-CD155 immune-activating pathway



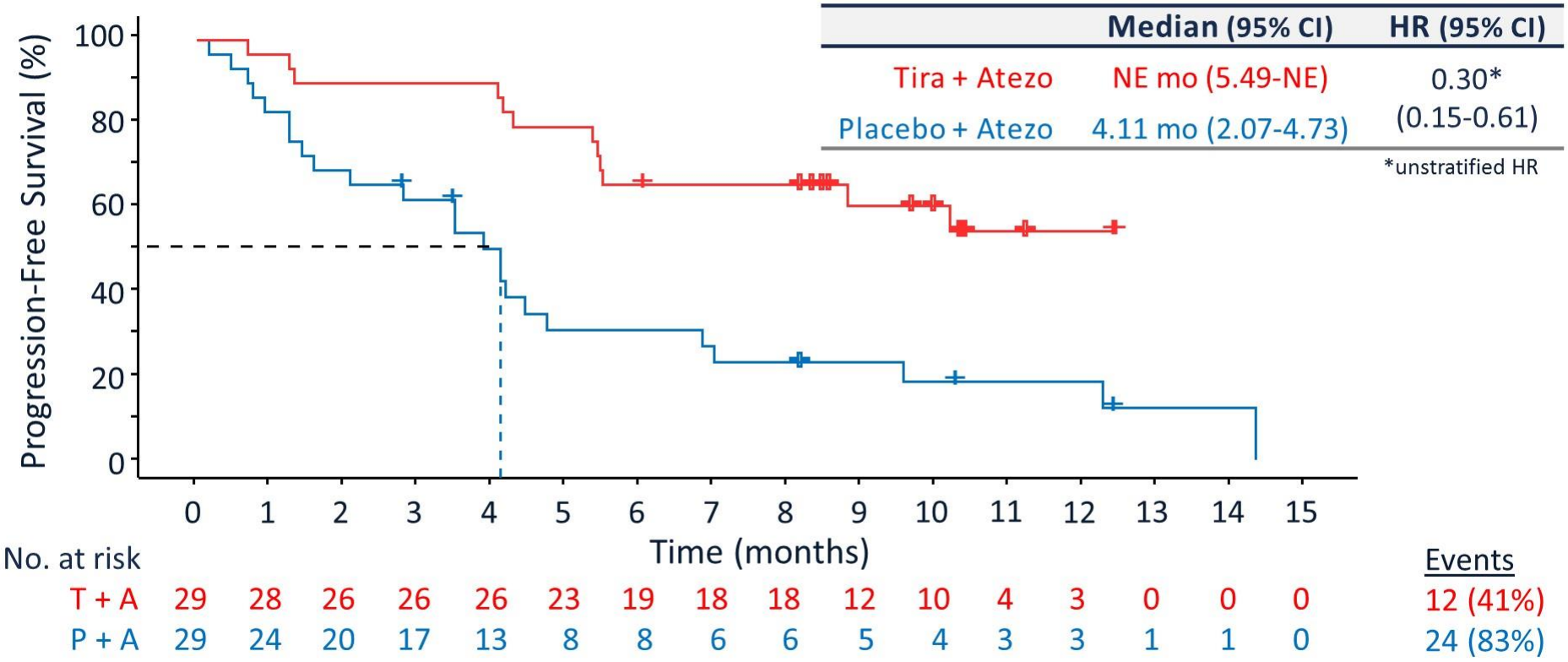
Competitors Rapidly Advancing Anti-TIGIT mAbs

- Genentech presented positive phase 2 results in 1L NSCLC at ASCO 2020; greatest benefit in PD-L1+ population
- Roche currently running two new Phase 3 studies (SCLC, NSCLC) and four Phase 2 studies (Cervical, PDAC, GC/EC and UC)
- Merck reported early clinical activity from a Phase 1 study in solid tumors
- Since Dec. of 2019, Merck has initiated: 4 Phase 2 studies (1 in NSCLC and 3 in melanoma), and co-formulation studies with Pembrolizumab
- Additional competitors have also initiated several new studies, including: BMS, BMS/Compugen, BeiGene, Seattle Genetics, iTeos,

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Clear Evidence of Activity (1L NSCLC) from CITYSCAPE Trial (Tirago + Atezo)

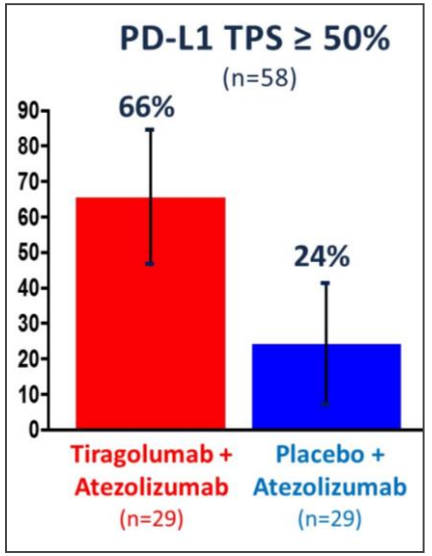
Updated Investigator-Assessed PFS: PD-L1 TPS ≥ 50%



NE = non-evaluable; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab; TPS = tumor proportion score

Follow data cutoff: 02 December 2019

Confirmed ORR

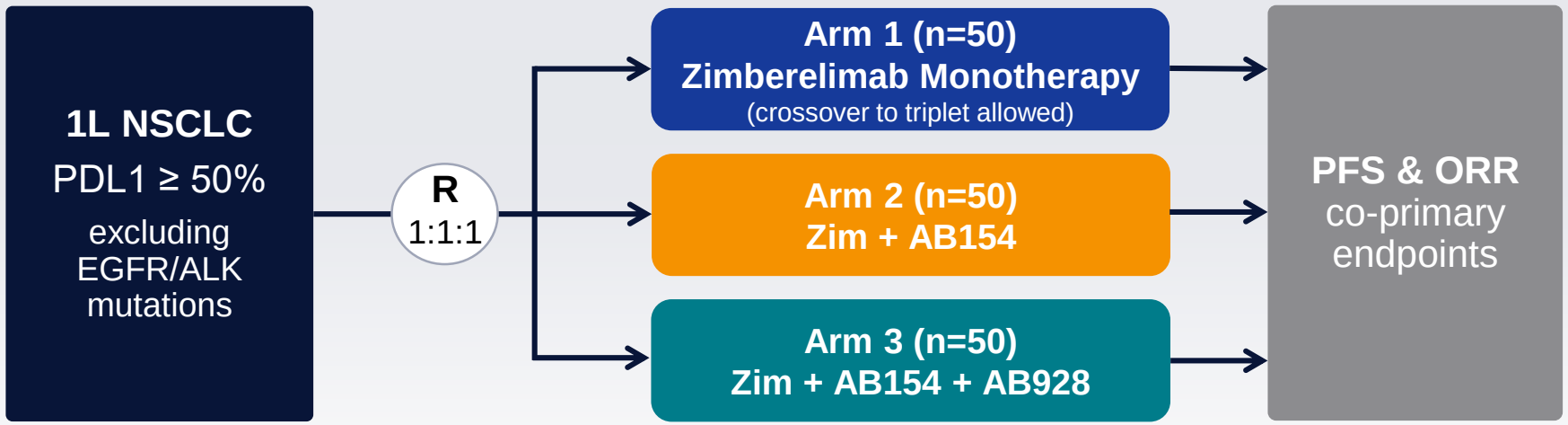


Rodriguez-Abreu et al.; ASCO (2020)

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Phase 2 Open to Evaluate Two Combinations: AB154+Zim and AB154+AB928+Zim vs Zim Mono in 1L NSCLC

Randomized Phase 2 Study of Combinations with Zimberelimab, AB154, and AB928 in 1L NSCLC



- **Study now open in US and Asian-Pacific sites**
- **Early randomized data expected in 4Q20**

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Oncology Discovery Programs

HIF-2α Inhibitor

Transcription factor

HIF-2α is a master transcriptional regulator of multiple genes involved in tumor progression

Cancer cell intrinsic target;
potential non-oncology indications

PI3Kγ Inhibitor

Glycolipid kinase

PI3Kγ is required for the immunosuppressive activity of tumor-infiltrating macrophages and myeloid-derived suppressor cells

Immune (TAM, MDSC) target

AXL Inhibitor

Tyrosine kinase

AXL overexpression is associated with tumor resistance to chemotherapy and IO drugs

Cancer cell intrinsic target

PAK4 Inhibitor

Serine kinase

PAK4 overexpression is responsible for T-cell exclusion from immune desert tumors

Cancer cell intrinsic target

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