

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

NYSE: RCUS

JANUARY 2020

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Our Vision

World Class Discovery Engine

Leverage underexploited biologic pathways to create molecules with outstanding clinical profiles and best-in-class potential

Combining to Cure

Deploy rationally designed studies of combinations in the pursuit of cures

Fully Integrated Biopharmaceutical Company

Become a leader in creating best-in-class cancer therapies that transform patients' lives

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Our Vision: Combining to Cure With Best-in-Class Cancer Therapies

Four Molecules in Expansion and Randomized Studies	• **AB928**: $A_{2a}R$ / $A_{2b}R$ antagonist – first and only dual antagonist in the clinic • **AB680**: CD73 inhibitor – first in the clinic (pancreatic) with exceptional potency • **AB154**: anti-TIGIT mAb – rapidly advancing in randomized combinations • **Zimberelimab (formerly AB122)**: anti-PD-1 mAb enabling portfolio combination strategies with clear line-of-sight to commercialization
Rapidly Advancing, Broad Clinical Portfolio	• High unmet need indications where we can deliver first- and/or best-in-class therapies • Flexible protocols designed for early generation of randomized data
Drug Discovery Engine	• Comprehensive, accomplished R&D team built from inception • Sustainable creation of 1-2 IND candidates per year
Proven Track Record	• Management team with extensive expertise in immuno-oncology / oncology • Demonstrated track record of success from discovery through commercialization
Well Capitalized	• $197 million in cash & investments (3Q19)

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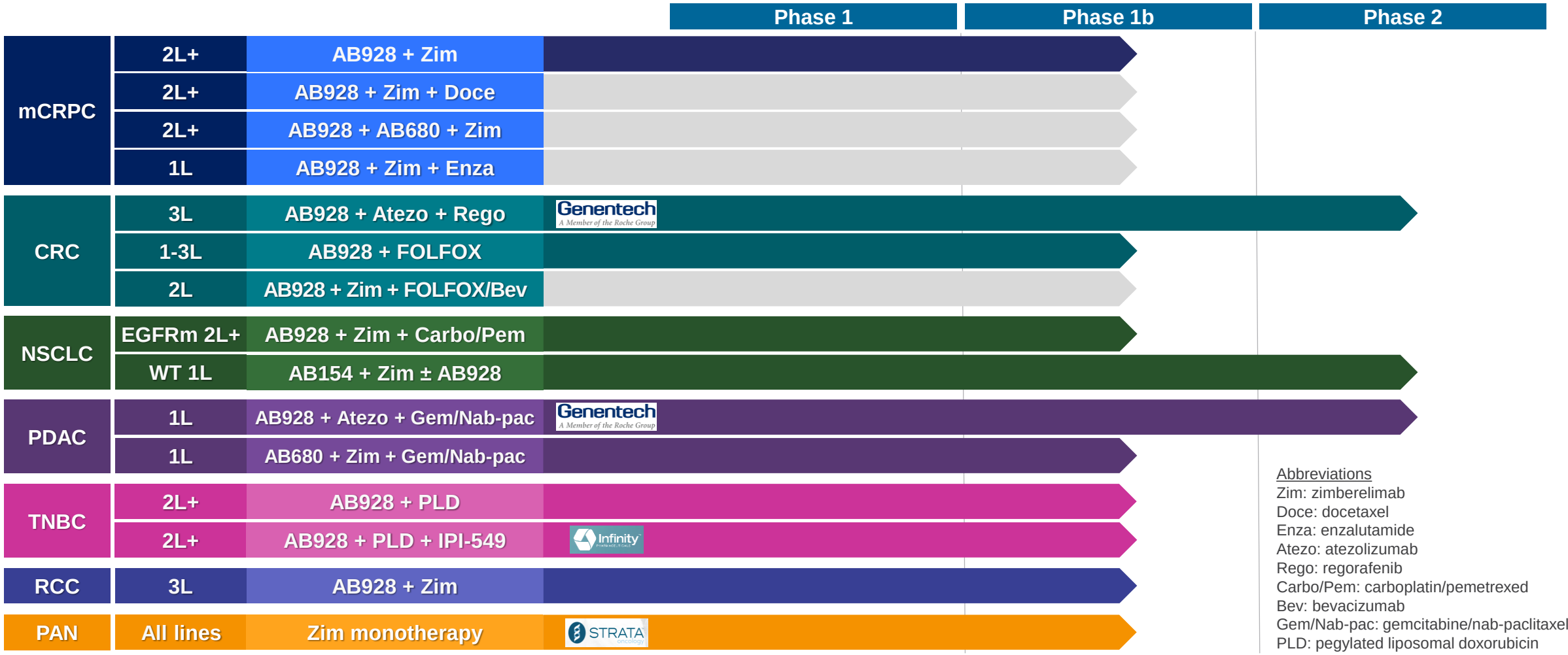
We Are Competing Aggressively in Multiple Settings with Significant Therapeutic and Commercial Potential



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

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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2020 Outlook Includes Four Clinical Programs with Multiple Readouts

- **AB928 ($A_{2a}R/A_{2b}R$ antagonist)**
  - Early Phase 1b expansion data (multiple tumor types) expected starting in mid-2020
  - Mature Phase 1b and early Phase 2 randomized data in multiple tumor types expected by 4Q20
- **AB154 (anti-TIGIT antibody)**
  - Phase 2 study in 1L NSCLC now open; early randomized data expected by 4Q20
- **AB680 (CD73 inhibitor)**
  - Early Phase 1b expansion data (pancreatic) starting in mid-2020
- **Zimberelimab (anti-PD-1 antibody)**
  - Execute plans for monotherapy development and approvals
- **Discovery Programs**
  - Several additional development programs (PI3Kγ; HIF-2α; Axl; PAK4) advancing towards the clinic
  - Clinical studies with at least two of these candidates are planned to begin within 12 months
- **Strategic business development in support of clinical programs; two types of relationships**
  - Partner jointly to advance clinical program as Arcus retains all commercial rights (e.g., AB928 collaboration with Genentech)
  - Well-defined partnership providing development resources and capital, with Arcus retaining substantial commercial rights

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AB928 & AB680

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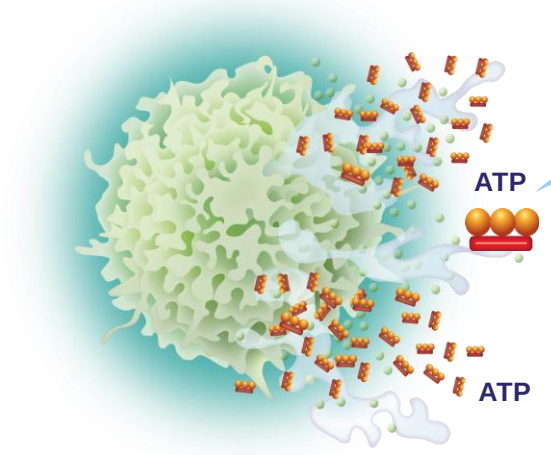
Arcus is a Leader in the Development of Therapeutics that Target the Adenosine Axis

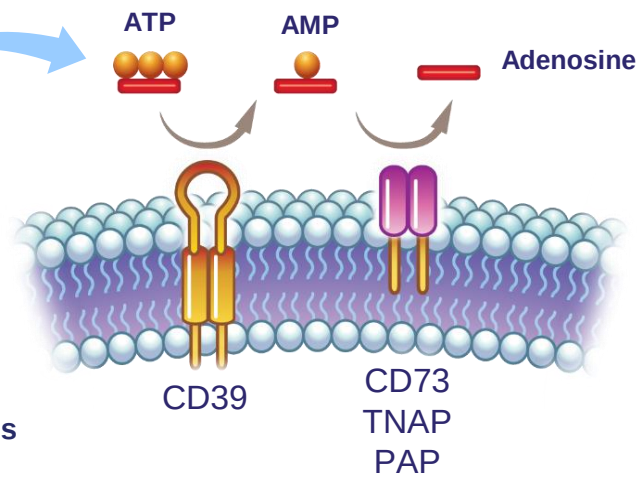
The Adenosine Axis

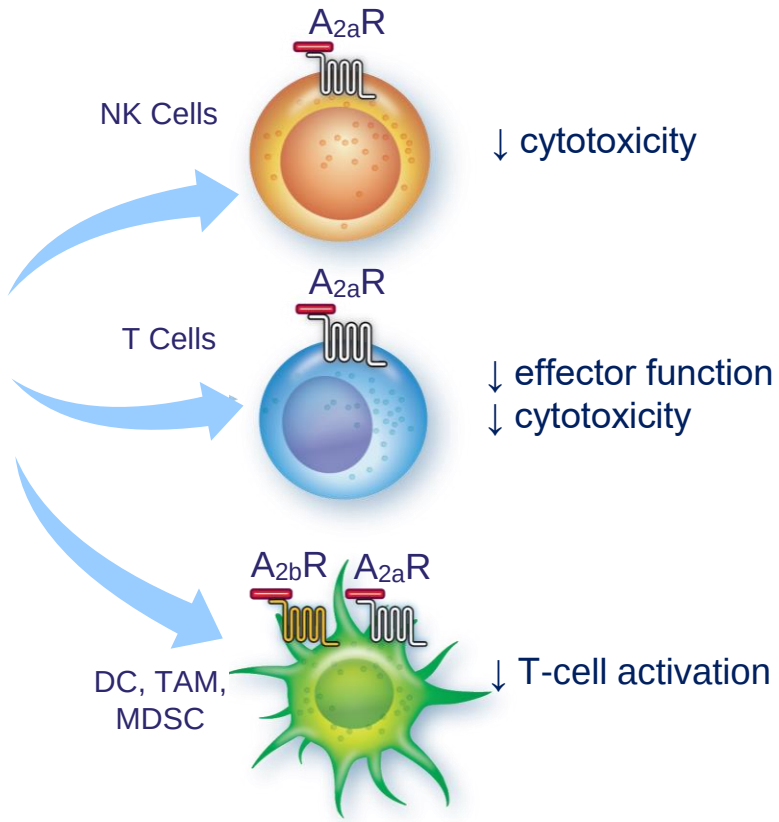
-- Well-established and Critical Role in Tumor-associated Immune Suppression --

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 chemo

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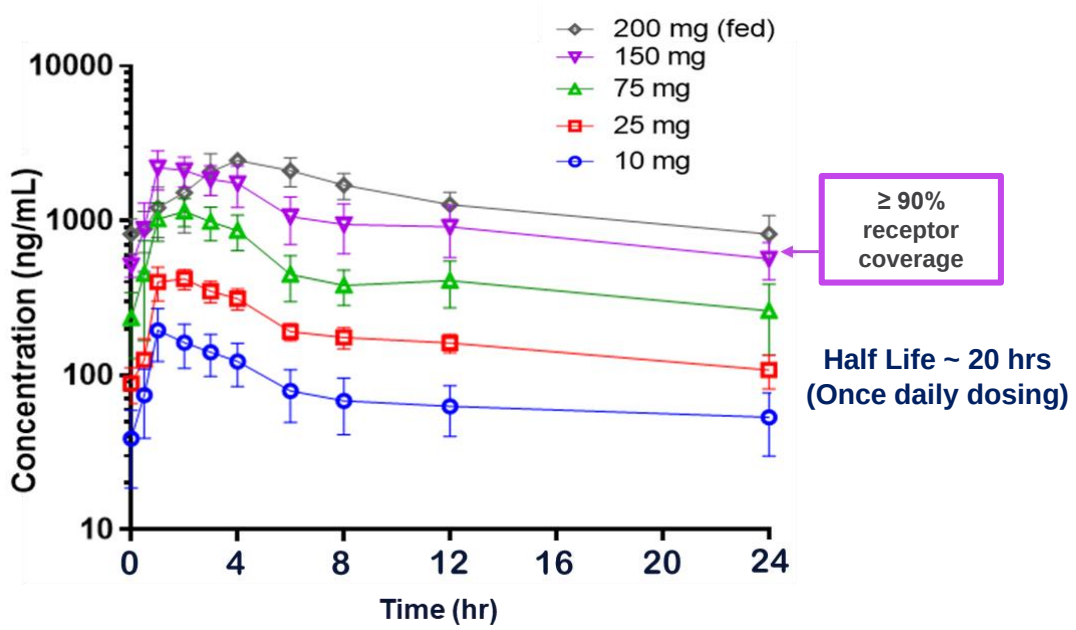
AB928:
Excellent Safety, PK/PD Profile, & “24/7” Target Coverage

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 the Safety of AB928 with Different Combination Backbones and Provide the Foundation for Ongoing Early 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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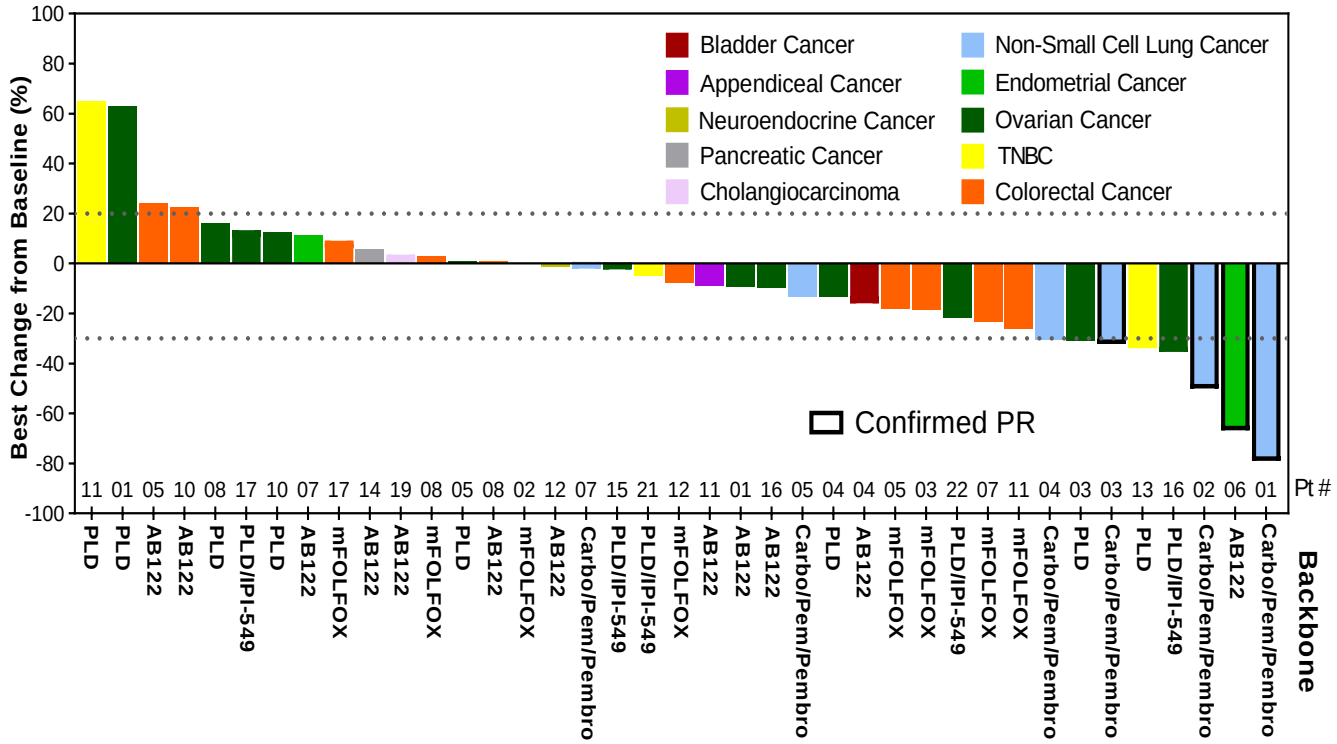
Phase 1 Combination Studies Designed To Evaluate Safety (Tolerability), PK and PD but Also Provided Early Efficacy Data Consistent with our Clinical Hypotheses

Waterfall Plot Across Evaluable Phase 1 Patients (Best Percent Change from Baseline)



Data cut-off (DCO) of 27 Dec 2019

TKI = tyrosine kinase inhibitor; PLD = Pegylated liposomal doxorubicin; CR = complete response; PR = partial response; SD = stable disease

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 44% (17 out of 39 evaluable patients)**
- **Extensive biomarker characterization of tissue and blood across the AB928 studies is ongoing**

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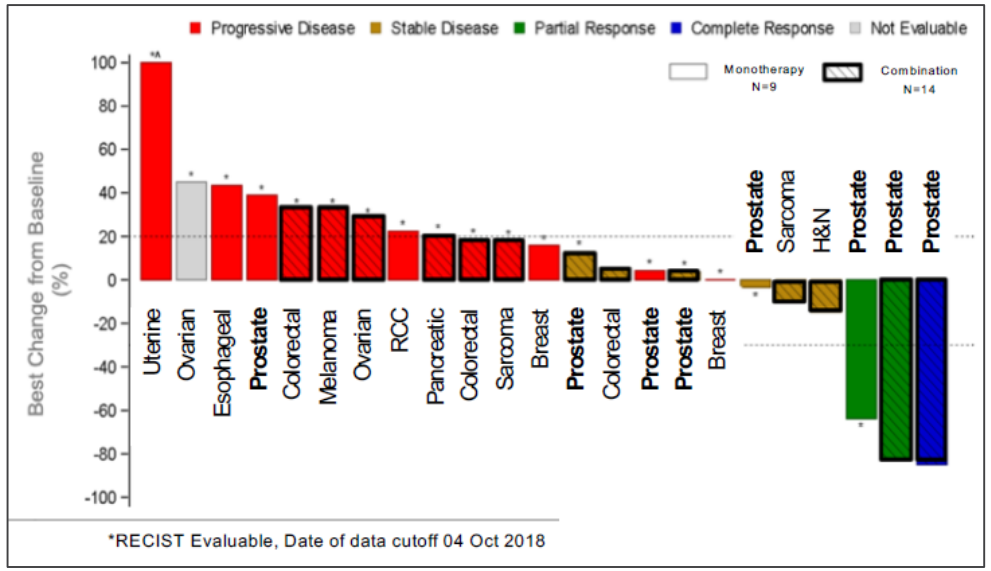
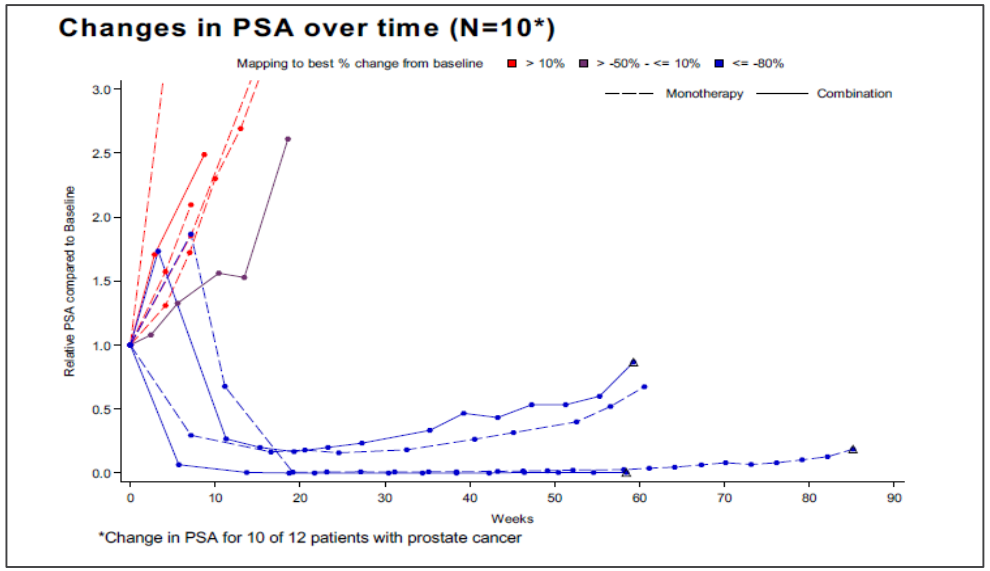
AZ Disclosed Activity of AZD4635 ($A_{2a}R$ Antagonist) in mCRPC, Leading to Broad Expansion of Studies in Prostate Cancer



Single Agent (N=4):
1 PR; 1 SD; 2 PD

Durva Combo (N=4):
1 CR; 1 PR; 2 SD



Bendell et al., (AACR 2019) Abstract CT026

Ongoing studies with >300 patients across 7 different cohorts in mCRPC alone

- 2L+ mCRPC: AZD4635 + enzalutamide
- 2L+ mCRPC: AZD4635 + abiraterone
- 2L+ mCRPC: AZD4635 (new formulation) + docetaxel
- 3L+ mCRPC: AZD4635 single agent
- 3L+ mCRPC: AZD4635 (new formulation) + durvalumab (PD-L1)
- 3L+ mCRPC: AZD4635 (new formulation) + oleclumab (CD73)
- 3L+ mCRPC: AZD4635 (new formulation) + oleclumab (CD73) + durvalumab (PD-L1)

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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
- **Phase 1b data expected in mid-2020**
- **Early randomized data expected by 4Q20**
- **Settings/combinations selection criteria:**
  - Observed clinical activity
  - CD73 and/or adenosine levels
  - High unmet need

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

Initiated | Planned

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
[2] Patients who have progressed on a checkpoint inhibitor

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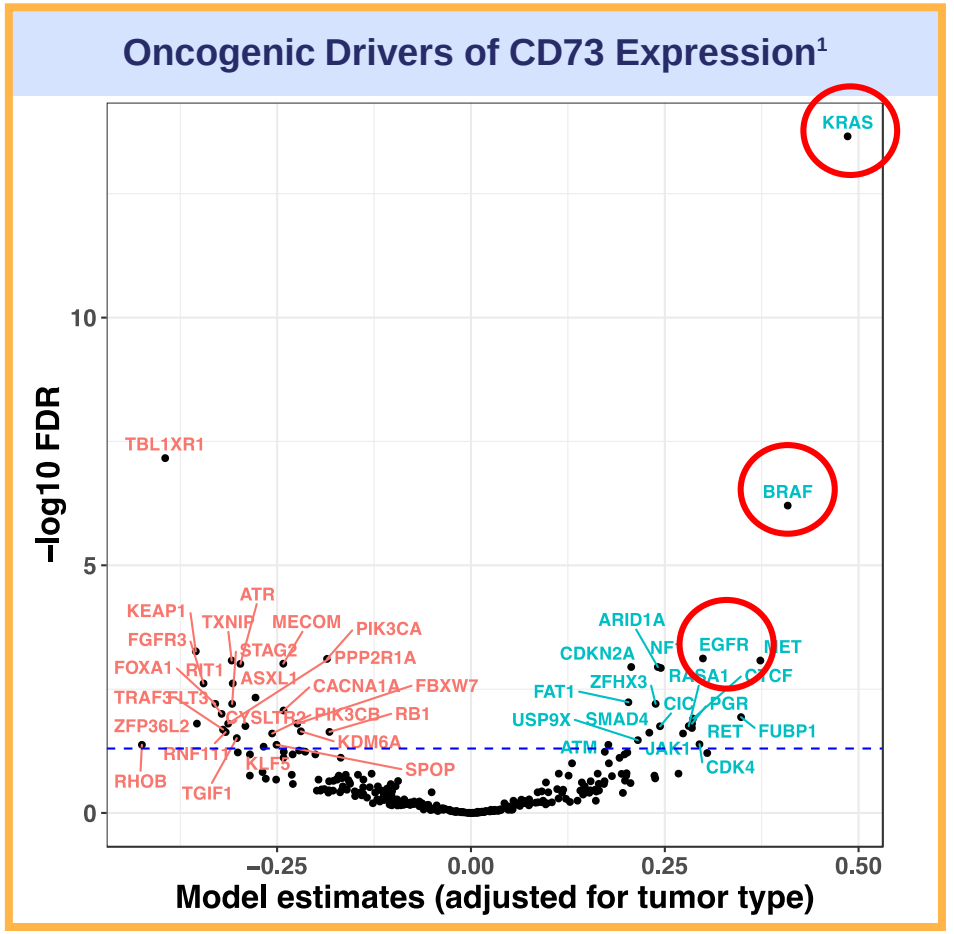
Exciting New Insights into Adenosine Biology in Oncogene-driven Tumors Suggest Important Role for $A_{2b}R$ Blockade in Combination Strategies

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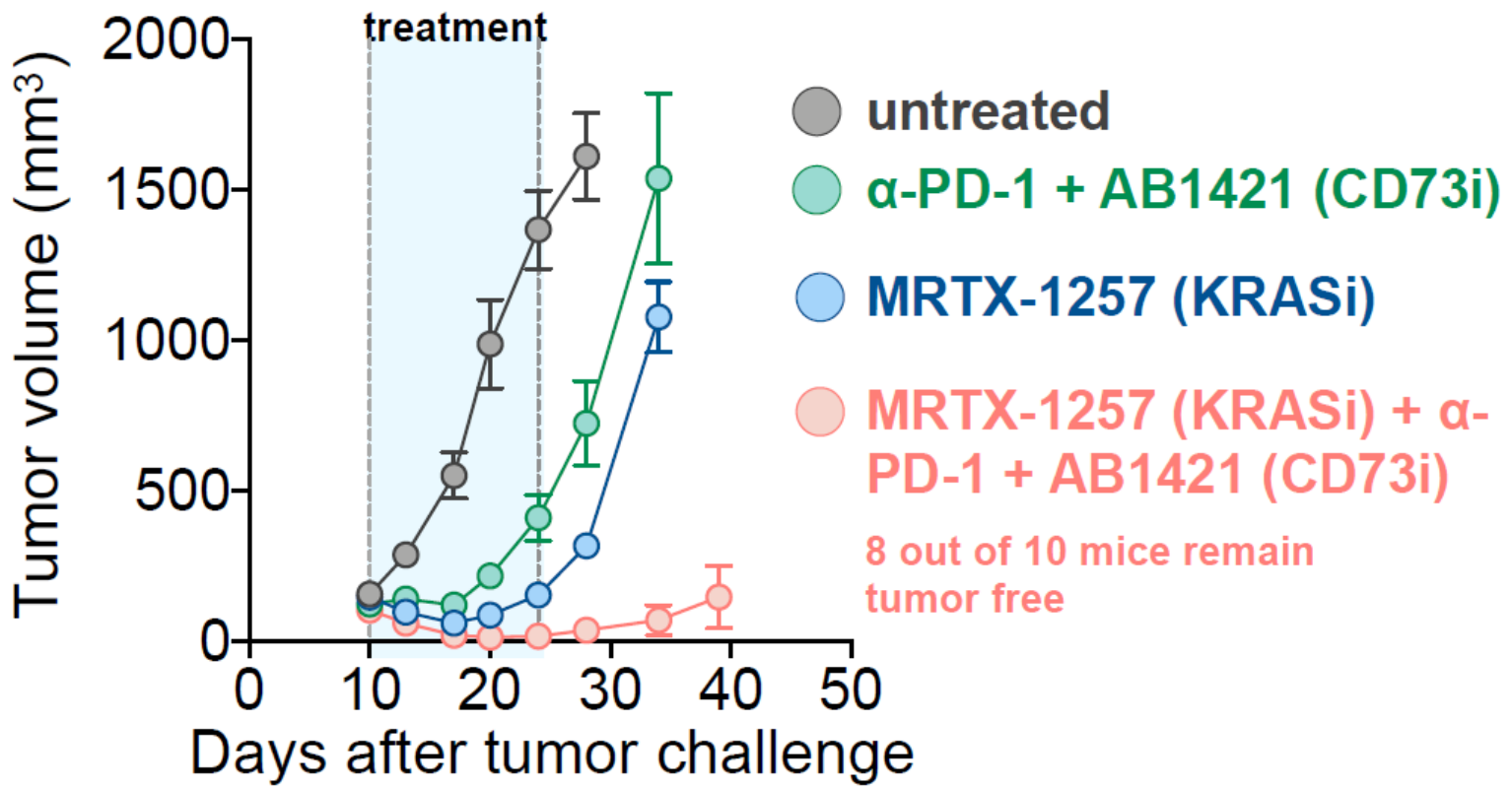
Co-targeting KRAS and CD73 Enhances Efficacy in a PDAC Mouse Model

$KRAS^{G12C}/TP53^{R172H/+}$ 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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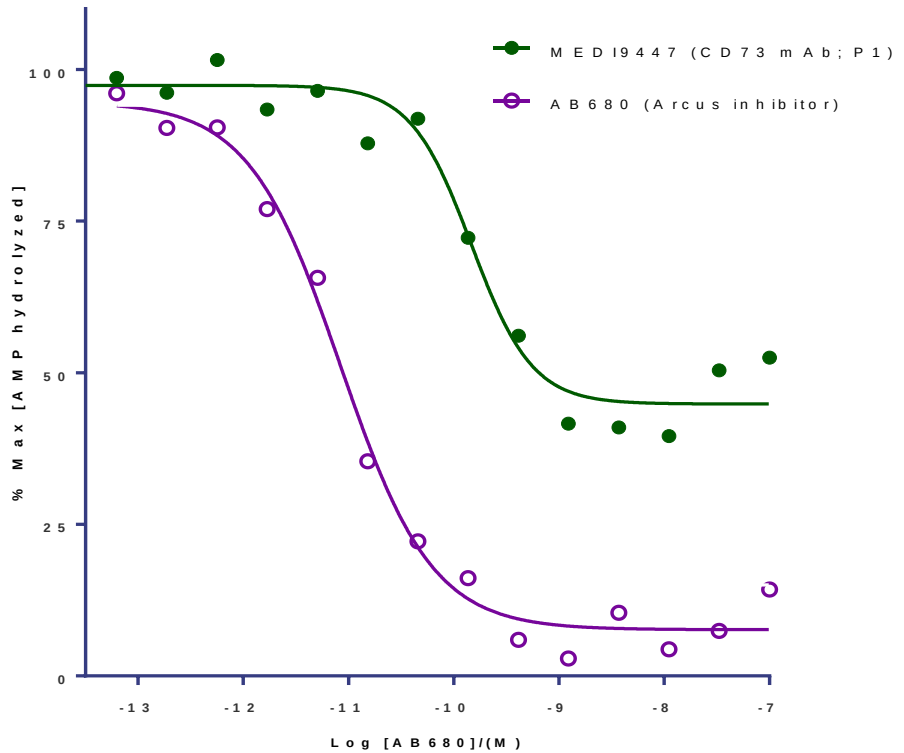
AB680: First Small-molecule CD73 Inhibitor to Enter Clinical Development

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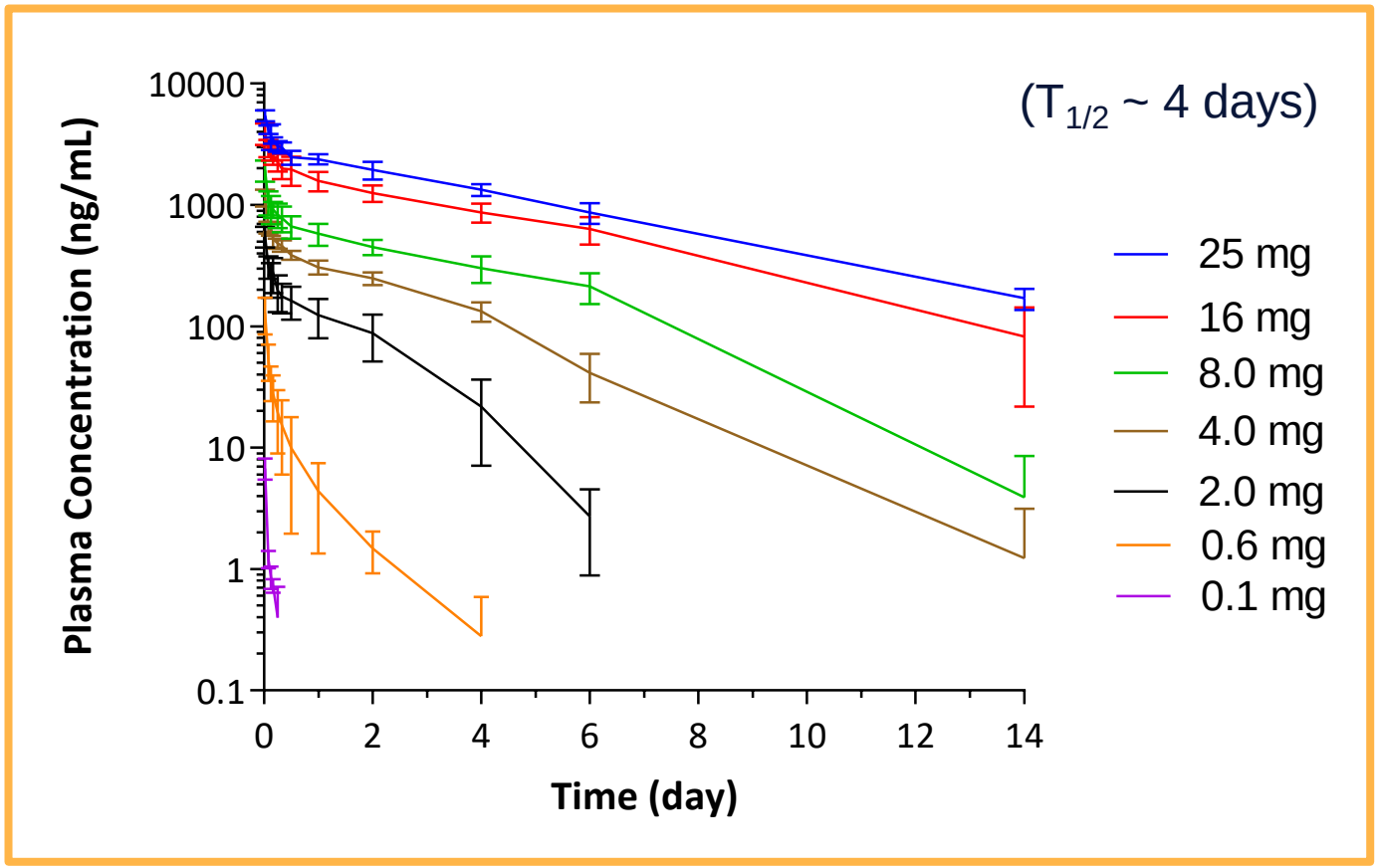
AB680 Displays Excellent PK Profile in Healthy Human Volunteers Consistent with q2w Dosing



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

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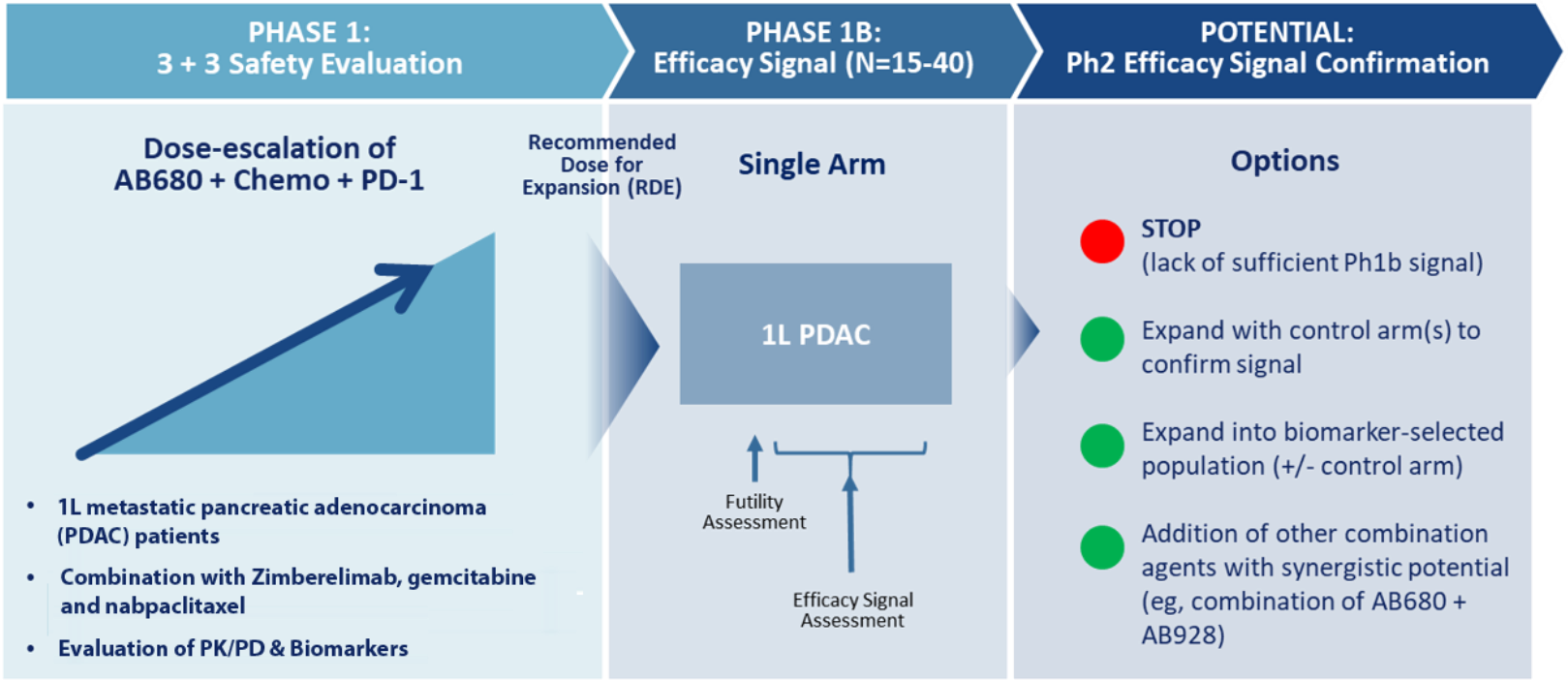
AB680 (CD73 inhibitor) Development Status

- **Evaluation in 1L pancreatic cancer in combination with Zim + gemcitabine/nab-paclitaxel**
  - Dose escalation ongoing
  - Early Phase 1b expansion data starting in mid-2020
- **Plans underway to evaluate AB680 in multiple combinations and indications (e.g., mCRPC)**



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ZIMBERELIMAB & AB154 DEVELOPMENT STRATEGY

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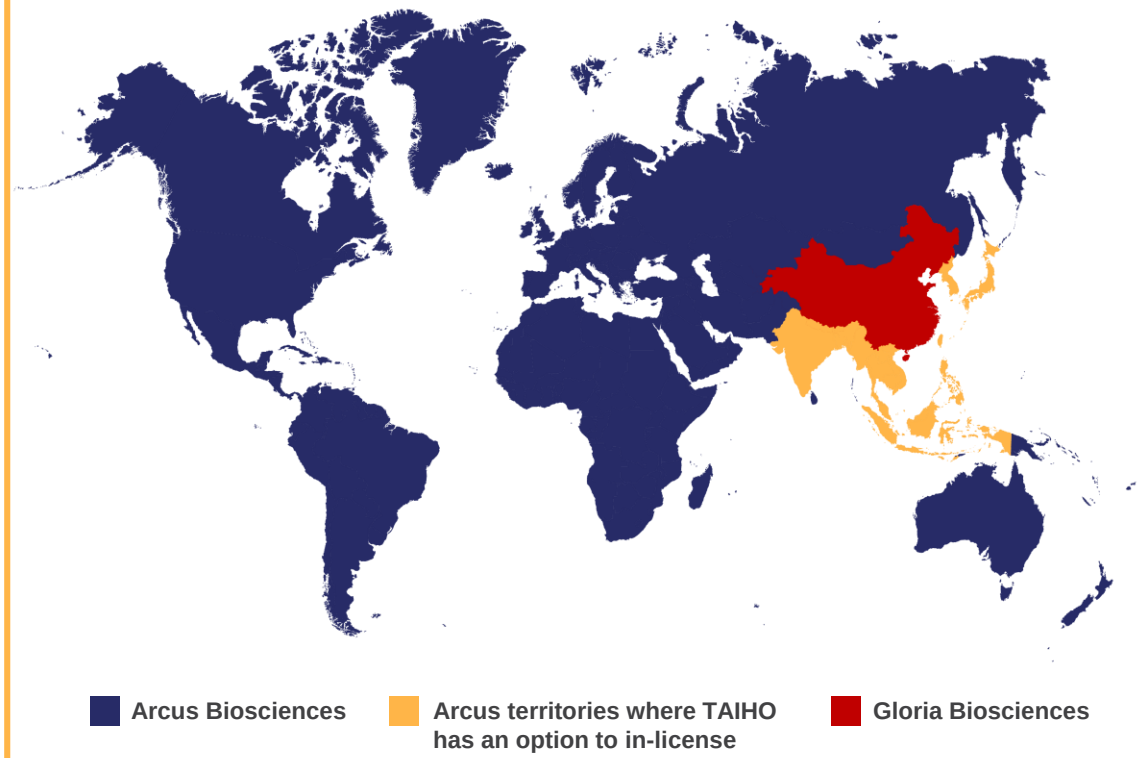
Zimberelimab (anti-PD-1) Provides Flexibility & Optionality in Clinical Development & Potential Commercialization

- **Strategic in-license enabling full control over combinations, full commercialization in US/EU[2]**
- **Zimberelimab profile is clinically similar to approved anti-PD-1 agents[1]**
- **Gloria Biosciences filing for NMPA China approval in 1Q20**
  - Over 200 patients treated in China alone[1]
  - ORRs similar to other checkpoint inhibitors[1]
    - >90% ORR in late-line classic Hodgkins lymphoma (cHL)
    - >15% ORR in late-line GI cancers (e.g., esophageal, cholangiocarcinoma and gastric)
- **Arcus developing strategic plans for gaining approvals of Zimberelimab in select indications (US, EU)**

Global Commercialization Rights to Zimberelimab



[1] Presentations by Gloria Biosciences at CSCO 2019. Gloria's studies are conducted independently of Arcus
[2] Arcus Biosciences obtained global commercialization rights outside of China and Thailand

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Gloria Biosciences Reported Results with Zimberelimab Demonstrating Impressive anti-Tumor Activity in Relapsed/ Refractory Classical Hodgkin's Lymphoma (cHL)[1]

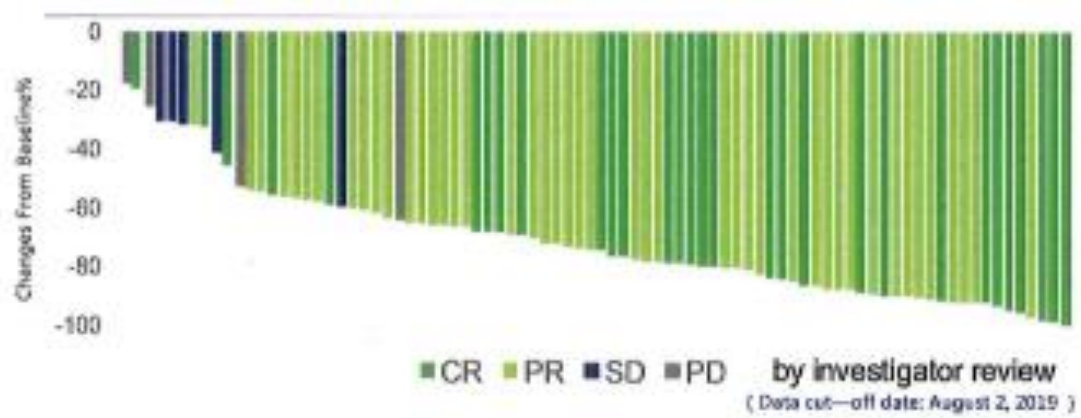
YH-S001-02 is a single-arm, multicenter, Phase 2 clinical study to evaluate the efficacy and safety of Zimberelimab (GLS-010/AB122) in the treatment of relapsed/refractory (r/r) cHL

Overall Response Rate (ORR) & Disease Control Rate (DCR)



Median Duration of Response (DOR) was not reached
Median Progression Free Survival was not reached

Waterfall Plot



100% of evaluable r/r cHL patients had a decrease in size of target lesions

[1] As presented at the China Showcase, JPM Conference (2020). Gloria's studies are conducted independently of Arcus
NCT number: NCT03655483

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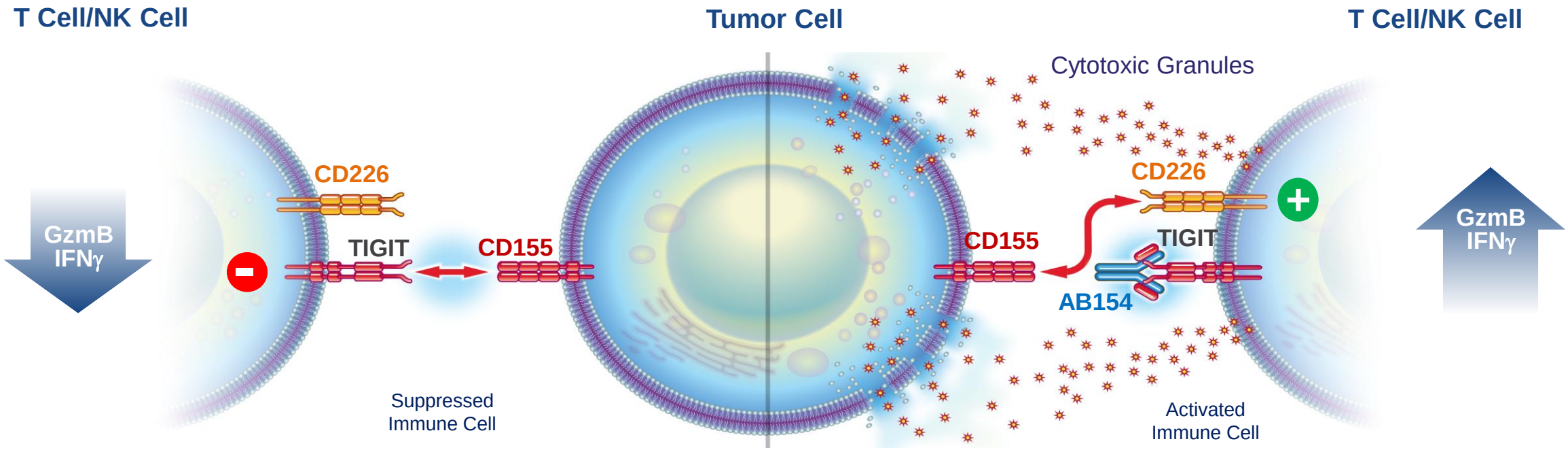
AB154 (anti-TIGIT): Next Potential I-O Backbone

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 completed enrollment of Phase 2 study in NSCLC; primary data completion April ’20 (clinicaltrials.gov)
- Merck reported early clinical activity from a Phase 1 study in solid tumors; Phase 2 study in NSCLC was initiated in 4Q19
- BMS, BeiGene and Astellas have Phase 1 studies in solid tumors ongoing (clinicaltrials.gov)

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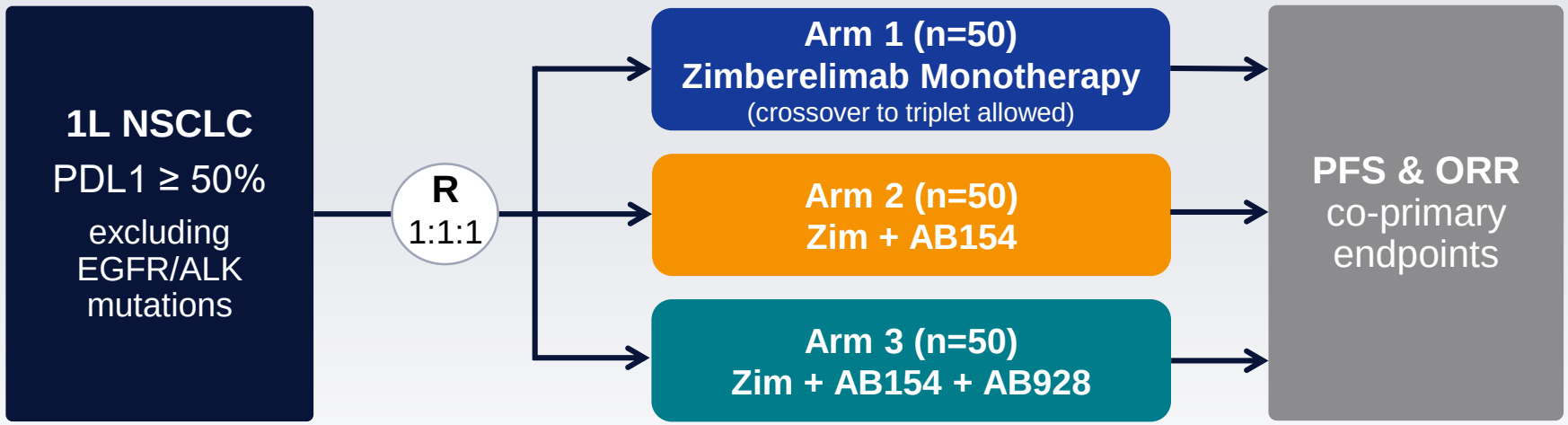
Phase 2 Open to Evaluate Two Combinations: AB154+Zim and AB154+AB928+Zim vs Zim Mono in 1L NSCLC

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



- **Study now open in US centers as of 1Q20**
- **US and Asia sites planned for enrollment**
- **Early randomized data expected by 4Q20**

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Oncology Discovery Programs

PI3Kγ Inhibitor

Glycolipid kinase

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

Immune (TAM, MDSC) target

PAK4 Inhibitor

Serine kinase

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

Cancer cell intrinsic target

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

Anti-TIM-3

Immune Checkpoint

TIM-3 is an immune checkpoint highly overexpressed by leukemic cells (e.g., MDS, AML) and exhausted T cells

Cancer cell intrinsic and immune (T cells) target

AXL Inhibitor

Tyrosine kinase

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

Cancer cell intrinsic target

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