

CREATING INNOVATIVE CANCER THERAPIES BY LEVERAGING UNDEREXPLOITED BIOLOGICAL OPPORTUNITIES

September 2019

NYSE: RCUS

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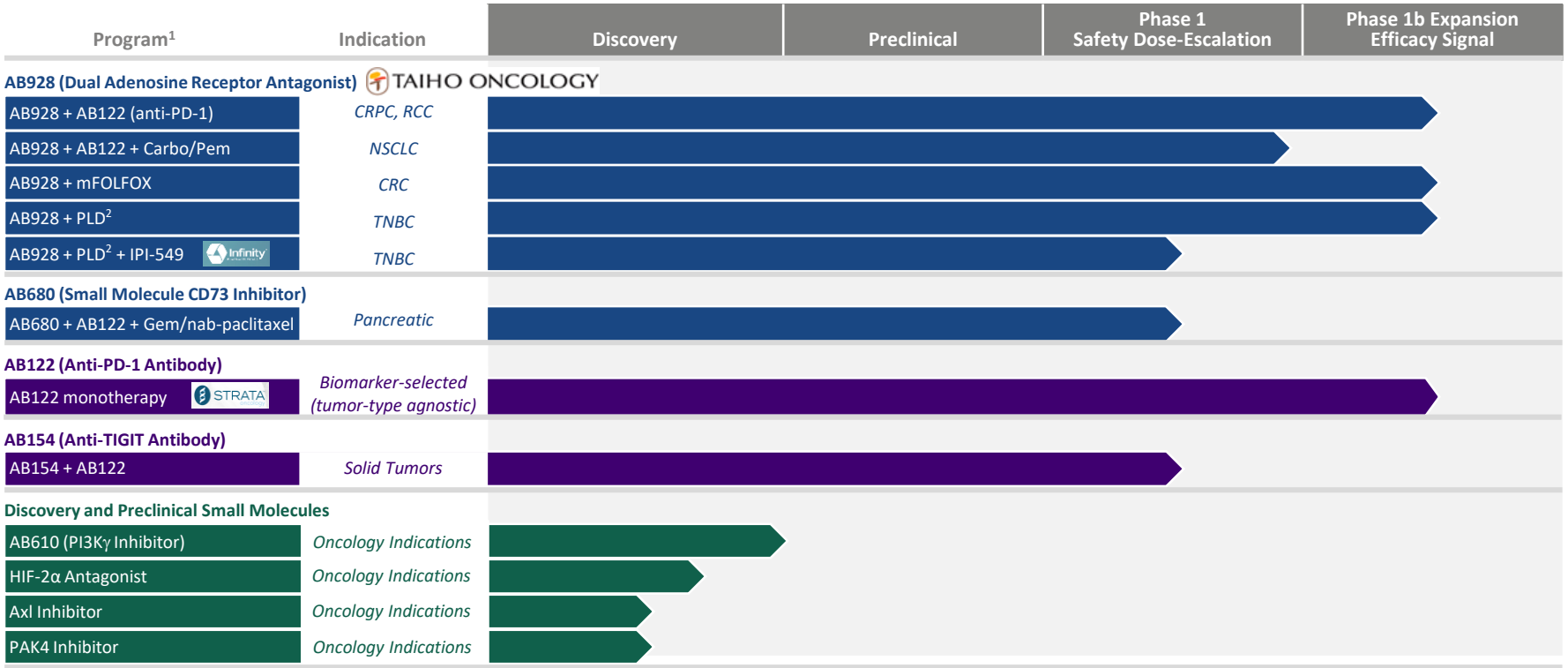
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CREATING INNOVATIVE BEST-IN-CLASS CANCER THERAPIES

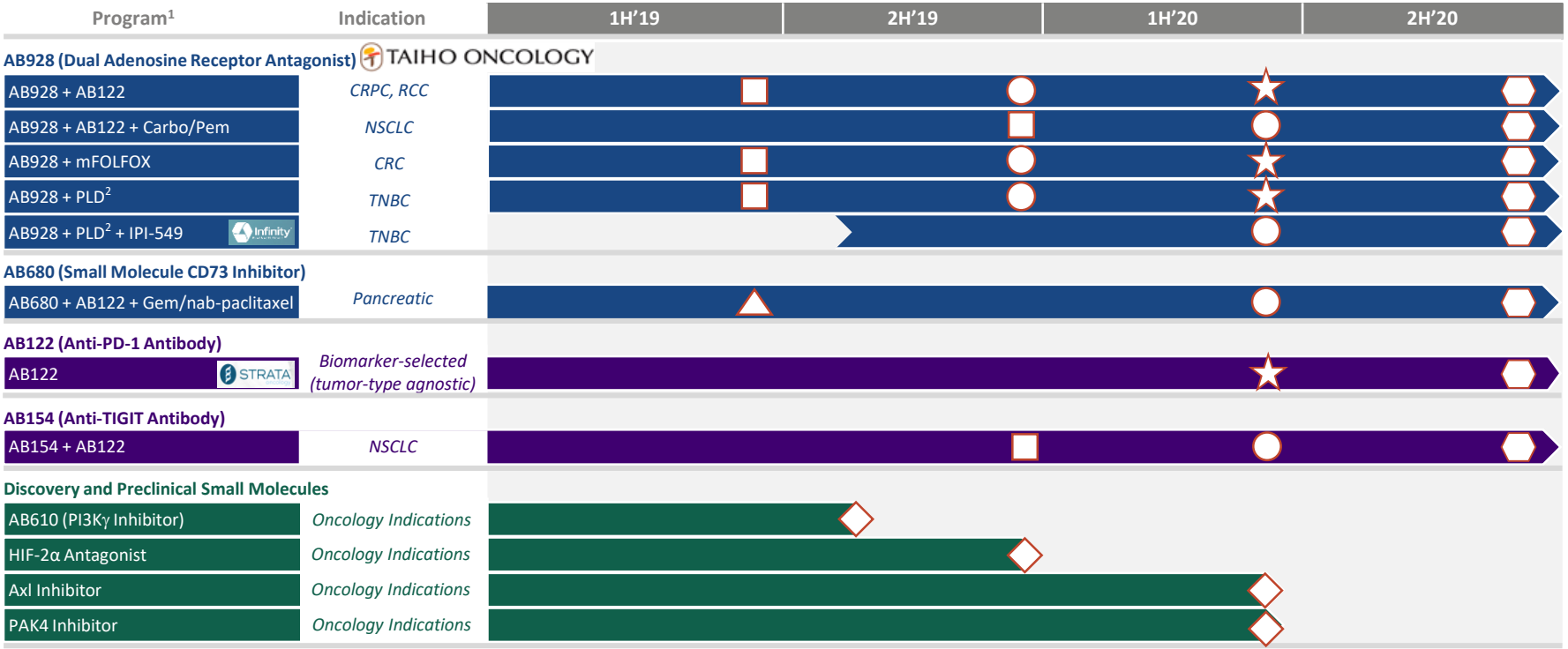
Leverage Underexploited Biological Targets in Promising Pathways	*Pioneering drug discovery efforts with initial focus on ATP-adenosine pathway*
Clinical Stage Pipeline	*Four clinical compounds; lead program advancing into multiple Ph1b expansion cohorts*
Broad Portfolio	*Ability to maximize development and commercial potential of combinations*
World-class Drug Discovery Engine	*Comprehensive and accomplished R&D team built from inception to support ongoing innovation*
Proven Track Record	*Successful management team with extensive expertise in immuno-oncology/oncology*
Well Capitalized	*$224.4 million in cash and investments at 6/30/19: sufficient to fund operations into 2021*

EXTENSIVE & EXPANDING PORTFOLIO OF ONCOLOGY PROGRAMS



1) Taiho has an option to Arcus's programs in Japan and certain other Asian territories (excluding China) over a 5-year term. Taiho partnership generates $35M in guaranteed payments over 3 years, additional opt-in payments, milestones and tiered-royalties. AB928 option exercised July 2018.
2) Pegylated liposomal doxorubicin.
CRPC = castration-resistant prostate cancer, RCC = renal cell cancer, NSCLC = Non-small cell lung cancer, CRC = colorectal cancer, GEC = gastric-esophageal cancer, TNBC = triple-negative breast cancer

EXTENSIVE & EXPANDING PIPELINE WITH MULTIPLE DATA READOUTS IN THE NEXT 12-18 MONTHS



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CRPC = castration-resistant prostate cancer, RCC = renal cell cancer, NSCLC = Non-small cell lung cancer, CRC = colorectal cancer, GEC = gastric-esophageal cancer, TNBC = triple-negative breast cancer

- Clinical Dev Candidate
- HV Ph1 dose-escalation data
- Initial Ph1 dose-escalation safety/PK/PD data
- Maturing Ph1 dose-escalation safety/PK/PD data
- Initial Ph1 expansion efficacy data
- Maturing Ph1 expansion efficacy data (randomized data possible in some studies)

KEY PROGRAM HIGHLIGHTS

AB928 ***Dual Adenosine Receptor Antagonist***	• **Excellent safety, PK, PK/PD profile established in 3 combination settings** • **Progressing into multiple Phase 1b expansion trials, including prostate cancer (across several lines of therapy), renal cell cancer, mut-EGFR NSCLC, triple-negative breast cancer, and colorectal cancer**
AB680 ***Small Molecule CD73 Inhibitor***	• **Excellent safety, PK, PK/PD profile in healthy volunteers supports advancement into cancer patients** • **Initiating Phase 1 safety dose-escalation in combination with AB122, gemcitabine and nab-paclitaxel in 1L metastatic pancreatic cancer**
AB122 ***Anti-PD-1 Monoclonal Antibody***	• **IND clearance to initiate a tumor-type agnostic biomarker-selected trial of AB122 monotherapy in advanced solid tumors (in collaboration with Strata Oncology)** • **Backbone for several of our combination trials**
AB154 ***Anti-TIGIT Monoclonal Antibody***	• **Phase 1 safety dose-escalation ongoing, currently in combination with AB122** • **Initiating an expansion study in combination with AB122 in NSCLC**
DISCOVERY & PRECLINICAL	• **Internal small-molecule drug discovery engine with multiple immuno-oncology and cancer cell-intrinsic targets** • **On track to identify a potentially best-in-class HIF-2α clinical development candidate in 2019**

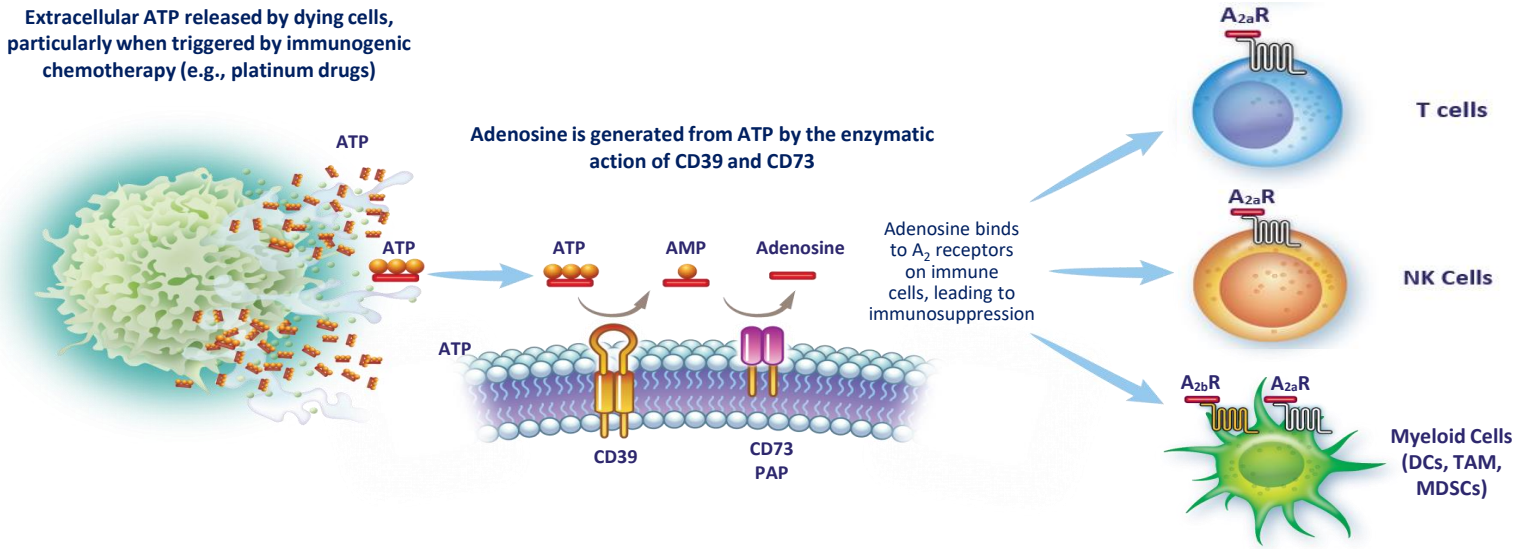


AB928

SMALL MOLECULE $A_{2a}R/A_{2b}R$ ANTAGONIST

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THE ATP-ADENOSINE PATHWAY PLAYS A WELL ESTABLISHED, CRITICAL ROLE IN IMMUNE SUPPRESSION



What we know about adenosine:

- High levels of adenosine are present in most tumors
- Adenosine directly blocks T-cell and NK-cell function and activation (mediated by $A_{2a}R$)
- Adenosine induces myeloid cells (dendritic cells, macrophages) to indirectly impair T-cell activation ($A_{2b}R$ effect)
- CD73, the enzyme that generates adenosine, could serve as a target for therapeutic intervention, as well as a biomarker for patient selection
- In certain tumor types, other enzymes (e.g., PAP in Prostate Cancer) can also convert AMP into adenosine

EFFORTS FOCUSED ON THE CD73-ADENOSINE PATHWAY ARE EXPANDING ACROSS THE INDUSTRY

Product (Company)	Target	Key Indications	Phase 1	Phase 2*	Commentary
AZD4635 (AstraZeneca)	$A_{2a}R$	CRPC NSCLC CRC		◆	Reported early efficacy signal in CRPC[1]; large (~280 patients) Phase 1b study (multiple cohorts) ongoing
NIR178 (Novartis)	$A_{2a}R$	NSCLC DLBCL TNBC	◆		Early signals of efficacy reported in NSCLC[2,3]
Oleclumab (AstraZeneca)	CD73 (antibody)	NSCLC Pancreatic TNBC Other solid tumors		◆	Early signals of activity in CRC and pancreatic cancer[4] ; 13 clinical trials ongoing, several of them randomized to combination partner
BMS-986179 (BMS)	CD73 (antibody)	Solid Tumors	◆		Phase 1 data in Apr-18 in combination with nivolumab[5]; currently in a Phase 1/2a trial
NZV930 (Novartis)	CD73 (antibody)	Solid Tumors	◆		Phase 1 study started in 2018; No data reported

* Phase 2 refers to existence of randomized trial in at least one setting

1.Bendell J, Bauer T, Patel M, Falchook G, Karlix JL, et al. 2019. *Cancer Research* 79 (13, suppl.): CT026
2.Chiappori A, Williams CC, Creelan BC, Tanvetyanon T, Gray JE, et al. 2018. *Journal of Clinical Oncology* 36: 9089
3.Chiappori A, Creelan B, Tanvetyanon T, Gray J, Haura E, et al. 2018. *Phase I/II study of the A2AR antagonist NIR178 (PBF-509) combined with the anti-PD-1 monoclonal antibody spartalizumab in patients with advanced NSCLC.*
4.Overman MJ, LoRusso P, Strickler JH, Patel SP, Clarke SJ, et al. 2018. *Journal of Clinical Oncology* 36: 4123
5.Siu LL, Burris H, Le DT, Hollebecque A, Steeghs N, et al. 2018. *Cancer Research* 78 (13, suppl.): CT180

Sources: https://www.clinicaltrials.gov/
CRPC = castration-resistant prostate cancer, NSCLC = Non-small cell lung cancer, CRC = colorectal cancer, DLBCL = diffuse large B-cell lymphoma, TNBC = triple-negative breast cancer

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** the $A_{2a}R$ and $A_{2b}R$ receptors

Multiple advantages over other $A_{2a}R$ antagonists in clinical development:

- Minimal shift in potency due to decreased non-specific protein binding
- Excellent penetration of tumor tissue
- Minimal CNS effects
- Excellent drug properties (PK, etc.)

Differentiated, highly efficient clinical development plan ongoing:

- Believed to be first clinical program to evaluate an A_2R antagonist with chemotherapy

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

Compound	$A_{2a}R$ (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

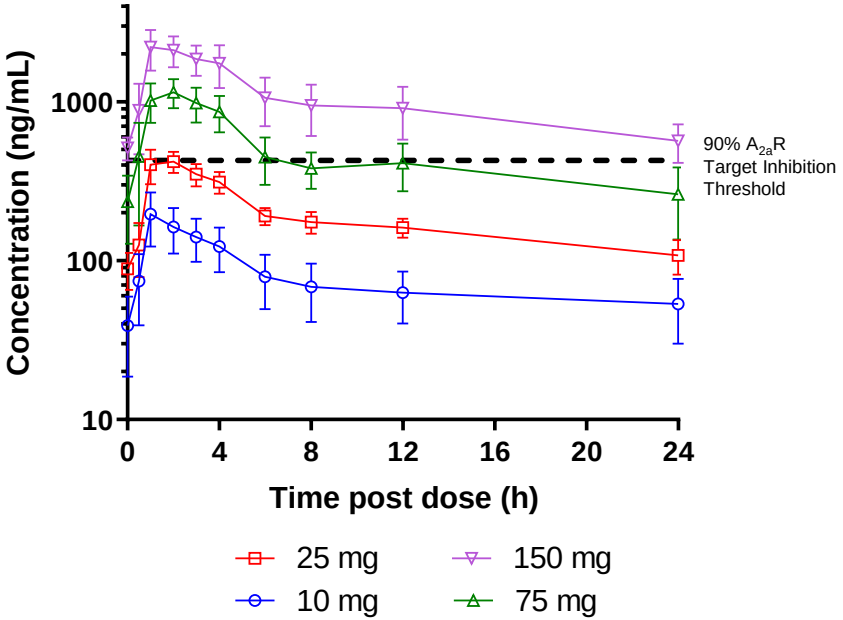
AB928 has ideal pharmacological properties for an oncology drug

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; PBF509: Believed to be NIR178 (based on Pat Appl WO2017025918 and WO2018146612), 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.

BASED ON THE HEALTHY VOLUNTEER DATA, TARGET INHIBITION OF $A_{2a}R$ IS ACHIEVED AT DOSES BETWEEN 75-150 mg QD

Excellent Pharmacokinetic Profile*



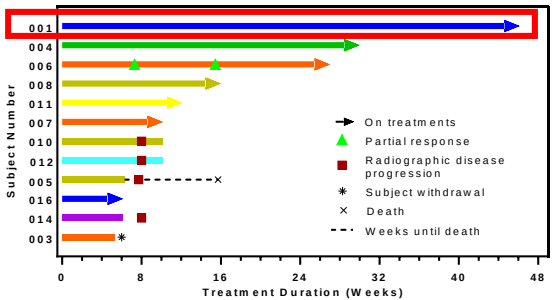
Dose QD	2-hr Post-Dose: AB928 Plasma Conc. (ng/mL)	2-hr Post-Dose: % Inhibition of 5 µM NECA	24-hr Post-Dose: AB928 Plasma Conc. (ng/mL)	24-hr Post-Dose: % Inhibition of 5 µM NECA	
150 mg	**2,113**	**100 %**	**566**	**≥ 90%**	**RDE Dose**
75 mg	**1,148**	**100 %**	**261**	**76 %**	Ph1 Starting Dose
25 mg	420	82 %	108	51 %	
10 mg	163	51 %	53	(12%)**	

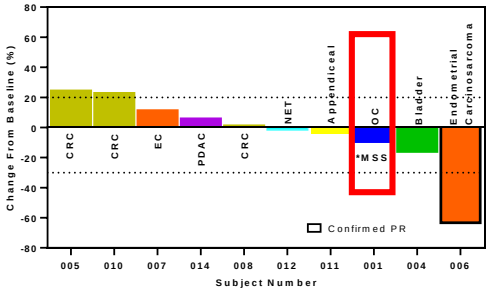
*Steady-state data shown

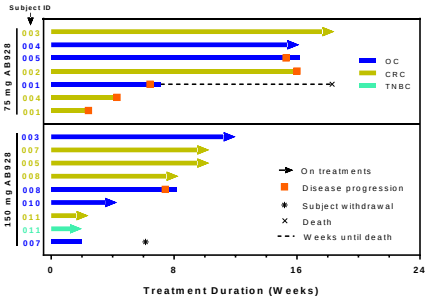
**Some or all dosed subjects were within the range of variation observed in placebo subjects (-39 to 30%). The PK/PD and safety data from the AB928 healthy volunteer study has been published; Seitz et al 2018 Invest. New Drugs doi: 10.1007/s10637-018-0706-6

EXCELLENT SAFETY, PK/PD & EVIDENCE OF IMMUNE RESPONSE DEMONSTRATED in PHASE 1 DOSE ESCALATION STUDIES

- Excellent safety, PK, PK/PD profile established in 3 combination settings
- AB928 + AB122 demonstrated tumor responses and disease stabilization in tumor types generally unresponsive to monotherapy checkpoint inhibition
- Confirmed partial response in a subject with Endometrial Carcinosarcoma (Malignant Mixed Mullerian Tumor), a tumor type with generally low levels of response to PD-(L)1 inhibitors
- Demonstrated evidence of an immune response in ovarian cancer subject (on treatment > 47 weeks as of data cutoff)
  - Subject was low TMB, PD-L1 TPS 1% and CPS 4% (by 22C3), MSS and had very high CD73 expression
  - Increase in activated intra-tumoral CD8+ cells in on-treatment biopsies







PRELIMINARY AB928 PH1 SAFETY DOSE-ESCALATION DATA: EXCELLENT SAFETY PROFILE OBSERVED THUS FAR

AB928-related ≥ Grade 3 Adverse Event Profile by Treatment Group

Number of Subjects with AE Preferred Term	AB928-002		AB928-003		AB928-004	AB928-005		
	75 mg (n=3)	150 mg (n=5)	75 mg (n=4)	150 mg (n=4)	75 mg (n=3)	75 mg (n=3)	150 mg (n=6)	200 mg (n=3)
Anemia	0	1	1	0	0	0	0	0
Fatigue	0	0	1	0	0	0	0	0
Leukopenia	0	1	0	0	0	0	0	0
Nausea	0	0	1	0	0	0	0	0
Neutropenia	0	1	0	0	0	0	0	0

Summary of Treatment Emergent Adverse Events in AB928 Dose Escalation

Number of Subjects with	AB928-002		AB928-003		AB928-004	AB928-005		
	75 mg (n=3)	150 mg (n=5)	75 mg (n=4)	150 mg (n=4)	75 mg (n=3)	75 mg (n=3)	150 mg (n=6)	200 mg (n=3)
TEAEs, n (%)	3 (100%)	5 (100%)	4 (100%)	4 (100%)	2 (67%)	3 (100%)	5 (83%)	2 (67%)
AB928-related TEAEs, n (%)	2 (67%)	3 (60%)	3 (75%)	4 (100%)	1 (33%)	3 (100%)	4 (67%)	0
Grade 1-2, n (%)	3 (100%)	5 (100%)	4 (100%)	4 (100%)	2 (67%)	3 (100%)	5 (83%)	1 (33%)
AB928-related Grade 1-2, n (%)	2 (67%)	3 (25%)	3 (75%)	4 (100%)	1 (33%)	3 (100%)	4 (67%)	0
Grade 3-4, n (%)	2 (67%)	2 (40%)	4 (100%)	2 (50%)	0	1 (33%)	1 (17%)	1 (33%)
AB928-related Grade 3-4, n (%)	0	2 (40%)	1 (25%)	0	0	0	0	0
SAE, n (%)	1 (33%)	0	2 (50%)	1 (25%)	0	2 (67%)	1 (17%)	0
AB928-related SAE, n (%)	0	0	0	0	0	0	0	0
DLT*, n	0	0	0	0	0	0	1	0

- No Grade 4 or 5 AB928-related AEs were reported across studies
- Maximum tolerated dose of AB928 in combination has not been reached

*DLT was a Gr 2 rash resulting in <80% of investigational product being delivered over the DLT period; Data Cut-off: 14JUN19

SUMMARY OF ONGOING AB928 TRIALS

	AB928 Trials	Status
STUDY 005	AB928 + AB122 (anti-PD1)	• **Initiated Phase 1b expansion in mCRPC (with plans for additional cohorts this quarter)** • **Phase 1b expansion in RCC ongoing**
STUDY 002	AB928 + PLD[1]	• **Initiated Phase 1b expansion in TNBC** • **Initiated Phase 1 safety dose-escalation with the addition of IPI-549, a PI3K*γ* inhibitor in TNBC**
STUDY 003	AB928 + mFOLFOX	• **Initiated Phase 1b expansion in CRC**
STUDY 004	AB928 + Carbo/Pem + AB122	• **Ongoing Phase 1 safety dose-escalation** • **Will soon initiate Phase 1b expansion in EGFR-mutated NSCLC in patients who have failed TKI therapy**

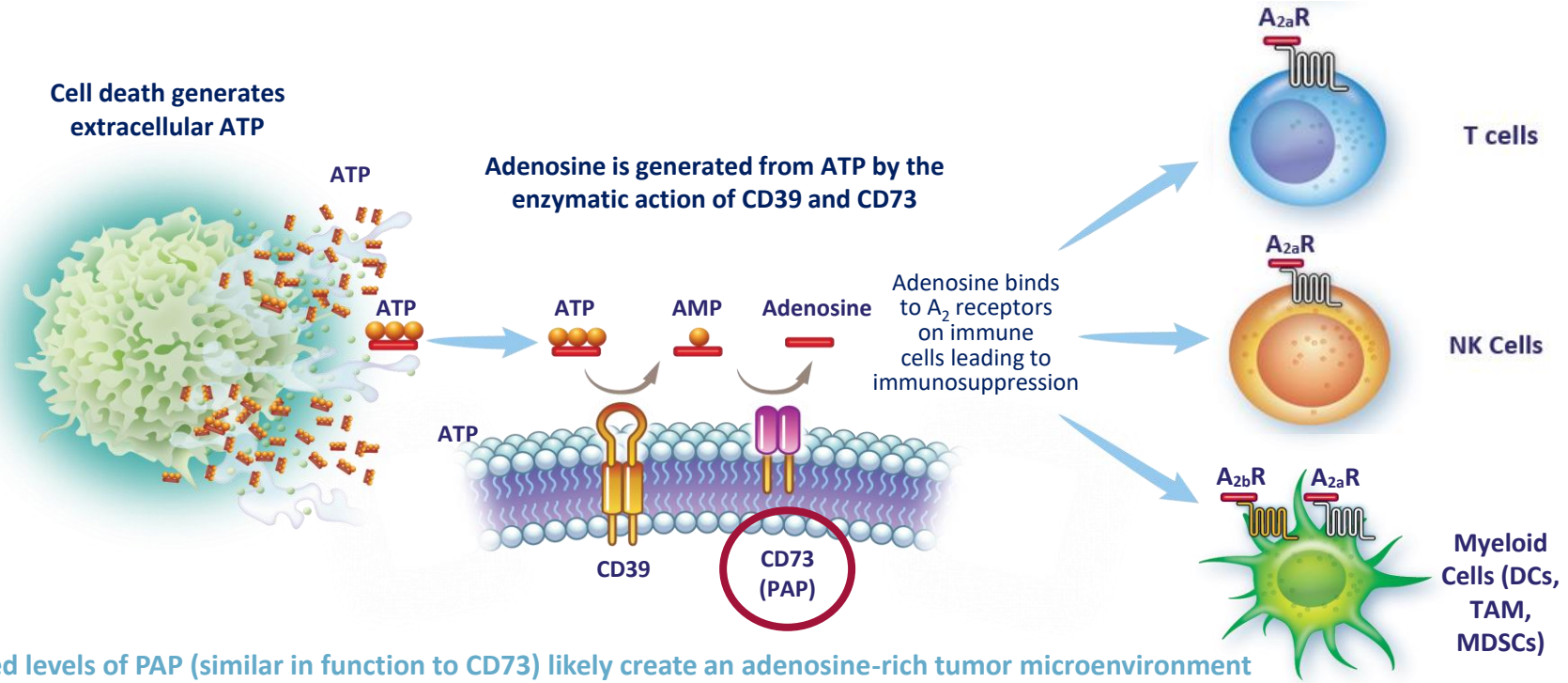
Flexible Trial Design

- Dose escalation cohorts designed to assess safety, PK, PD
- Expansion cohorts will assess futility after first 15 patients
- Expand to 40 patients if threshold response rate achieved and/or open up backbone-alone cohort (randomized comparison to combination)
- Opportunity for biomarker-based selection of patients at randomization stage

1) pegylated liposomal doxorubicin

mCRPC = metastatic castration-resistant prostate cancer, NSCLC = Non-small cell lung cancer, CRC = colorectal cancer, TNBC = triple-negative breast cancer, TKI = tyrosine kinase inhibitor

RATIONALE FOR INCLUSION OF A CASTRATION-RESISTANT PROSTATE CANCER ARM



Increased levels of PAP (similar in function to CD73) likely create an adenosine-rich tumor microenvironment

- Prostatic acid phosphatase (PAP) is an enzyme produced primarily by the prostate
- Increased levels of PAP are found in men who have prostate cancer, especially those with metastatic disease
- PAP breaks down extra-cellular AMP to produce adenosine

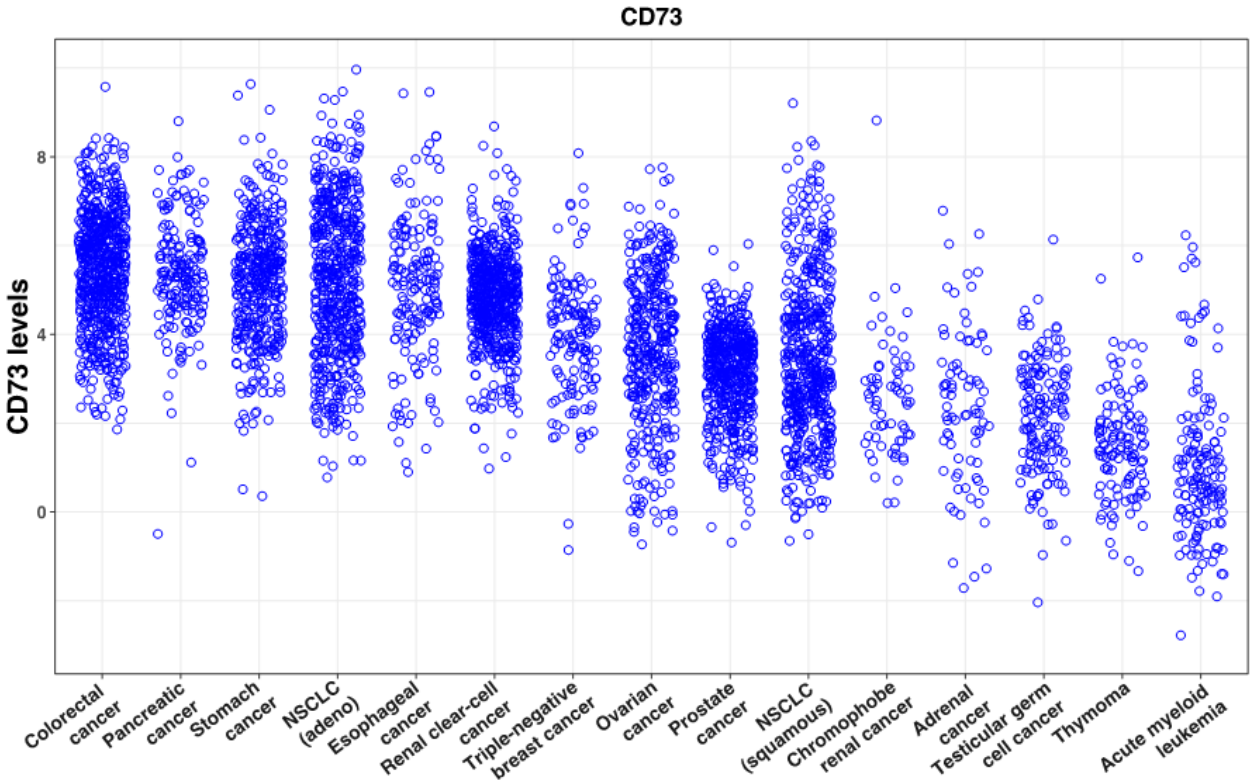


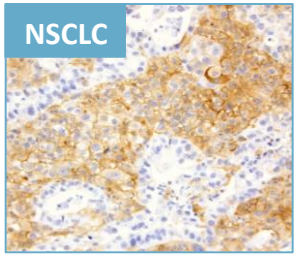
AB680

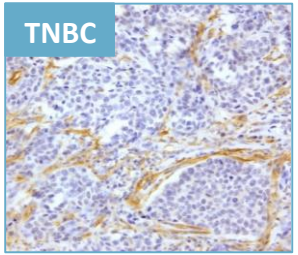
SMALL MOLECULE CD73 INHIBITOR

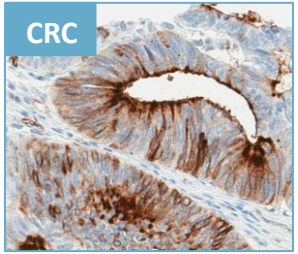
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CD73 IS BROADLY EXPRESSED ON MULTIPLE TUMOR TYPES





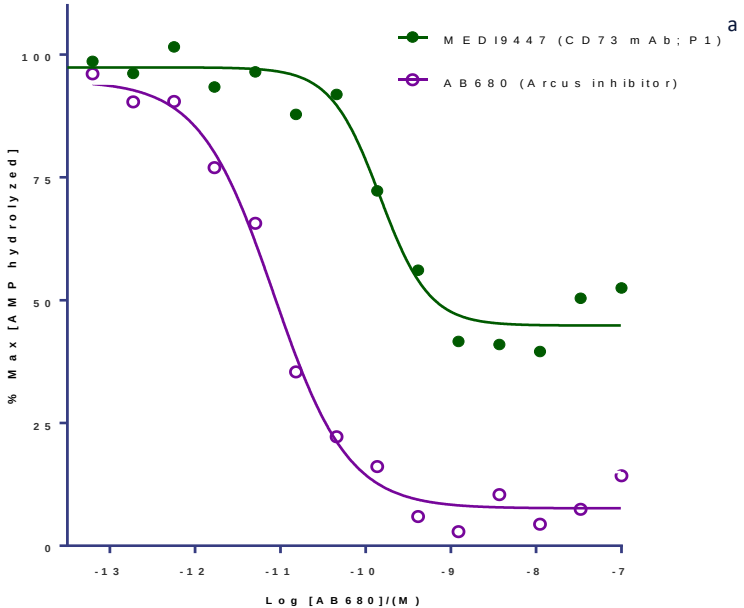




TCGA (The Cancer Genome Atlas)

AB680: FIRST SMALL-MOLECULE CD73 INHIBITOR TO ENTER CLINICAL DEVELOPMENT

AB680 Potently Inhibits CD73 Enzymatic Activity on CD8+ T Cells



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

AB680 potentially offers advantages over the anti-CD73 antibodies in development:

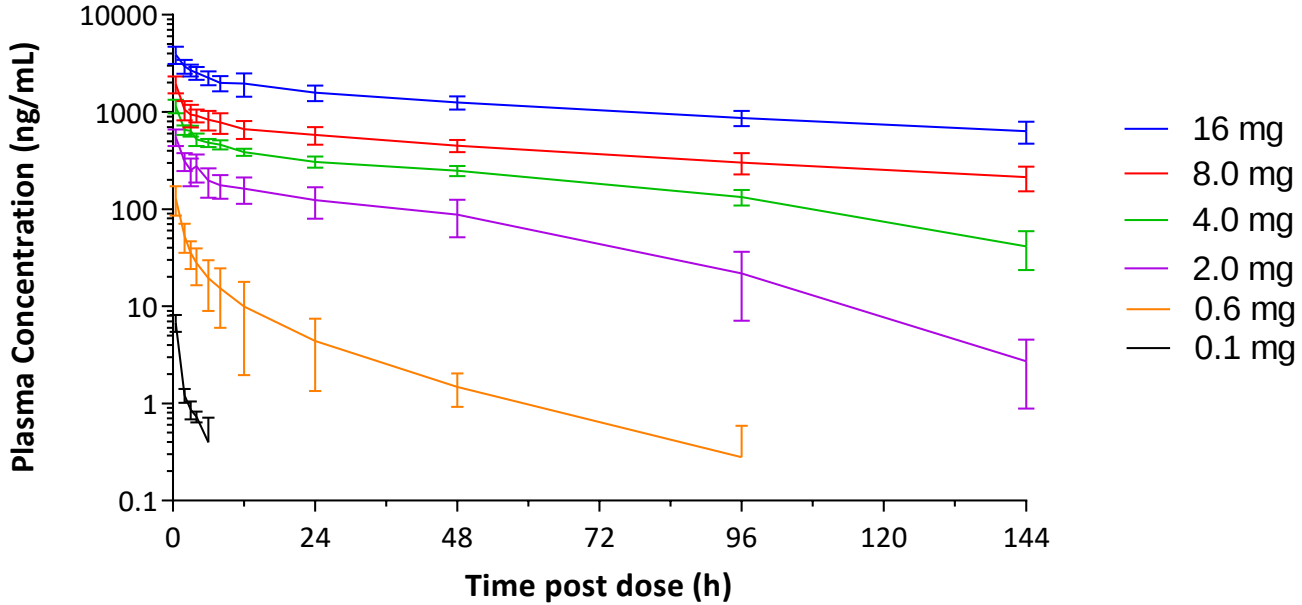
- Greater inhibition of CD73 enzymatic activity (soluble & cell-bound)
- Deeper tumor penetration
- IV and oral formulations

Unique small molecule properties

- Extraordinarily potent: IC_{50} = 0.008 nM (human T cells)
- Low clearance, long half-life molecule

Oral formulation in IND-enabling studies

AB680 IN PH1 HEALTHY VOLUNTEER STUDY: EXCELLENT SAFETY & PHARMACOKINETICS (PK) DATA OBTAINED



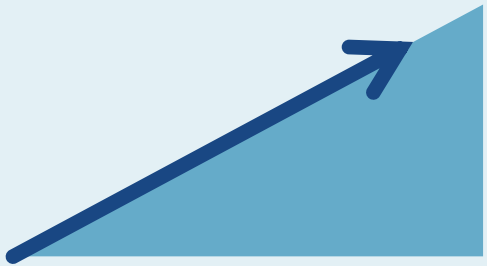
Design: Blinded, Healthy Volunteer study; n=6 participants dosed with AB680, and n=2 dosed with placebo

Initial Results: Support for Q2W dosing at pharmacologically relevant doses, with favorable safety profile across all cohorts

AB680: INITIAL STUDY TARGETING FIRST-LINE PANCREATIC CANCER

PHASE 1: 3 + 3 Safety Evaluation

Dose-escalation of AB680 + Chemo + PD-1



- **1L metastatic pancreatic adenocarcinoma (PDAC) patients**
- **Combination with AB122, gemcitabine and nab-paclitaxel**
- **Evaluation of PK/PD & Biomarkers**

Recommended Dose for Expansion (RDE)

PHASE 1B: Efficacy Signal (N=15-40)

Single Arm

1L PDAC

Futility Assessment

Efficacy Signal Assessment

POTENTIAL: Ph2 Efficacy Signal Confirmation

Options

- **STOP** (lack of sufficient Ph1b signal)
- Expand with control arm(s) to confirm signal
- Expand into biomarker-selected population (+/- control arm)
- Addition of other combination agents with synergistic potential (eg, combination of AB928 + CD73i)



AB122

ANTI-PD-1 ANTIBODY

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AB122 (ANTI-PD-1 mAb) PROVIDES FLEXIBILITY & OPTIONALITY IN CLINICAL DEVELOPMENT & POTENTIAL COMMERCIALIZATION

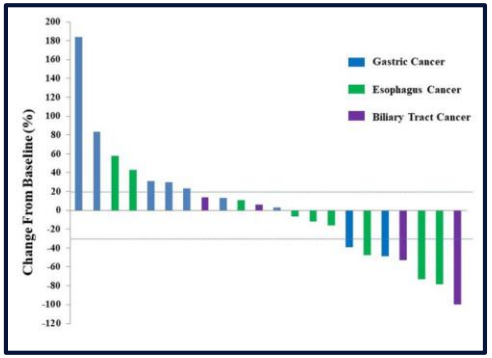
- Strategic in-license early in company evolution
- Enables full control over approaches to development, commercialization and pricing of anti-PD-1 containing combination therapies
- Pursuing targeted opportunities to obtain single-agent approval for AB122 in settings that are under-served by current agents and development strategies
- Initiating tumor-type agnostic biomarker-selected trial of AB122 in advanced solid tumors, in collaboration with Strata Oncology

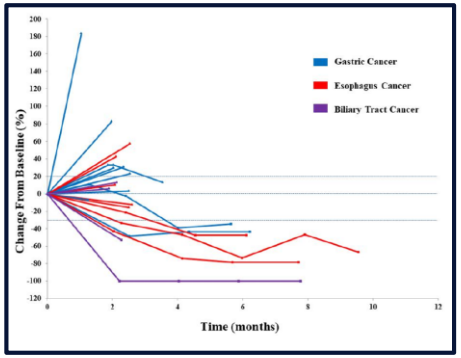


AB122 DEMONSTRATES ACTIVITY SIMILAR TO THAT OF APPROVED ANTI-PD-1 ANTIBODIES

GLORIA BIOSCIENCES*

ASCO-GI 2019 Update: Ph1b Trial in Advanced GI Tumors





ASCO GI, 2019

Best overall response rates:

- Gastric Cancer (N=10): 20%
- Esophageal Cancer (N=10): 30%
- Biliary Tract Cancer (N=4): 50%

Gloria ASCO 2019 Update: Ph2 Trial in Chinese r/r cHL

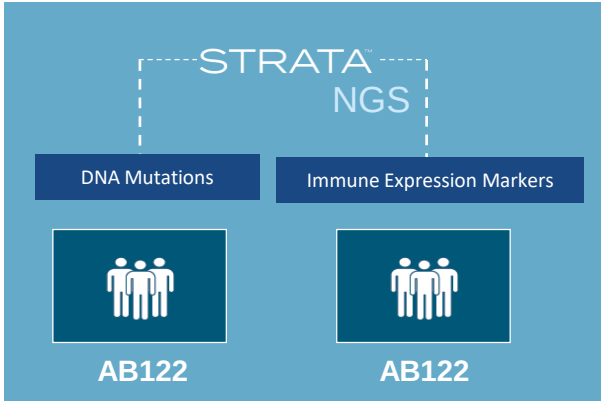
- Objective response in 88.3% of patients (15/17)
- Safety profile similar to that previously reported for PD-(L)1 inhibitors in this population

*Studies are being conducted independently of Arcus Biosciences

DEVELOPMENT OF AB122 IN A TUMOR-AGNOSTIC FASHION USING STRATA'S MOLECULAR BIOMARKERS

Unique Opportunity - Precision Medicine Approach

- Leading Next-generation sequencing (NGS) technology partner with unique practical advantages
- Minimal Arcus investment to efficiently reach decision points
- Leverage Strata's access to large number of cancer patients/year across 20 healthcare systems nationwide in order to quickly identify biomarker-positive patients for our trial
- Ability to target patients with great medical need that suffer from a diverse set of tumor types that have not previously received approvals for PD-1 treatment





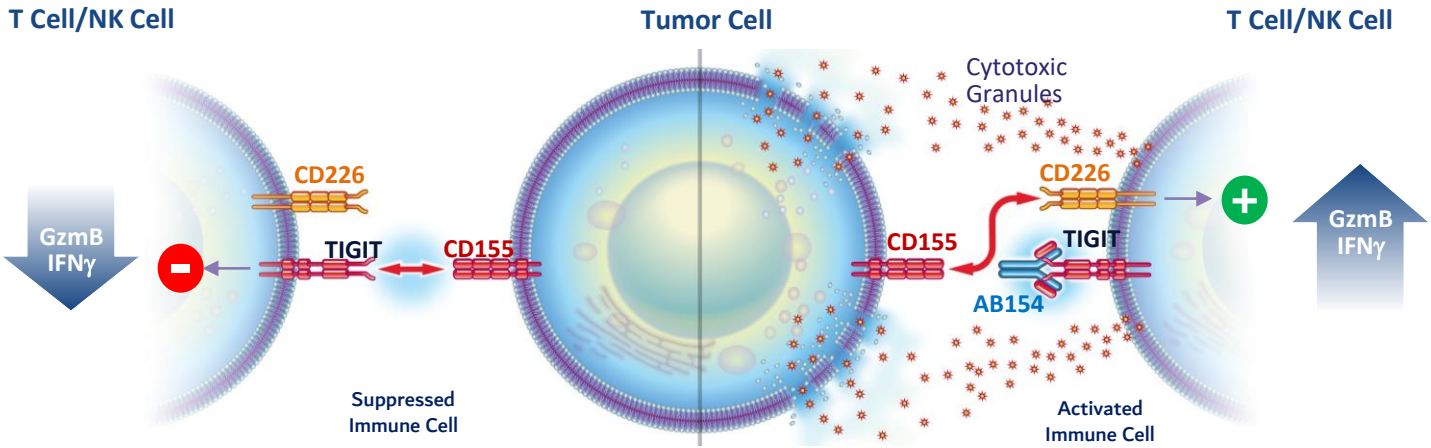
AB154

ANTI-TIGIT ANTIBODY

ARCUS BIOSCIENCES

AB154 (TIGIT): THE NEXT POTENTIAL I-O BACKBONE DUAL MECHANISM OF ACTION REFLECTS THE UNIQUENESS OF THE TIGIT PATHWAY

Blocking TIGIT inhibits an immuno-suppressive pathway **while freeing up CD155 to bind to CD226,** which is an immune-activating pathway



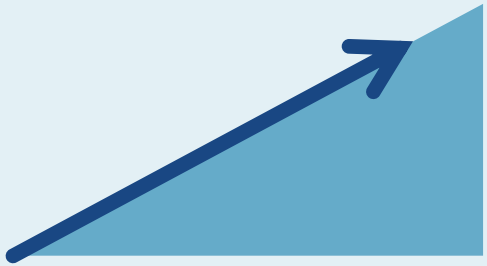
- AB154 is a humanized anti-TIGIT antibody designed to lack effector function
- AB154 reverses immune inhibition and provides tumor-selective immune stimulation
- Experiments in immune assays demonstrate synergy with AB680 (CD73) and AB122 (anti-PD-1)

AB154: INITIAL STUDY TARGETING SOLID TUMORS

PLANNED STUDY DESIGN

PHASE 1: 3 + 3 Safety Evaluation

Dose-escalation of AB154 + AB122 (α-PD-1)



Typical Patients in Ph1 Portion:

- Metastatic
- Late line-of-therapy

Evaluation of PK/PD & Biomarkers

Recommended Dose for Expansion (RDE)

PHASE 1B: (N=15-40)

Single Arm

NSCLC

Futility Assessment

Efficacy Signal Assessment

POTENTIAL: Ph2 Signal Confirmation

Options

- **STOP** (lack of sufficient Ph1b signal)
- Expand with control arm(s) to confirm signal
- Expand into biomarker-selected population (+/- control arm)
- Addition of other combination agents with synergistic potential

EXPANDING DISCOVERY PORTFOLIO

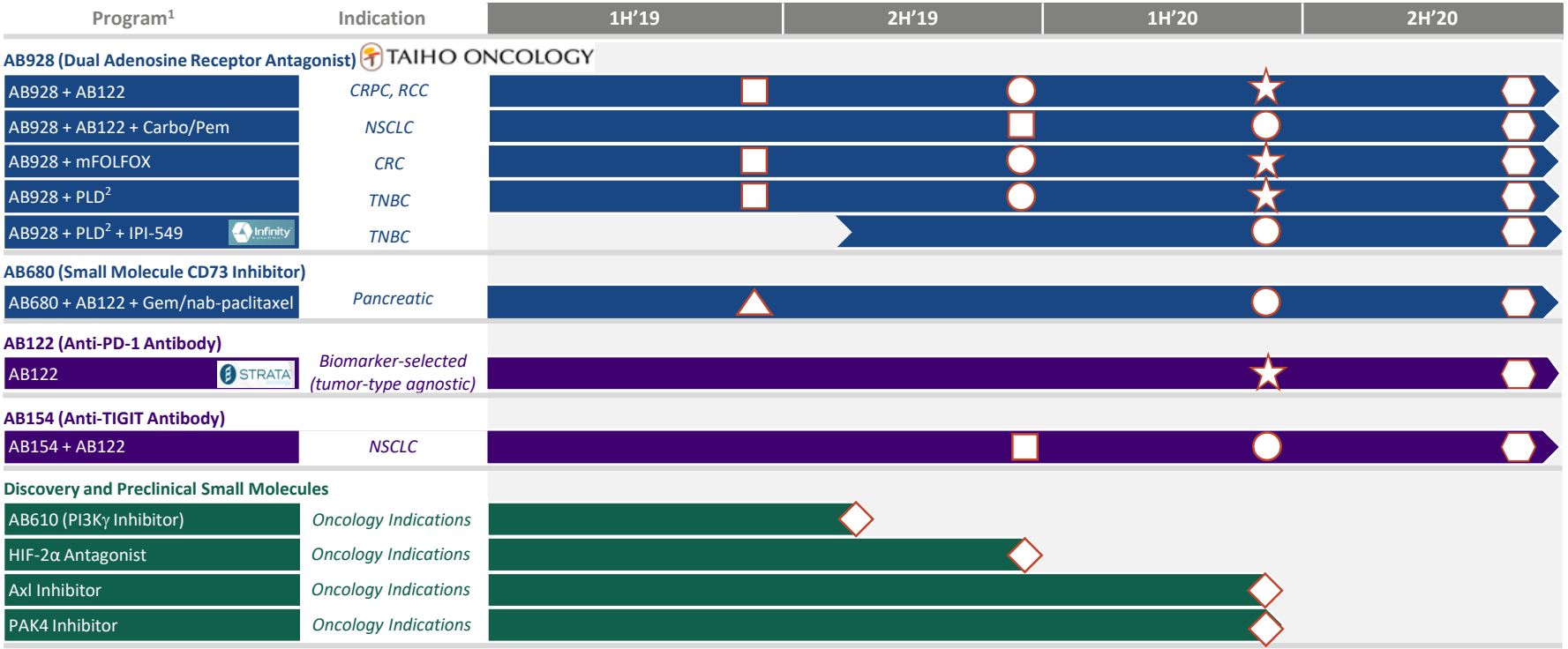
	HIF-2α	PI3Kγ	Axl	PAK4
Target Rationale	• Interfere with tumor pseudo-hypoxia; potential synergy with adenosine agents • HIF-2α plays a role in a variety of human cancers, including RCC, but broader activity expected in other HIF-2α driven tumors • Recent clinical POC generated by competitor compound	• Interfere with tumor myeloid cells in multiple tumor types (e.g., TNBC)	• Reverse tumor chemo/IO resistance	• PAK4 over-expression involved in T-cell exclusion from tumors discovered by our advisor (Ribas) • PAK4 inhibition as a way to sensitize "cold tumors" towards PD-(L)1 mAbs
Program Status	• Potentially best-in-class development candidate by 2H2019 • Plan to advance into clinical trials by mid-2020	• AB610 selected as development candidate • Advancement dependent on availability of data clinically validating the target	• Identify development candidate in 1H2020 • Potential first-in-human (FIH) dosing in late 2020	• Potential development candidate during 1H2020 • Potential FIH in late 2020

TAIHO PARTNERSHIP PROVIDES NON-DILUTIVE CAPITAL WHILE RETAINING SIGNIFICANT RIGHTS FOR ARCUS

TAIHO ONCOLOGY
Making the human connection

- Partnership initiated September 2017
- Option to Arcus programs in Japan and certain other Asian territories (excluding China) over a 5-year term
- $35mm in guaranteed payments over 3 years ($30 M received to date)
- Opt-in payments ranging from $3 to $15mm depending on when exercised
- **Exercised option to AB928 in July 2018**
- Up to $275mm in development, regulatory and commercial milestones per program
- Tiered royalties from high-single digit to mid-teens on net sales

EXTENSIVE & EXPANDING PIPELINE WITH MULTIPLE DATA READOUTS IN THE NEXT 12-18 MONTHS



1) Taiho has an option to Arcus's programs in Japan and certain other Asian territories (excluding China) over a 5-year term. Taiho partnership generates $35M in guaranteed payments over 3 years, additional opt-in payments, milestones and tiered-royalties. AB928 option exercised July 2018. 2) Pegylated liposomal doxorubicin.

CRPC = castration-resistant prostate cancer, RCC = renal cell cancer, NSCLC = Non-small cell lung cancer, CRC = colorectal cancer, GEC = gastric-esophageal cancer, TNBC = triple-negative breast cancer

- Clinical Dev Candidate
- HV Ph1 dose-escalation data
- Initial Ph1 dose-escalation safety/PK/PD data
- Maturing Ph1 dose-escalation safety/PK/PD data
- Initial Ph1 expansion efficacy data
- Maturing Ph1 expansion efficacy data (randomized data possible in some studies)