

CREATING INNOVATIVE CANCER THERAPIES BY LEVERAGING UNDEREXPLOITED BIOLOGICAL OPPORTUNITIES

July 2019

NYSE: RCUS

ARCUS BIOSCIENCES

FORWARD-LOOKING STATEMENTS/SAFE HARBOR

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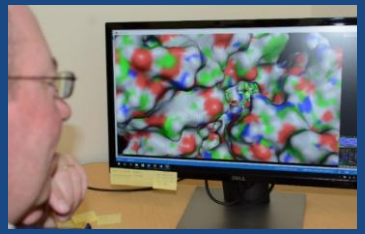
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CREATING INNOVATIVE CANCER THERAPIES

Leverage Underexploited Biological Targets in Promising Pathways	*Initial focus on* ***ATP-adenosine pathway***
Clinical Stage Pipeline	*Four clinical compounds with* ***multiple data readouts in 2019***
Broad Portfolio	*Ability to* ***maximize development*** *and* ***commercial*** *potential of combinations*
World-class Drug Discovery Engine	***Small-molecule discovery engine*** *to enable pipeline expansion*
Proven Track Record	*Successful management team with* ***10+ years working together in multiple companies***

OUR COMPETITIVE ADVANTAGES

BEST-IN-CLASS CHEMISTRY



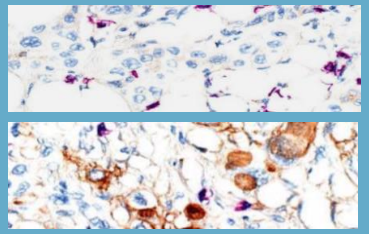
Rationally designed, potentially best-in-class small molecules for oncology

PORTFOLIO BREADTH AND DEPTH



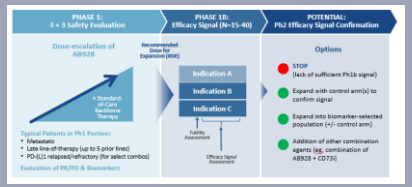
Enables development of multiple intra-portfolio combinations

TRANSLATIONAL SCIENCE



Extensive biomarker analysis to enrich clinical trials/inform clinical decisions

CLINICAL APPROACH



Clinical expertise in developing novel oncology combinations and seamless clinical trial platforms to enable early-stage decisions and increase late-stage trial success

BUILD LEADERSHIP TEAM WITH SIGNIFICANT CONTENT EXPERTISE EARLY-ON TO ENSURE LONG-TERM SUCCESS

ARCUS BIOSCIENCES



Terry Rosen, Ph.D.
Chief Executive Officer & Founder

30+ years leading, founding and building successful biopharma organizations, including founding and $1.25B sale of Flexus to BMS

FLEXUS BIOSCIENCES
AMGEN
Tularik
Pfizer
Abbott



Juan Jaen, Ph.D.
President & Founder

30+ years founding successful biopharma organizations and developing novel molecules, including founding and $1.25B sale of Flexus to BMS

FLEXUS BIOSCIENCES
ChemoCentryx
AMGEN
Tularik
WARNER LAMBERT



Rekha Hemrajani
Chief Operating & Financial Officer

Expertise in business development, finance and strategic planning within oncology/immuno-oncology

ONYX PHARMACEUTICALS
FLX BIO
EXELIXIS
CREDIT SUISSE FIRST BOSTON
LEHMAN BROTHERS



William Grossman, M.D., Ph.D.
Chief Medical Officer

Expertise leading global immuno-oncology clinical organizations, including direct accountability 50+ early-to-late-stage trials

Genentech
A Member of the Roche Group
Bellicum PHARMACEUTICALS
Roche
abbvie
MERCK

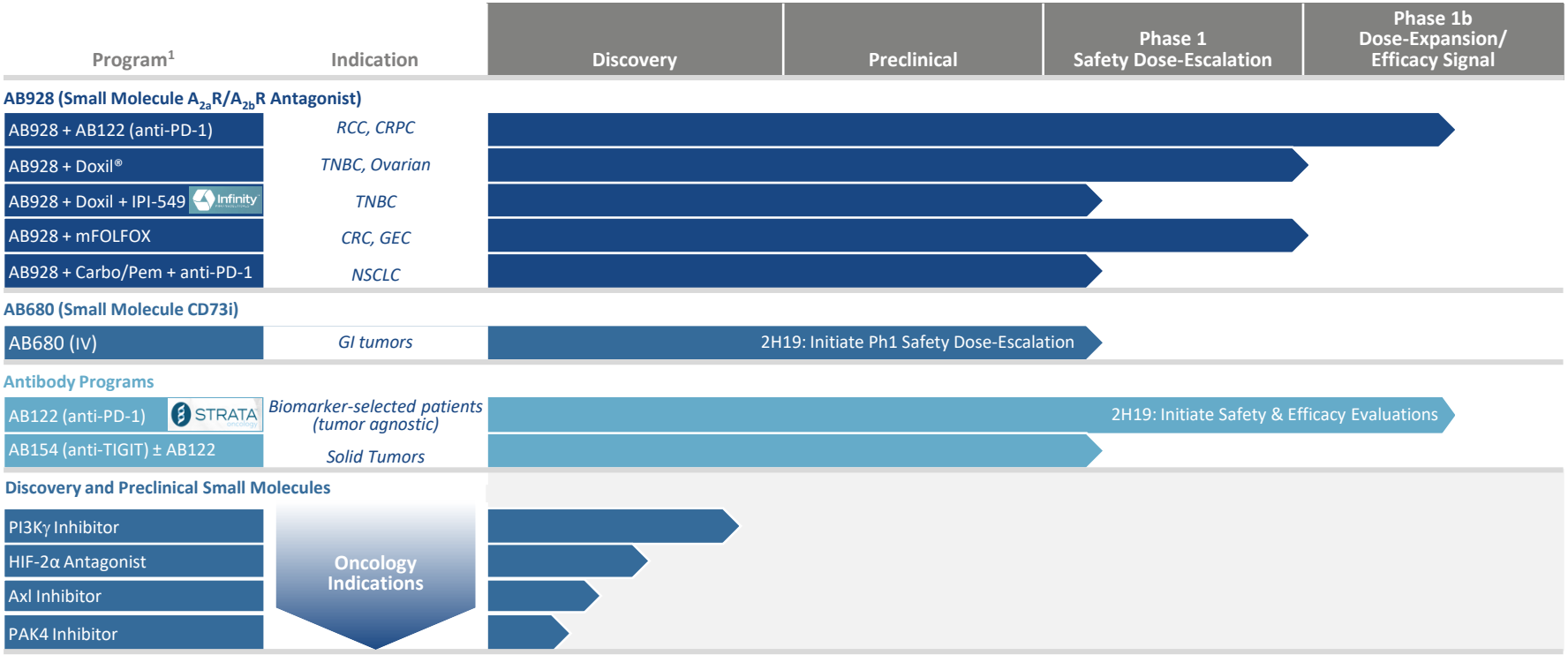


Eric Hoefer
Chief Commercial Officer

Expertise leading global immuno-oncology commercial organizations and development strategies, including the launch of 15 new medicines

AstraZeneca
Genentech
A Member of the Roche Group
Roche
INTERMUNE
GlaxoWellcome

BROAD 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.

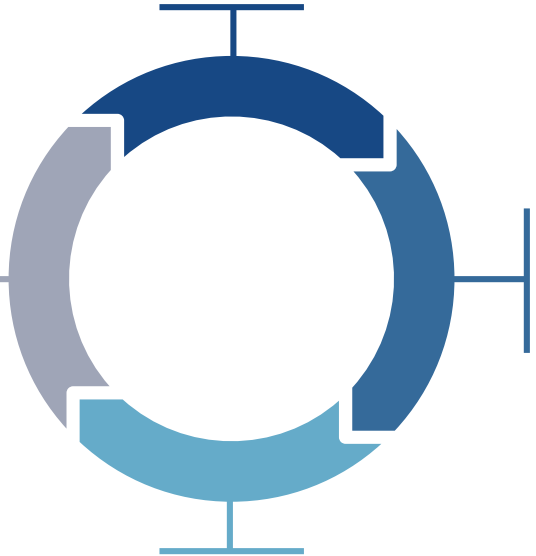
KEY PROGRAM HIGHLIGHTS

AB928	• Excellent safety, PK, PK/PD profile established in 3 combination settings • Recommended Dose for Expansion (RDE) selected as 150mg QD for first 3 combinations • Progressing into 6 dose expansion cohorts
AB680	• Excellent safety, PK, PK/PD profile in HV supports advancement into cancer patients • First study planned to start in 2H 2019 (combination in 1L Pancreatic Cancer)
AB122	• Clinically active molecule • Q2W and Q3W fixed-dose schedules selected • Backbone for several of our combination trials and moving into biomarker-selected monotherapy trial
AB154	• Phase 1 safety evaluation ongoing in combination with AB122
DISCOVERY & PRECLINICAL	• Internal small-molecule drug discovery engine • Multiple IO and cancer cell-intrinsic targets • Plan for HIF-2α inhibitor to enter clinic in mid-2020

RATIONALLY-SELECTED TUMOR INDICATIONS AND COMBINATIONS

Tumor types with high-levels of adenosine and/or CD73, or similar adenosine-related biology

Biomarker selected patient populations to enhance the potential efficacy benefit for patients and accelerate clinical development



Combinations with therapies that are expected to be complementary to targeting the CD73 adenosine axis

Indications where there continues to be significant unmet medical need

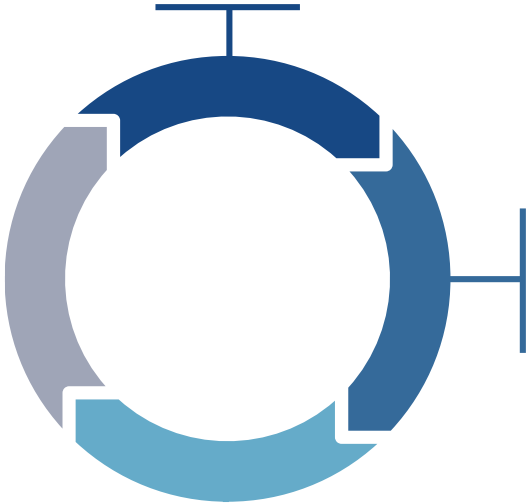
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RATIONALLY-SELECTED TUMOR INDICATIONS AND COMBINATIONS

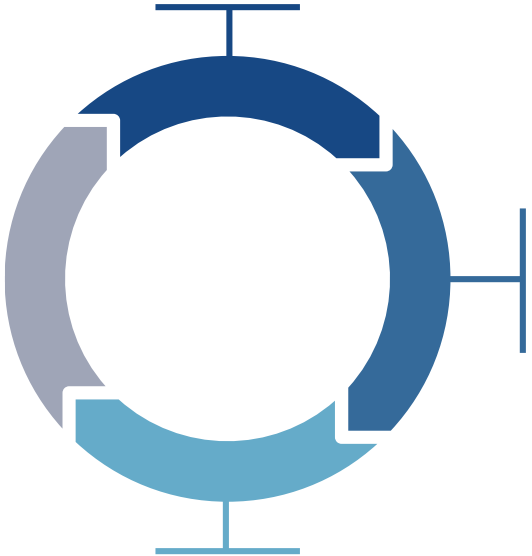
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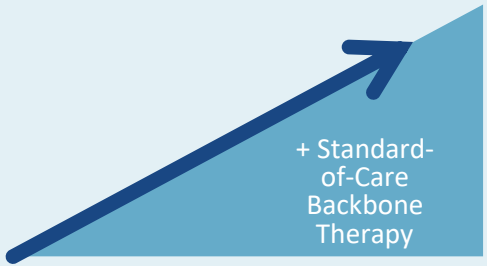
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Indications where there continues to be significant unmet medical need

CLINICAL PROGRAM OVERVIEW: GENERAL SEAMLESS CLINICAL TRIAL DESIGN

PHASE 1:
3 + 3 Safety Evaluation

Dose-escalation of AB928



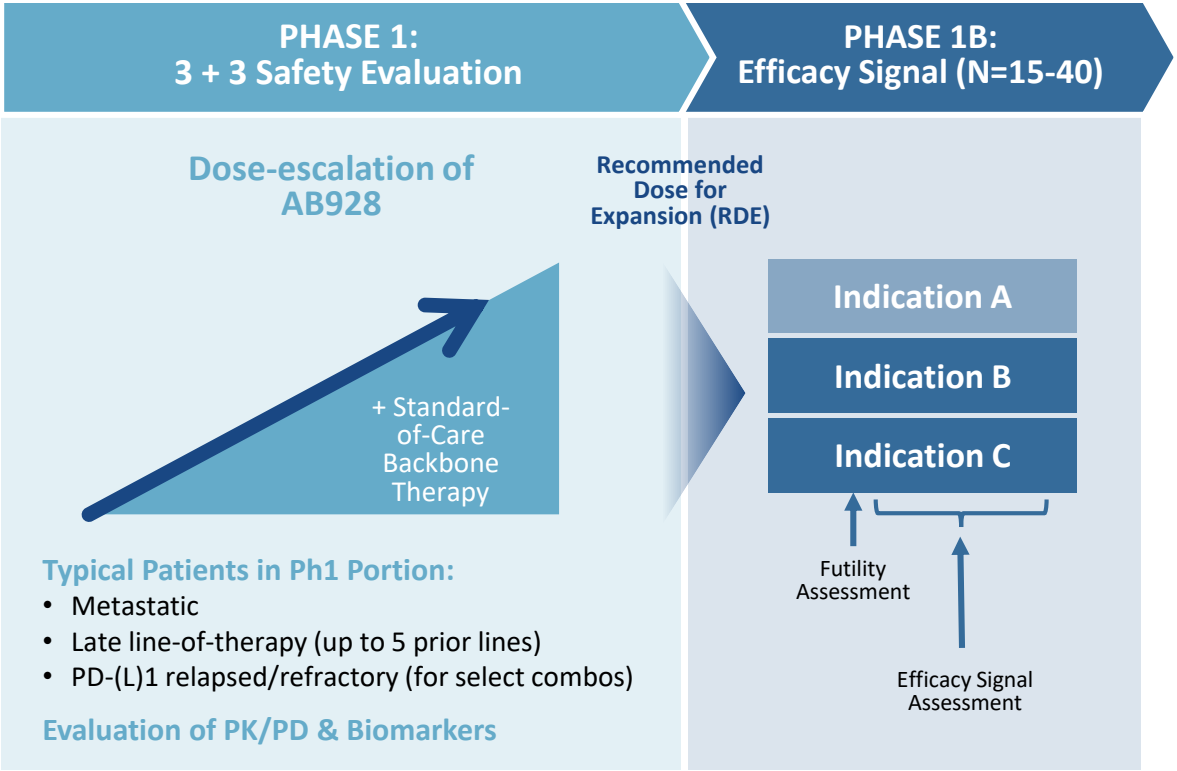
Recommended Dose for Expansion (RDE)

Typical Patients in Ph1 Portion:

- Metastatic
- Late line-of-therapy (up to 5 prior lines)
- PD-(L)1 relapsed/refractory (for select combos)

Evaluation of PK/PD & Biomarkers

CLINICAL PROGRAM OVERVIEW: GENERAL SEAMLESS CLINICAL TRIAL DESIGN

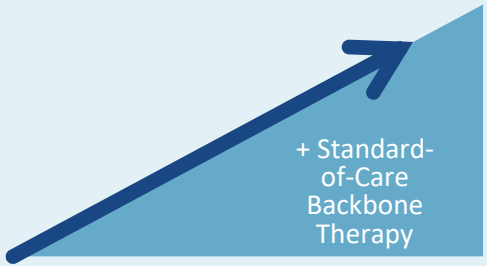


CLINICAL PROGRAM OVERVIEW: GENERAL SEAMLESS CLINICAL TRIAL DESIGN

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PHASE 1: 3 + 3 Safety Evaluation

Dose-escalation of AB928



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- Metastatic
- Late line-of-therapy (up to 5 prior lines)
- PD-(L)1 relapsed/refractory (for select combos)

Evaluation of PK/PD & Biomarkers

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

Recommended Dose for Expansion (RDE)

- Indication A
- Indication B
- Indication C

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 (eg, combination of AB928 + CD73i)

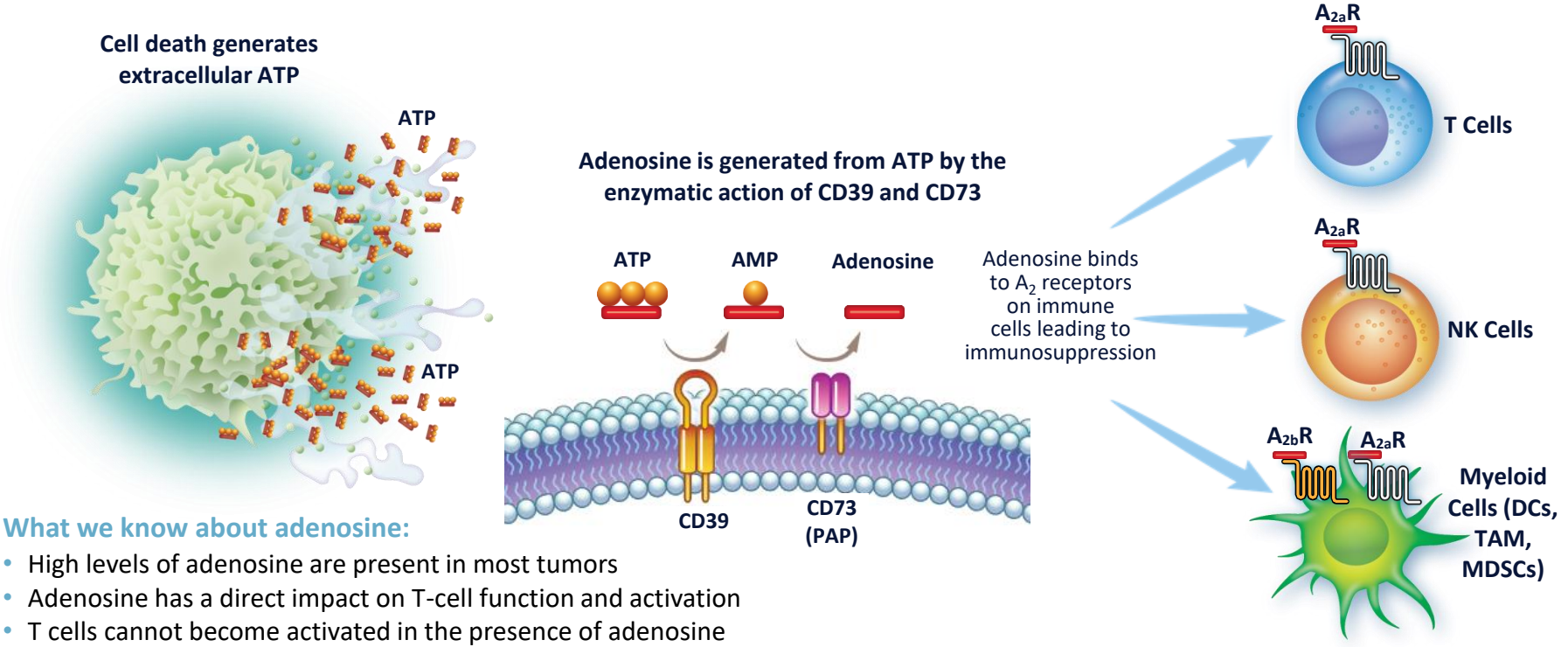


AB928

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 has a direct impact on T-cell function and activation
- T cells cannot become activated in the presence of adenosine
- CD73, the enzyme that generates adenosine, could serve as a target for therapeutic intervention as well as a biomarker for patient screening

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} and A_{2b} receptors

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

- Minimal shift in potency due to decreased non-specific protein binding
- Minimal penetration of intact blood brain barrier
- Excellent drug properties (PK, etc.)

Differentiated, highly efficient clinical development plan is 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	$A_{2a}R$ (K_B, nM)[c]	$A_{2b}R$ (K_B, nM)[c]
AB928 *(Arcus)*	**1.4**	**2.4**
CPI-444 [a,b] *(Corvus)*	5.4	493
AZD 4635 [a,b] *(AstraZeneca)*	1.7	64
NIR178 [a,b] *(Novartis)*	58	189
Preladenant [a,b] *(Merck)*	3.3	3,121

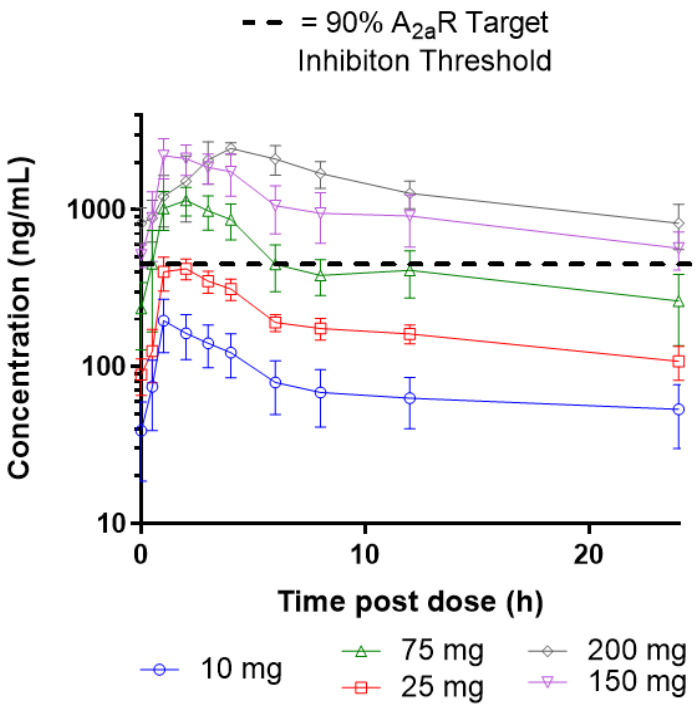
AB928 has ideal pharmacological properties for an oncology drug

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	≥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: was purchased from Ark Pharma (AK-43905).
[c] 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 75-150mg QD

Excellent Pharmacokinetic Profile*

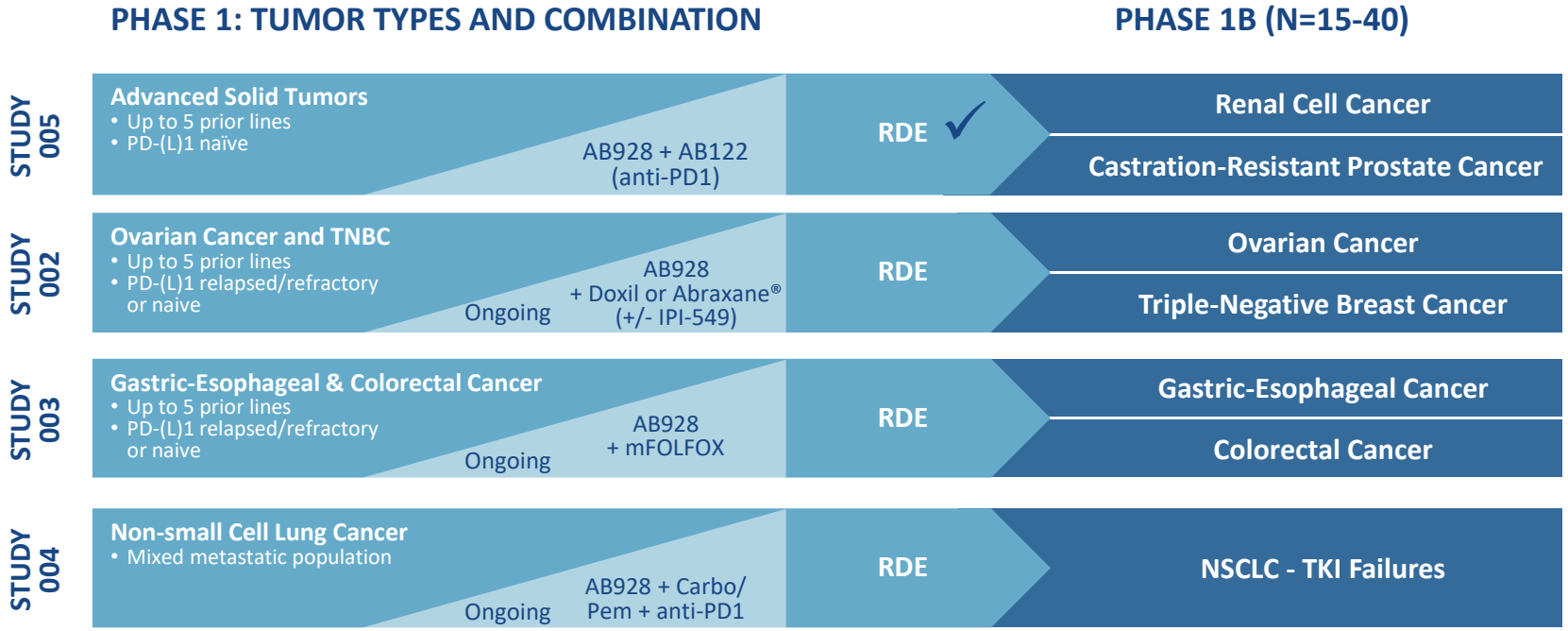


*Steady-state data shown

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	
10 mg	163	51 %	53	(12%)**	
25 mg	420	82 %	108	51 %	
75 mg	**1,148**	**100 %**	**261**	**76 %**	Ph1 Starting Dose
150 mg	**2,113**	**100 %**	**566**	**≥ 90%**	**RDE Dose**
200 mg	**1,517**	**≥ 90 %**	**819**	**≥ 90%**	Continued Evaluation

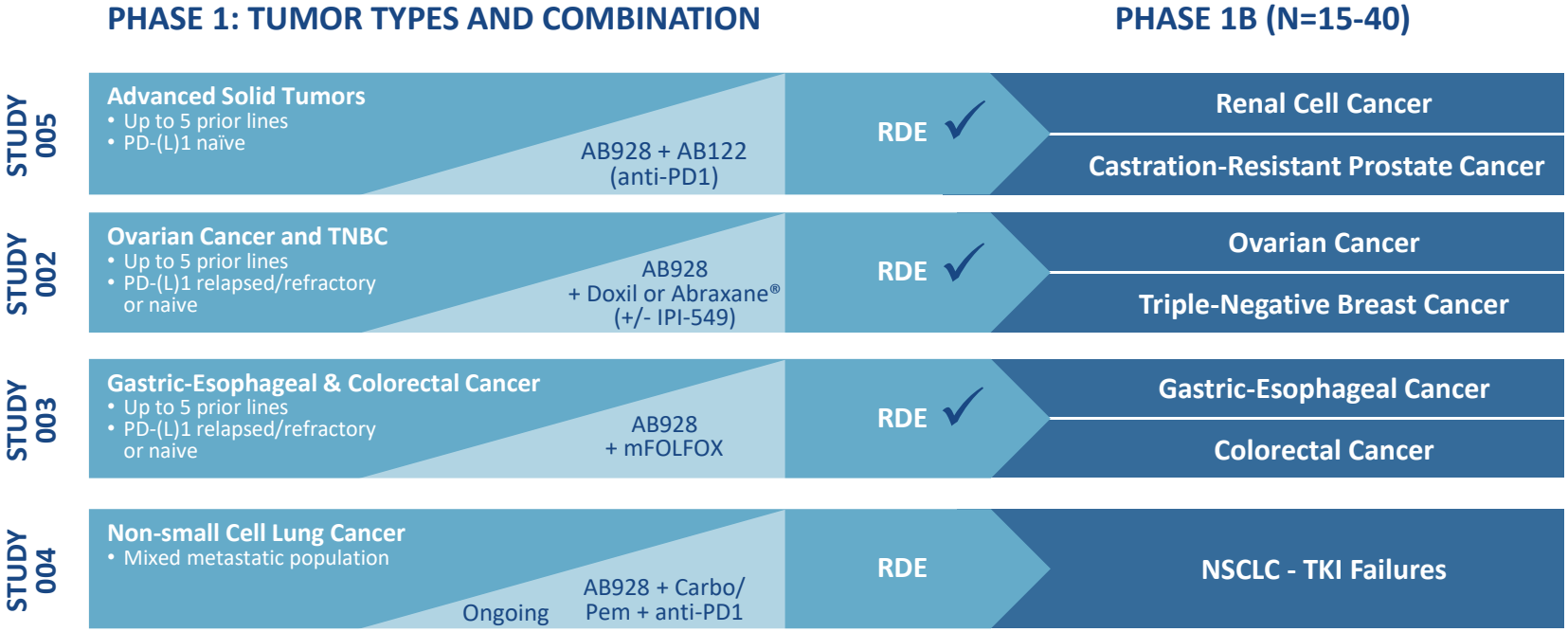
**Some or all dosed subjects were within the range of variation observed in placebo subjects (-39 to 30%).
The PK/PD and safety data from the AB928 healthy volunteer study has been published;
Seitz et al 2018 Invest. New Drugs doi: 10.1007/s10637-018-0706-6

BROAD PORTFOLIO OF AB928 CLINICAL TRIALS TARGETING HIGH ADENOSINE-CD73 TUMOR INDICATIONS



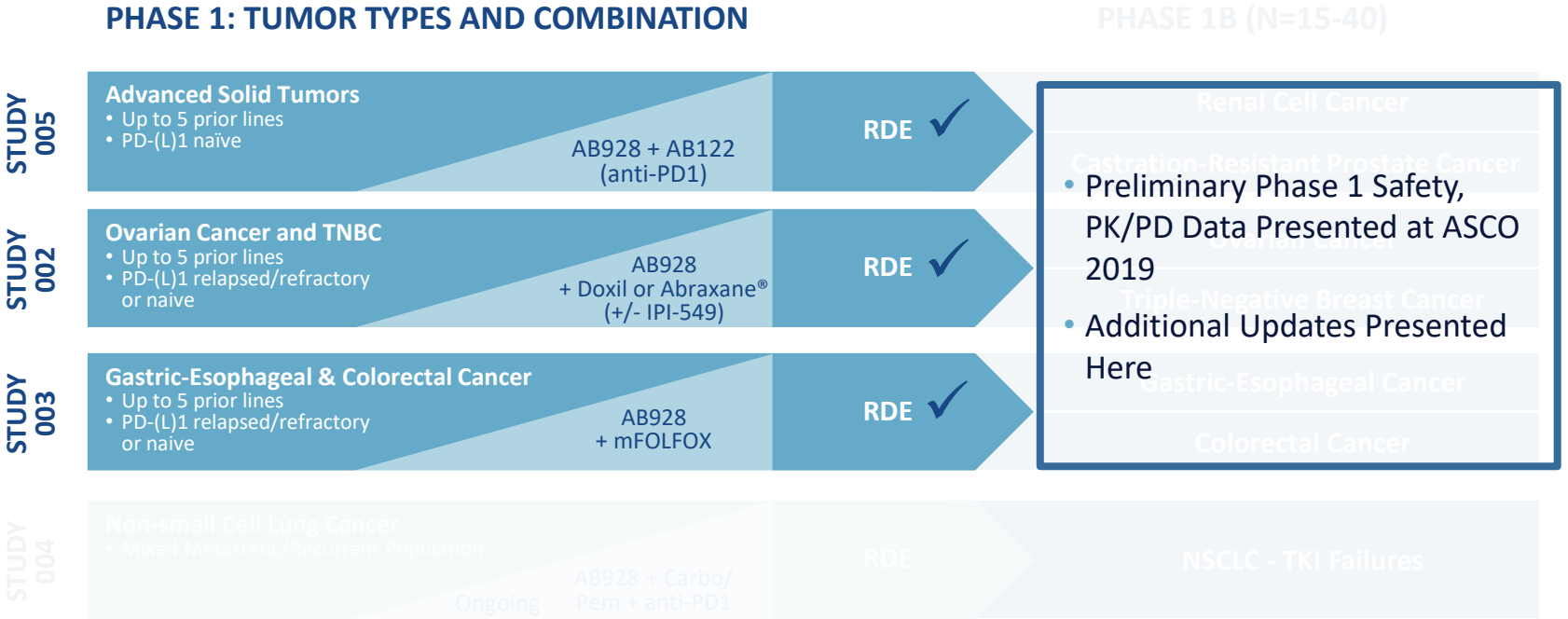
Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

POST-ASCO 2019: ADDITIONAL COMBINATIONS HAVE ESTABLISHED RECOMMENDED DOSE FOR EXPANSION



Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

BROAD AB928 PORTFOLIO OF CLINICAL TRIALS TARGETING HIGH ADENOSINE-CD73 TUMOR INDICATIONS



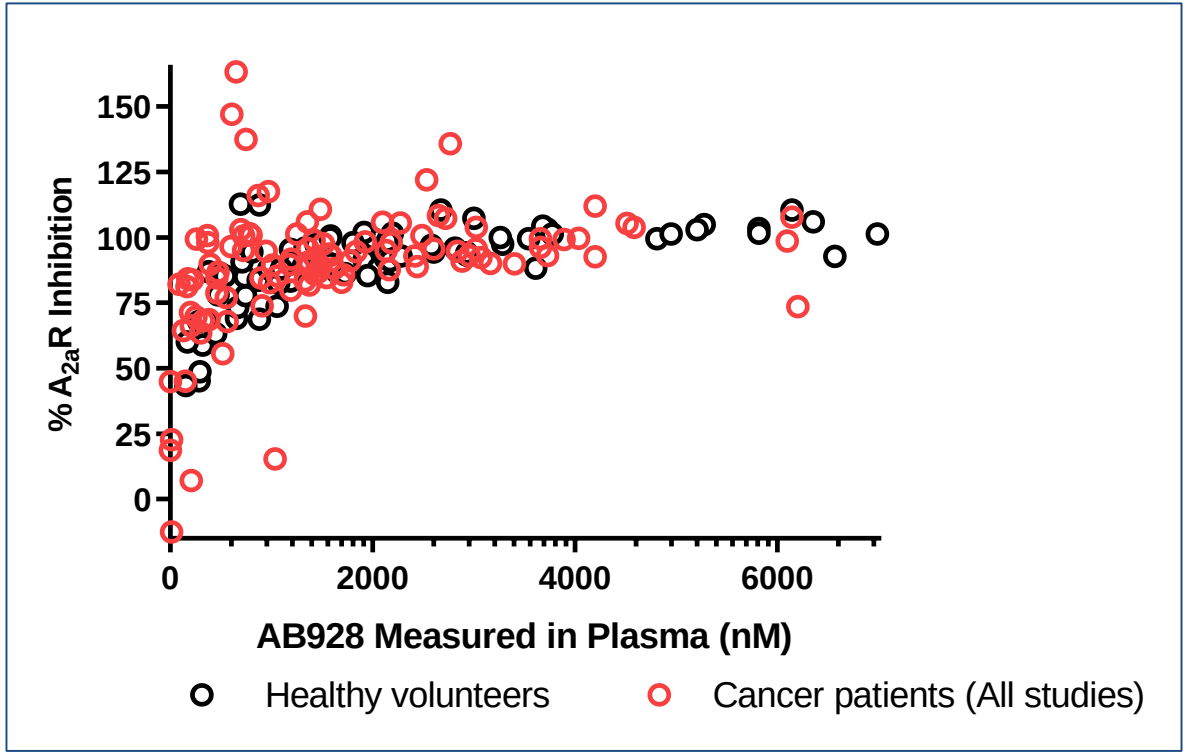
Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

PRELIMINARY AB928 PH1 SAFETY DOSE-ESCALATION DATA: CROSS-STUDY PATIENT DEMOGRAPHICS

Characteristics		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)
Median (range) age, years		66 (40-68)	68 (57-80)	52 (37-59)	55 (39-62)	62 (50-80)	73 (56-79)	64 (50-66)	71 (57-77)
Biological sex, n (%)	Female	3 (100%)	5 (100%)	2 (50%)	1 (25%)	1 (33%)	2 (67%)	5 (83%)	3 (100%)
	Male	0 (0%)	0 (0%)	2 (50%)	3 (75%)	2 (67%)	1 (33%)	1 (17%)	0 (0%)
Tumor types*		OC n=3	OC n=4, TNBC n=1	CRC n=4	CRC n=4	NSCLC n=3	OC, EC, Bladder	CRC n=3, EC n=2, NET	AP, PDAC, OC
Prior LOT (median)		3		3		N/A		2	
Time on Treatment for mITT** (range, weeks)		7.1-16.1	2.0-12.9	2.4-18.4	2.4-12.0	1.0-10.0	5.3-47	6.3-27.0	6.0-12.1

*OC=Ovarian Cancer, CRC=Colorectal Cancer, EC=Endometrial Cancer, NET=Neuroendocrine Tumor, AP=Appendiceal Cancer, PDAC=Pancreatic Ductal Adenocarcinoma; **mITT=modified intent-to-treat population; Data Cut-off 14JUN19

AB928 PK/PD: $A_{2a}R$ INHIBITION IN ONCOLOGY SUBJECTS IS EQUIVALENT TO THAT SHOWN IN HEALTHY VOLUNTEERS



PRELIMINARY AB928 PH1 SAFETY DOSE-ESCALATION DATA: CROSS-STUDY DATA

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

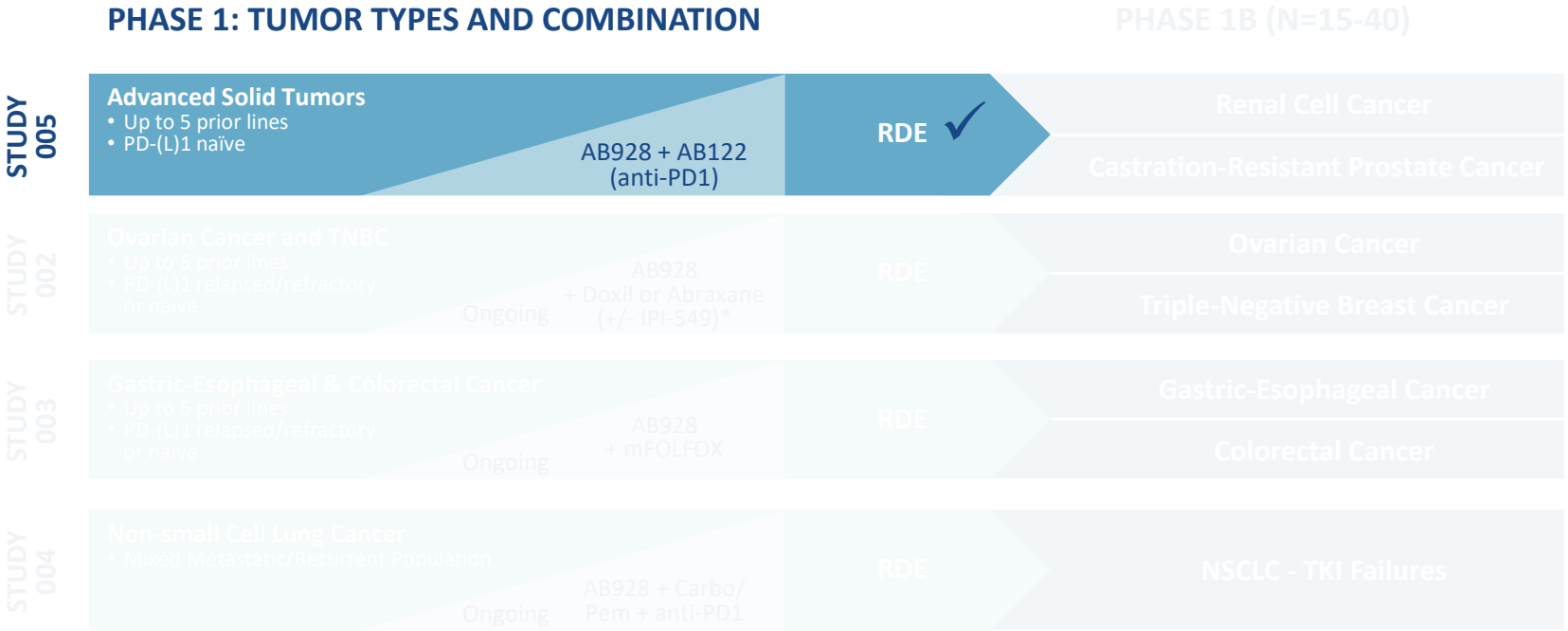
Summary of Treatment Emergent Adverse Events in AB928 Dose Escalation

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

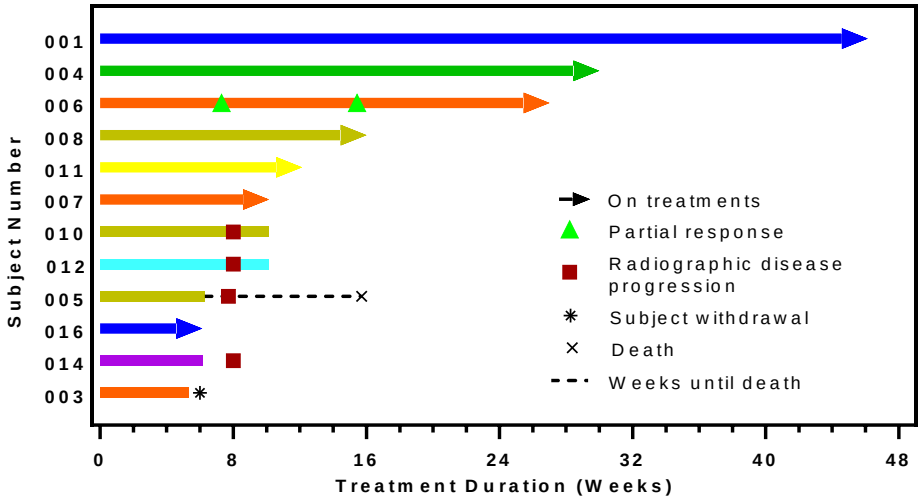
*DLT was a Gr 2 rash resulting in <80% of investigational product being delivered over the DLT period; Data Cut-off: 14JUN19

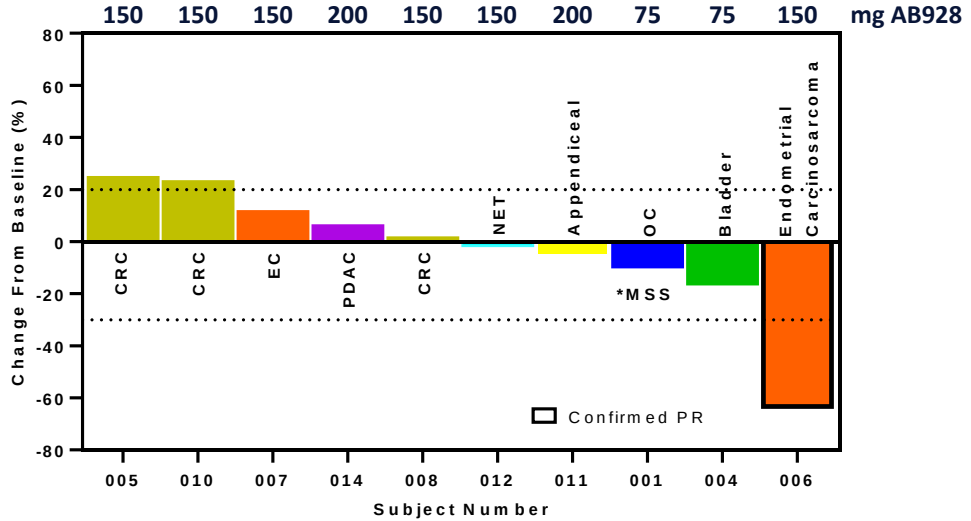
PRELIMINARY PH1 SAFETY DOSE-ESCALATION DATA: AB928 + AB122 IN ADVANCED SOLID TUMORS



Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

POST-ASCO 2019: PRELIMINARY PH1 TUMOR ASSESSMENTS: AB928 + AB122 IN ADVANCED SOLID TUMORS





- Initial clinical evaluation of AB928 + AB122 demonstrates tumor responses and disease stabilization in tumor-types generally unresponsive to monotherapy checkpoint inhibition
- Confirmed partial response in an Endometrial Carcinosarcoma subject (Malignant Mixed Mullerian Tumor), a tumor type with generally low levels of response to PD-(L)1 inhibitors

Data Cut-off: 14JUN19; Tumor Histology colors on Waterfall correspond to those of Swimlane

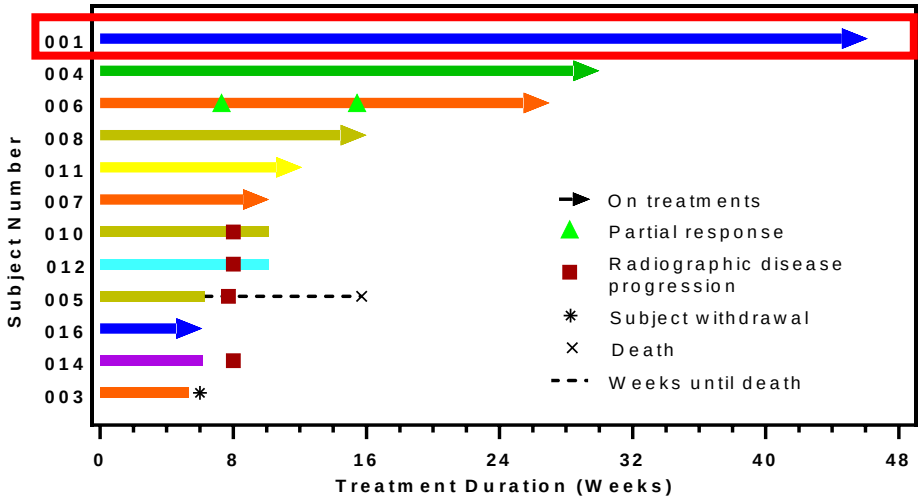
EXTENSIVE BIOMARKER PROGRAM IMPLEMENTED ACROSS AB928 TRIALS

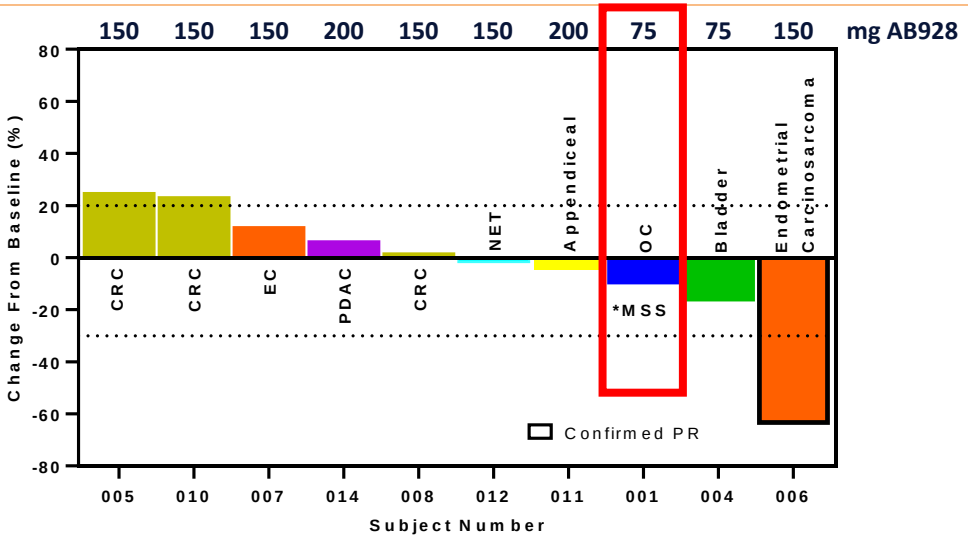
POTENTIAL PREDICTIVE BIOMARKERS	
BIOMARKER READOUT	**KEY OBJECTIVE(S)**
CD73 status • Tumor (IHC & mRNA) • Blood (ELISA & Enzymatic Assay)	• Determine relationship between CD73 expression (tumor, soluble) and clinical activity • Assess potential of CD73 biomarker as a patient selection tool
Tumor expression (mRNA) of *Adenosine Fingerprint genes**	• Assess relationship between clinical activity and various elements of this gene expression profile

IMMUNE MARKERS	
BIOMARKER READOUT	**KEY OBJECTIVE(S)**
T cell clonality (tumor & blood) • neoantigen-specific T cell clonal expansion	• Determine if tumor responses correlate with increases/changes in (neoantigen-specific) T cell populations
Immunophenotyping (blood) and serum cytokines	• Quantify activation of immune pathways • Assess effects on immune cell activity/function

* Collection of 9 proteins involved in the generation, degradation and signaling of adenosine in the tumor

CASE STUDY OF AB928 + AB122 COMBINATION: EVIDENCE OF IMMUNE RESPONSE

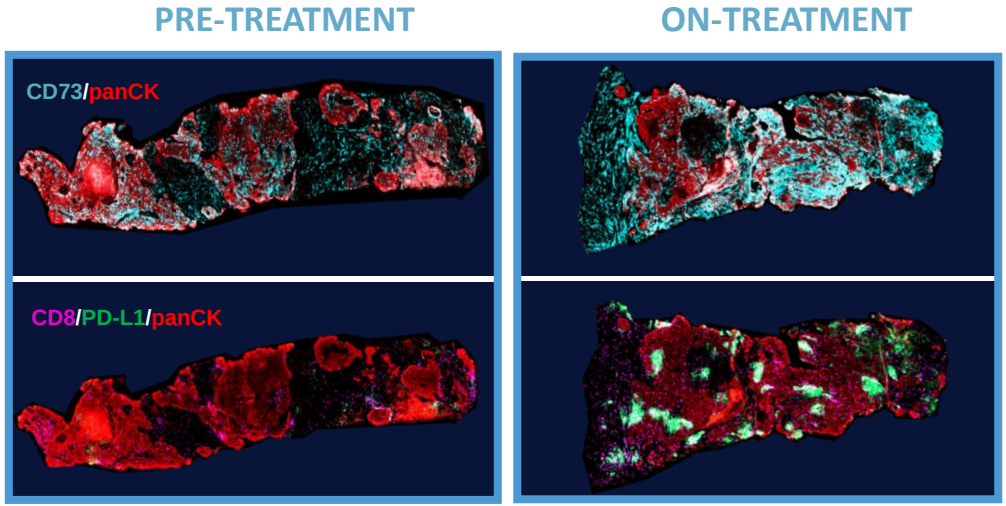




- Subject 001: Case Study of AB928 + AB122 Demonstrating Evidence of an Immune Response to the Combination

Data Cut-off: 14JUN19; Tumor Histology colors on Waterfall correspond to those of Swimlane

CASE STUDY OF AB928 + AB122 COMBINATION: EVIDENCE OF IMMUNE RESPONSE

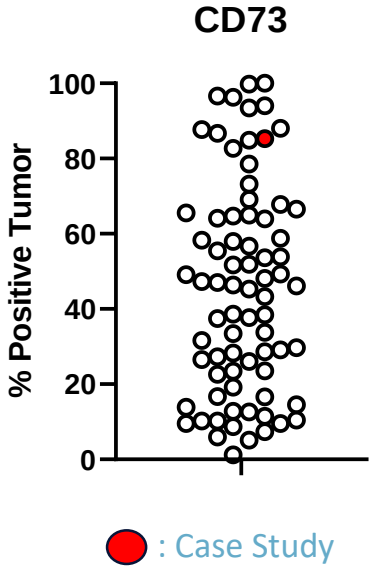


Case Report: Biomarker data is from an ovarian carcinoma subject treated with AB928 + AB122

- Diagnosed May 2016; received 3 prior lines of therapy (Carbo/PLD, PARPi, Carbo/Gemzar®) in the recurrent/metastatic setting, naïve to α-PD(L)-1 treatment
- Baseline tumor characteristics: low TMB, PD-L1 TPS 1% and CPS 4% (by 22C3), MSS
- Subject continues on-treatment (47 weeks) as of June 14th, 2019

TMB: tumor mutation burden; TPS: tumor proportion score; CPS: combined positive score; MSS: microsatellite stable

Case study has some of the highest CD73 expression relative to other ovarian cancer specimens*

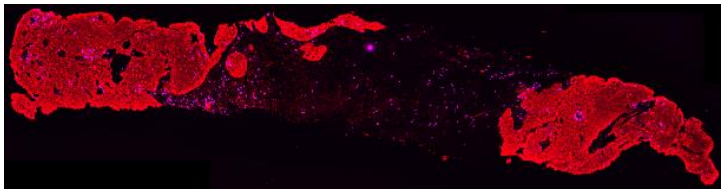


*white circles represent ovarian cancer patient samples obtained from a commercial source

CASE STUDY OF AB928 + AB122 COMBINATION: INCREASE IN ACTIVATED INTRA-TUMORAL CD8+ CELLS IN ON-TREATMENT BIOPSIES

IHC assay can distinguish CD8+ T cells within the tumor tissue (PanCK)

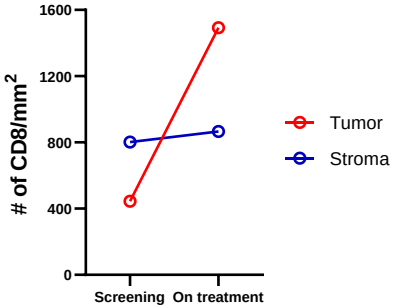
PRE-TREATMENT



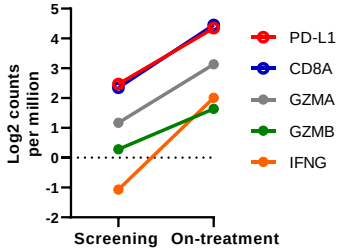
ON-TREATMENT



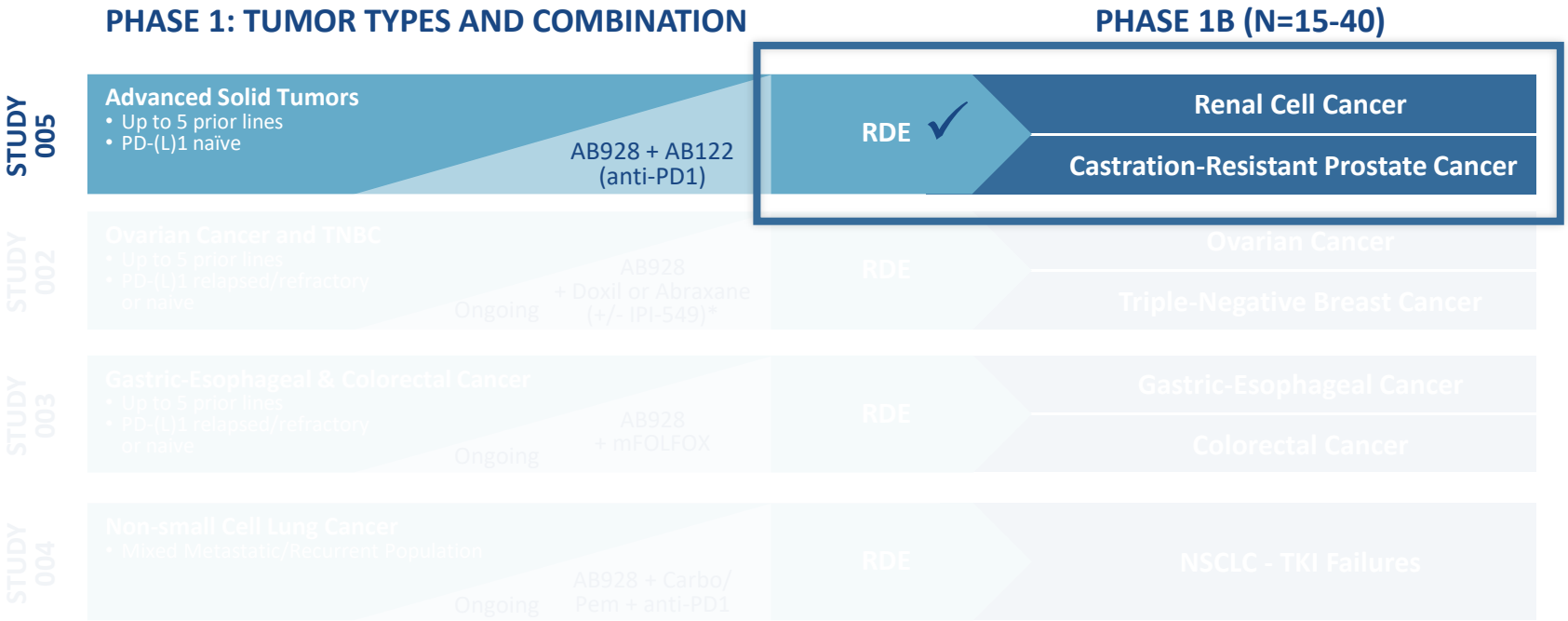
Quantification of CD8+ T cells Pre- vs. Post- treatment



AB928 + AB122 Induces Upregulation of T cell Associated Effector Genes

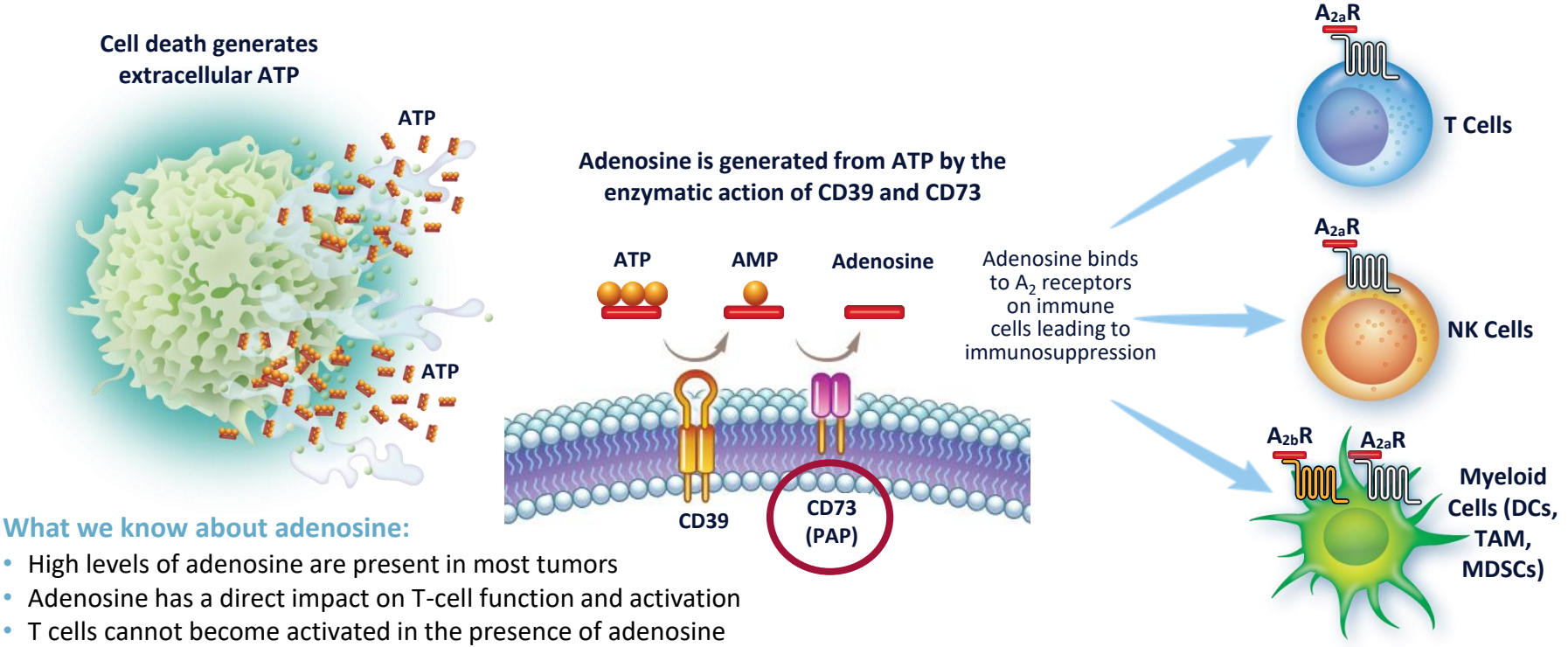


NEXT STEP: PH1B EFFICACY SIGNAL EVALUATION



Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

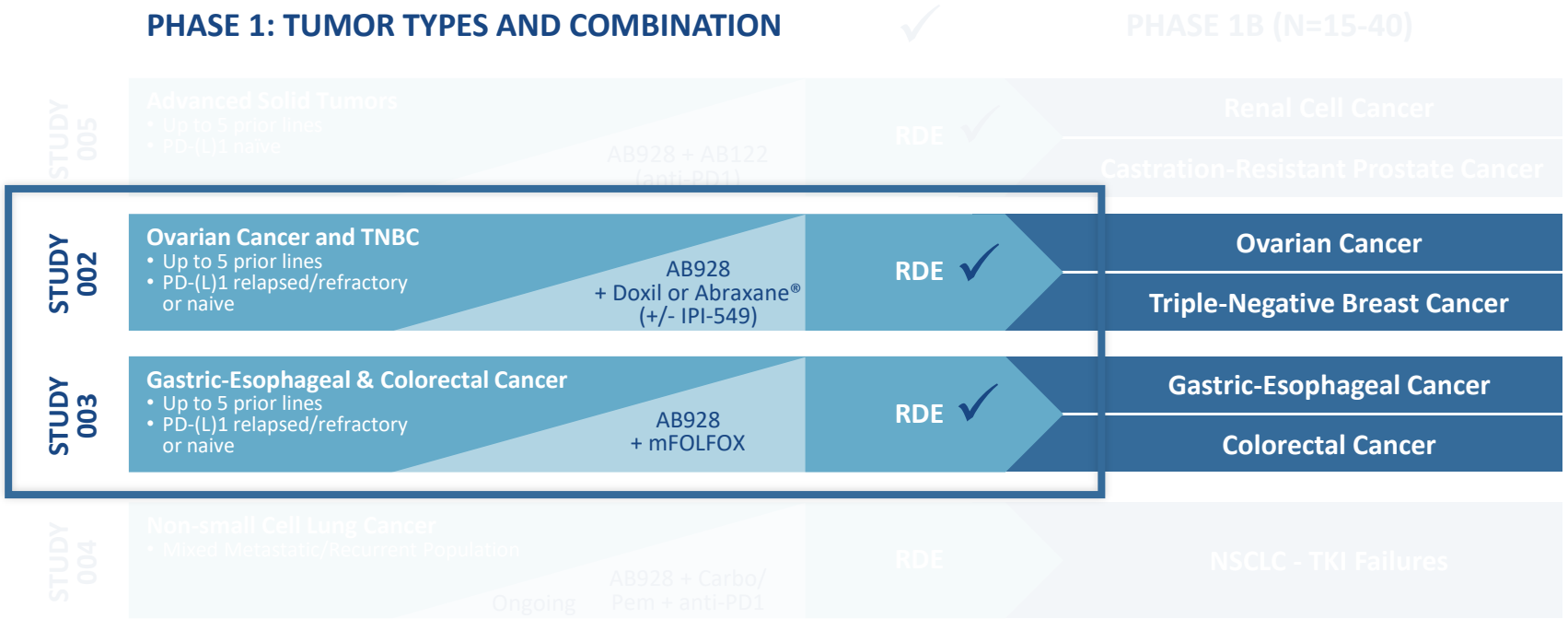
THE ATP-ADENOSINE PATHWAY PLAYS A WELL ESTABLISHED, CRITICAL ROLE IN IMMUNE SUPPRESSION



What we know about adenosine:

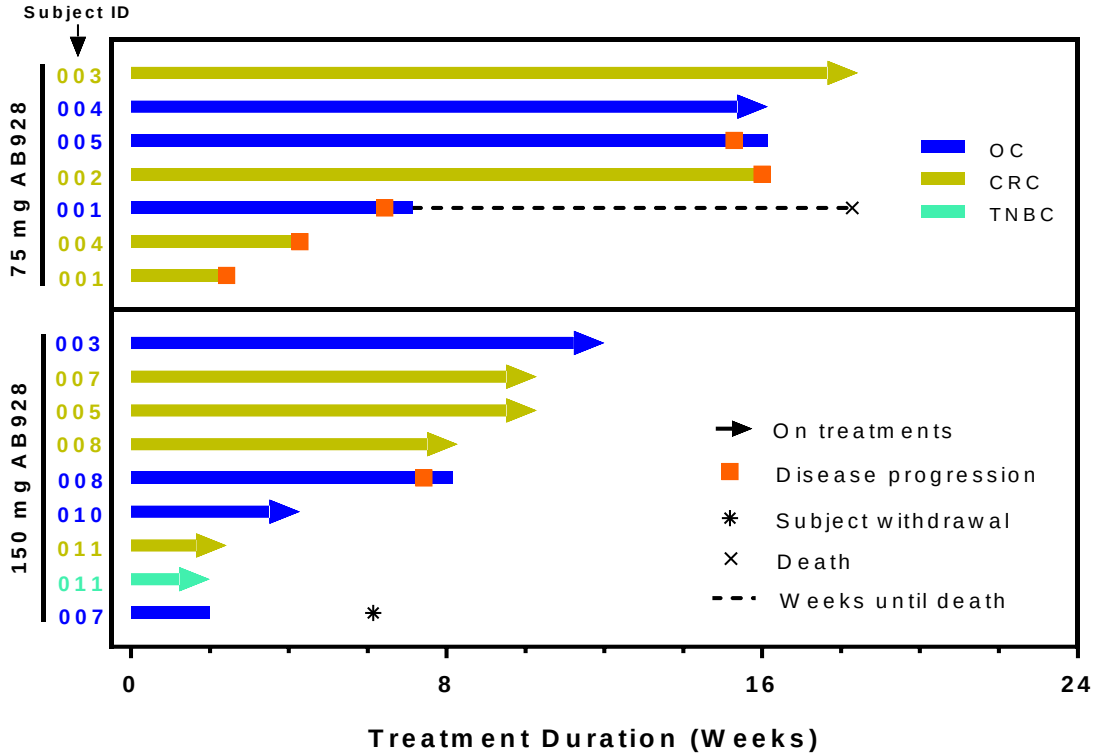
- High levels of adenosine are present in most tumors
- Adenosine has a direct impact on T-cell function and activation
- T cells cannot become activated in the presence of adenosine
- CD73, the enzyme that generates adenosine, could serve as a target for therapeutic intervention as well as a biomarker for patient screening

POST-ASCO 2019 UPDATE: PRELIMINARY PH1 SAFETY DOSE-ESCALATION FOLLOW-UP OF AB928-002 (AB928 + DOXIL) AND AB928-003 (AB928 + mFOLFOX)



Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

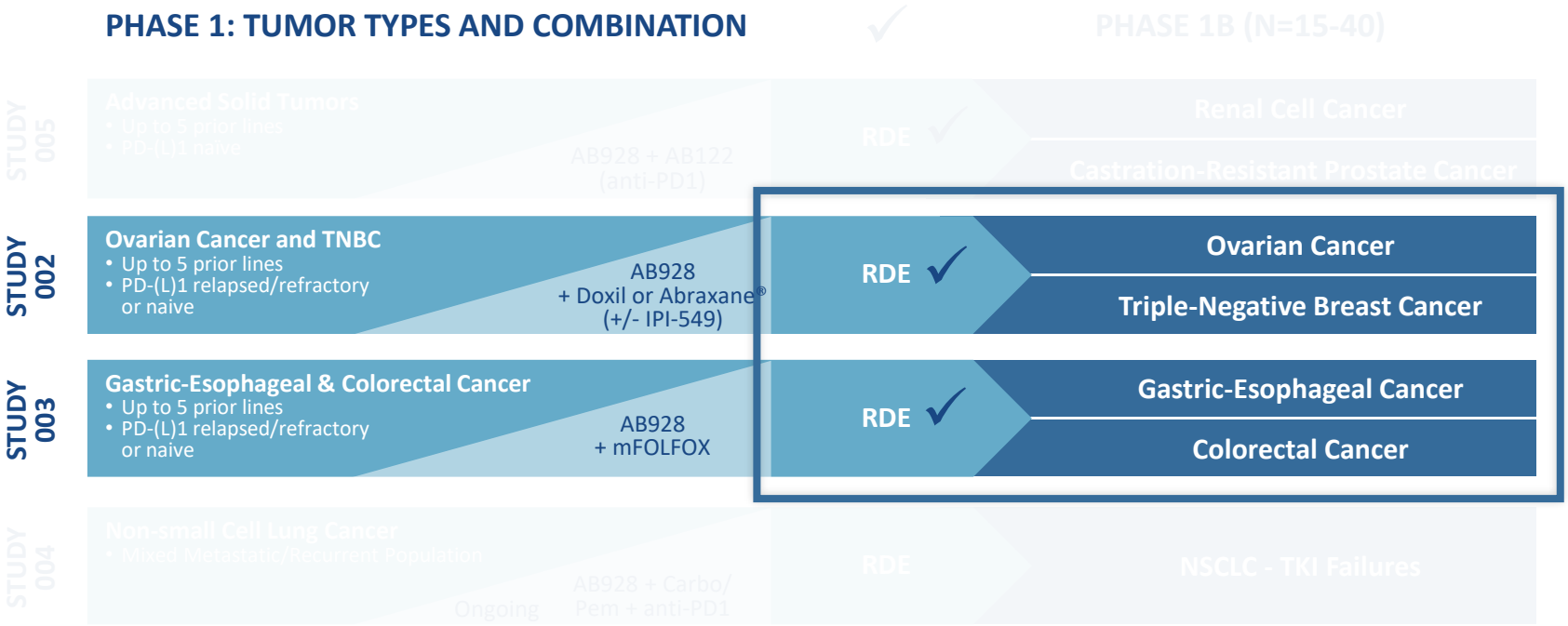
POST-ASCO 2019: PRELIMINARY PH1 TIME ON TREATMENT FOR AB928-002 (AB928 + DOXIL) AND AB928-003 (AB928 + mFOLFOX)



- Preliminary phase 1 safety evaluation of AB928 + Doxil and AB928 + mFOLFOX illustrates participants early in their course of treatment, with the majority of subjects still on therapy

Data Cut-off: 14JUN19

NEXT STEPS FOR STUDIES AB928-002 & 003: PH1B EFFICACY SIGNAL EVALUATION



Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

PHASE 1 SAFETY DOSE-ESCALATION FOLLOW-UP: AB928 + CARBO/PEM + ANTI-PD-1 IN NON-SMALL CELL LUNG CANCER

PHASE 1: TUMOR TYPES AND COMBINATION

PHASE 1B (N=15-40)

STUDY 005	Advanced Solid Tumors • Up to 5 prior lines • PD-(L)1 naive	AB928 + AB122 (anti-PD1)	RDE	Renal Cell Cancer Castration-Resistant Prostate Cancer
STUDY 002	Ovarian Cancer and TNBC • Up to 5 prior lines • PD-(L)1 relapsed/refractory or naive	Ongoing AB928 + Doxil or Abraxane (+/- IPI-549)*	RDE	Ovarian Cancer Triple-Negative Breast Cancer
STUDY 003	Gastric-Esophageal & Colorectal Cancer • Up to 5 prior lines • PD-(L)1 relapsed/refractory or naive	Ongoing AB928 + mFOLFOX	RDE	Gastric-Esophageal Cancer Colorectal Cancer
STUDY 004	**Non-small Cell Lung Cancer** • Mixed metastatic population	Ongoing AB928 + Carbo/ Pem + anti-PD1	**RDE**	**NSCLC - TKI Failures**

Mature Data expected for Dose-Escalation Cohorts in 2H-2019 & Preliminary Data expected for Dose Expansion Cohorts in 1H-2020

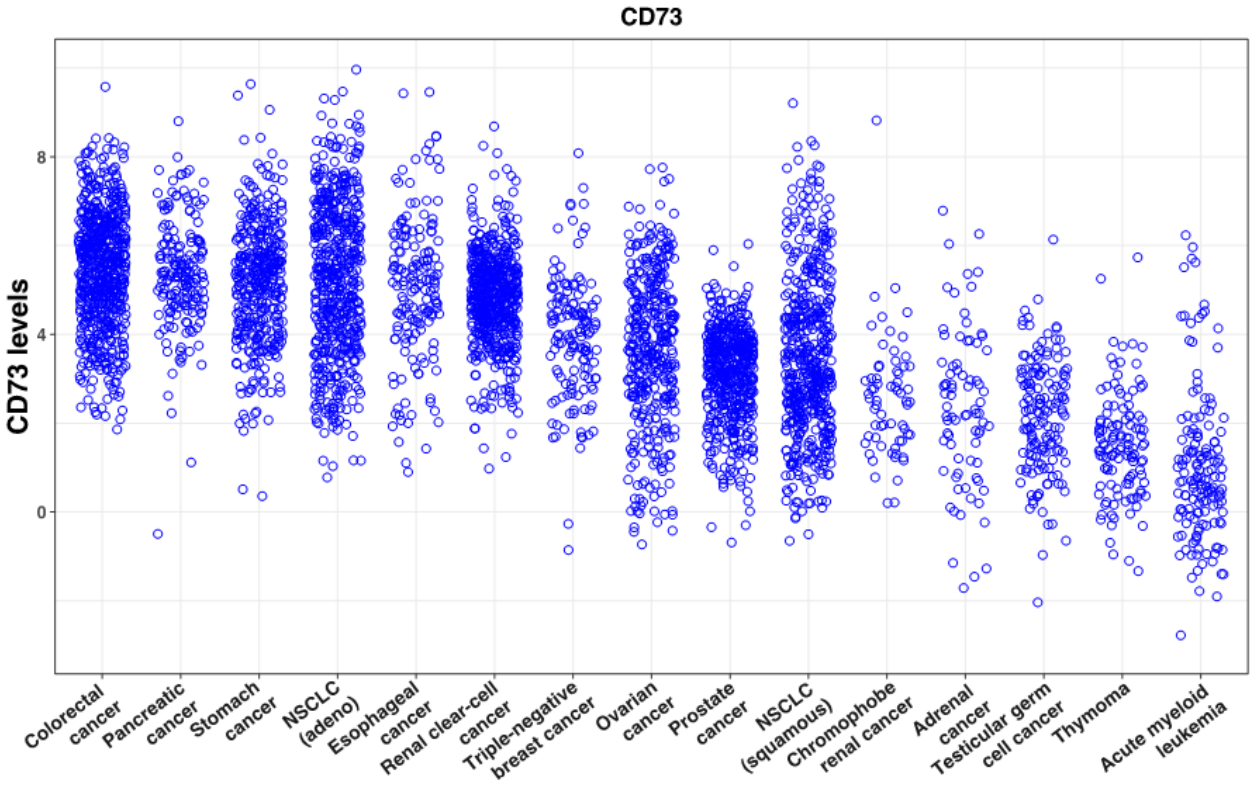


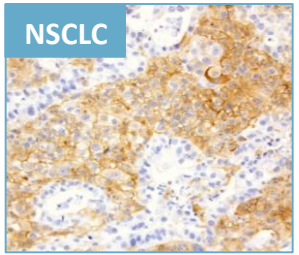
AB680

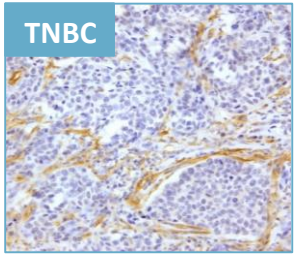
SMALL MOLECULE CD73 INHIBITOR

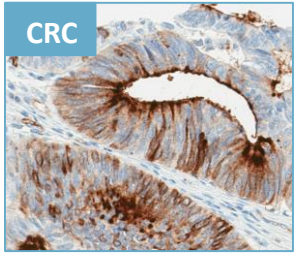
ARCUS BIOSCIENCES

CD73 IS BROADLY EXPRESSED ON MULTIPLE TUMOR TYPES



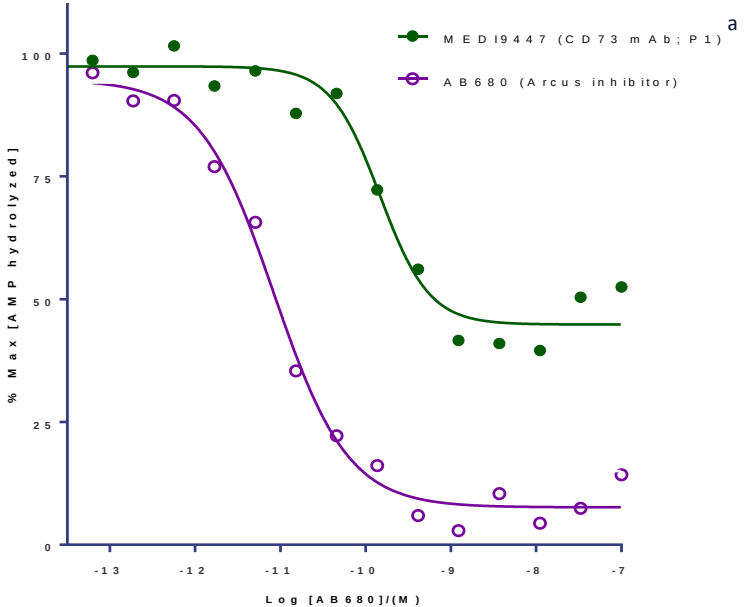






AB680: FIRST SMALL-MOLECULE CD73 INHIBITOR TO ENTER CLINICAL DEVELOPMENT

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.

ARCUS BIOSCIENCES

AB680 OVERVIEW

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

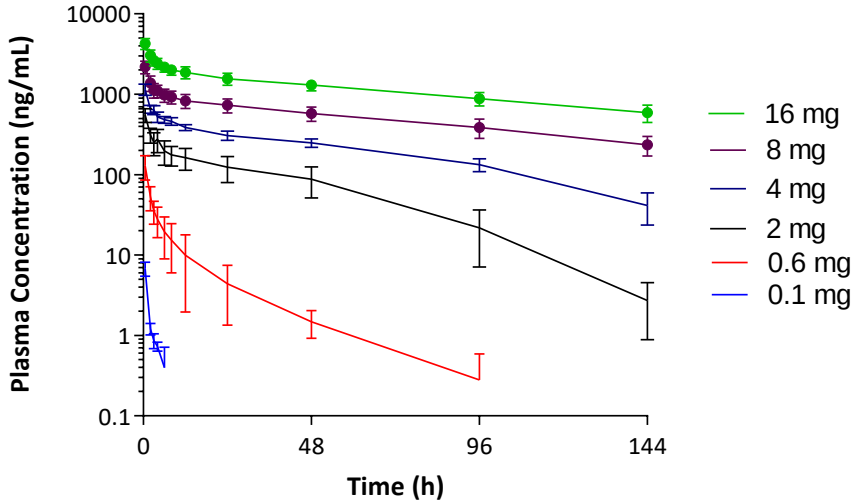
- Greater inhibition of CD73 enzymatic activity (soluble & cell-bound)
- Deeper tumor penetration
- IV + oral formulations

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 HAS A HALF-LIFE OF ~4 DAYS IN HEALTHY VOLUNTEERS



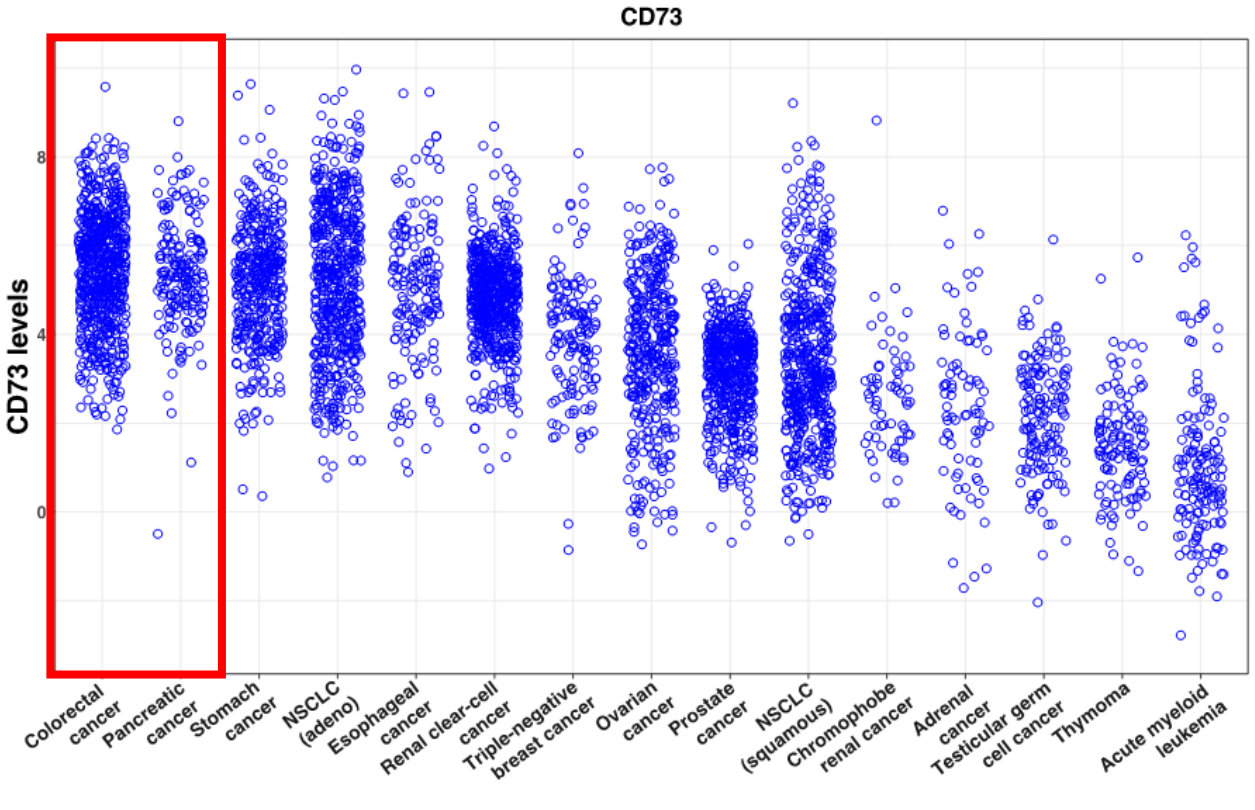
Dose (mg)	Effective $T_{1/2}$ (h)
16	85
8	74
4	34
2	21
0.6	20
0.1	4

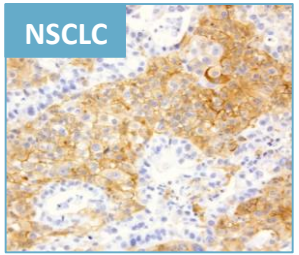
Design: Blinded, Healthy Volunteer study; n=6 participants dosed with AB680, and n=2 dosed with placebo

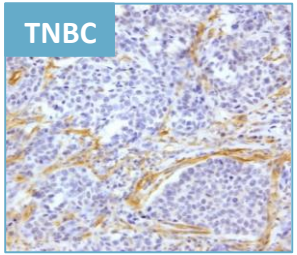
Initial Results: Higher doses support a $T_{½}$ of 4 days and Q2W dosing with favorable safety profile across all cohorts

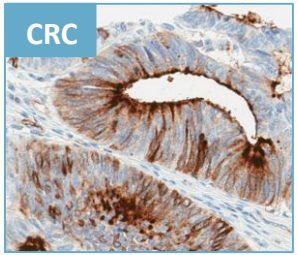
16 and 8 mg dose plasma levels measured at Arcus; remaining values determined at CRO (Covance)

CD73 IS BROADLY EXPRESSED ON MULTIPLE TUMOR TYPES

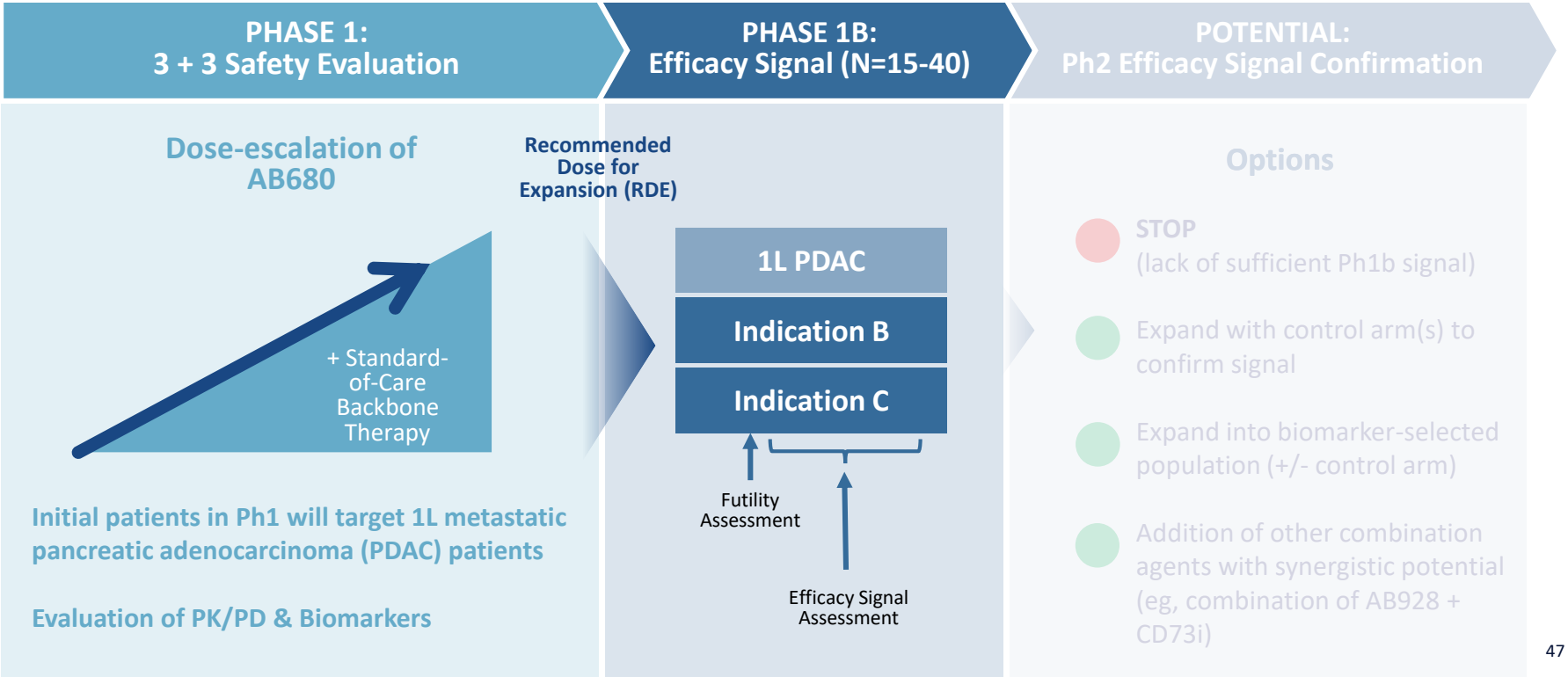








AB680: INITIAL STUDY TARGETING FIRST-LINE PANCREATIC CANCER



*Pending FDA Clearance (IND Submitted)



AB122

ANTI-PD-1 ANTIBODY

ARCUS BIOSCIENCES

AB122: ANTI-PD-1 ANTIBODY WITH PROPERTIES SIMILAR TO THOSE OF APPROVED AGENTS

- **Fully human antibody similar to pembrolizumab and nivolumab, with clinical monotherapy activity**

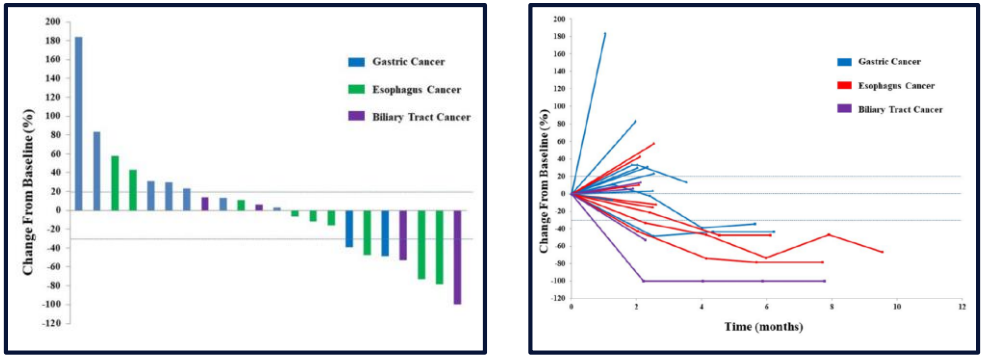
- **Key elements of our strategy for AB122 include:**
  1. Maximizing our development and commercial control over PD-1 containing combinations with our proprietary drug combinations
  2. Pursuing targeted opportunities to obtain approval for AB122

Strata Collaboration: Strategic biomarker-driven basket trial to evaluate AB122 in molecularly defined patient populations



GLORIA BIOSCIENCES: INTERIM CLINICAL STUDY RESULTS OF GLS-010 (AB122) IN ADVANCED GI TUMORS & RELAPSED/ REFRACTORY CLASSICAL HODGKIN'S LYMPHOMA (R/R CHL)

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



ASCO GI, 2019

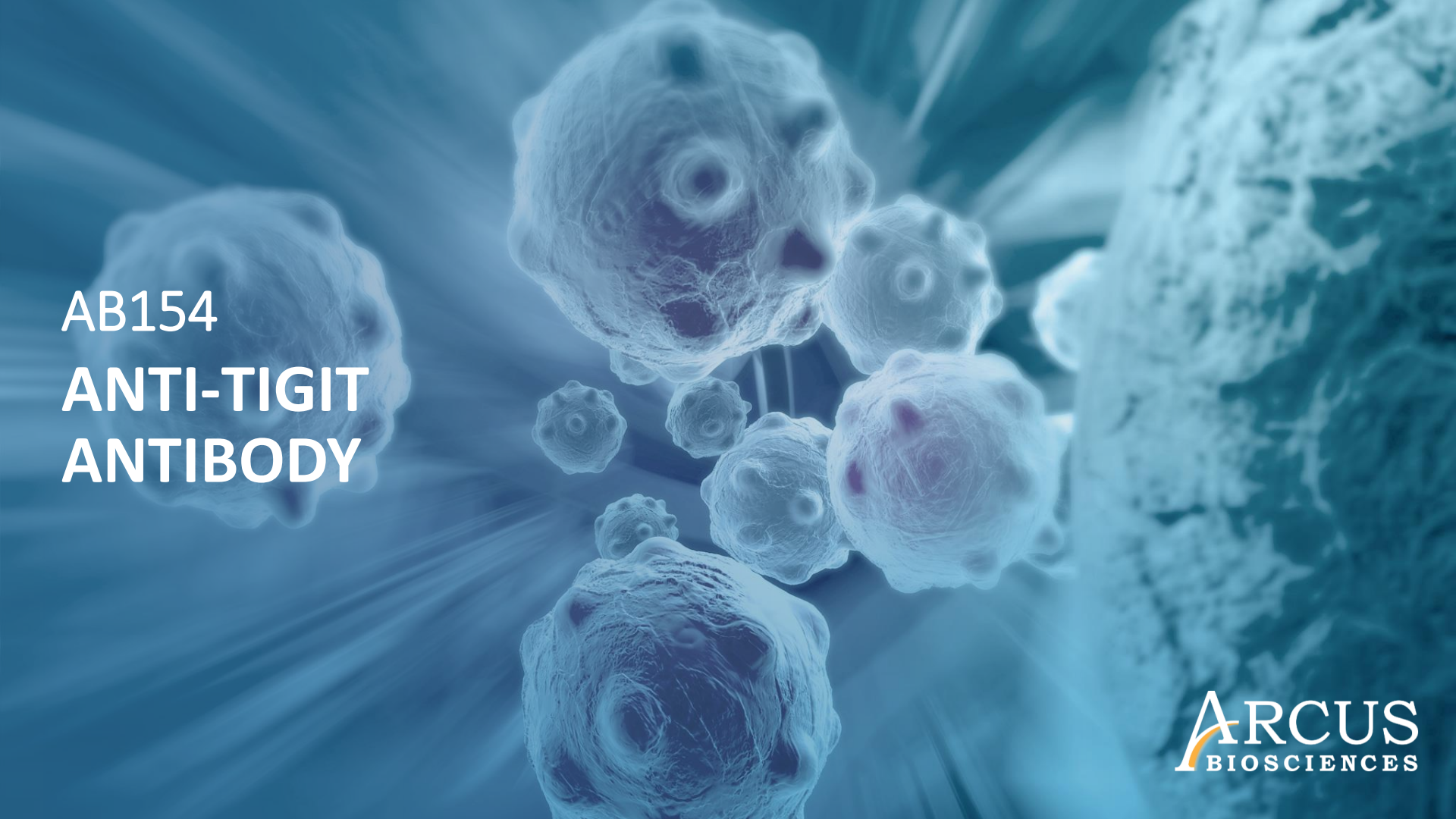
Best overall response rates:

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

ASCO 2019 Update: Ph2 Trial in r/r cHL

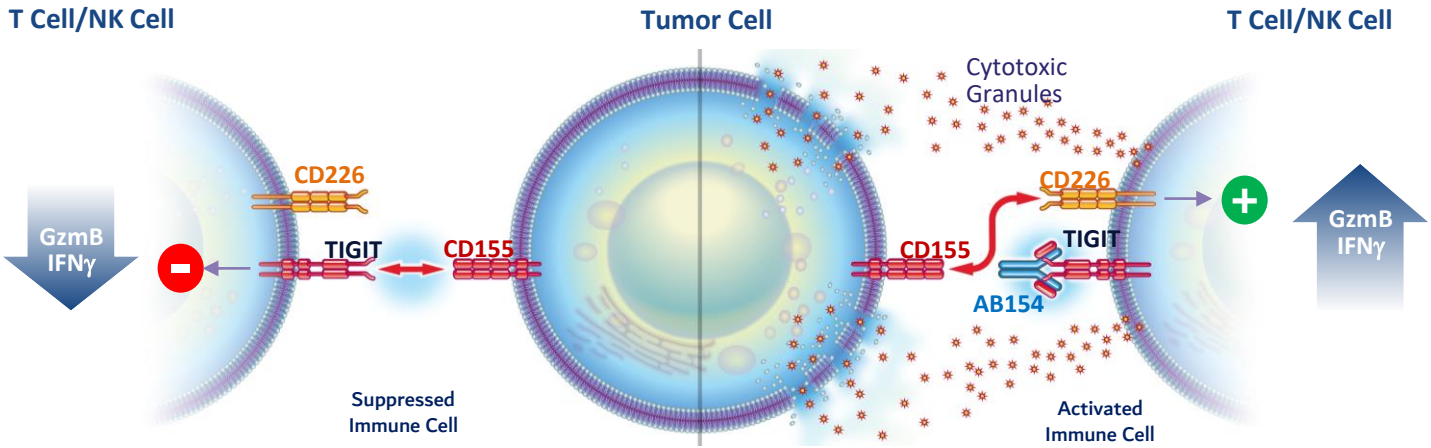
- Ongoing Phase 2 clinical trial in Chinese r/r cHL patients (pts)
- All pts enrolled received GLS-010 240mg every 2 weeks
- 39 pts were enrolled in this ongoing study
- Of 17 evaluable subjects, an objective response was reported in 15 patients (88.3%):
  - 4 pts (23.5%) with a complete response (CR)
  - 11 pts(64.7%) with a partial response (PR)
- Safety profile was similar to that previously reported PD-(L)1 inhibitors in r/r cHL

Studies are being conducted independent of Arcus Biosciences


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



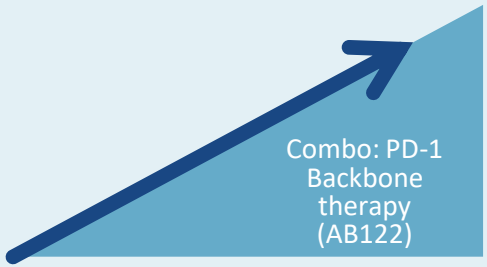
- AB154 is a humanized anti-TIGIT antibody designed to lack effector function
- AB154 reverses immune inhibition and provides tumor-selective immune stimulation
- Experiments in immune assays demonstrate synergy with AB680 (CD73) and AB122 (anti-PD-1)

AB154: INITIAL STUDY TARGETING SOLID TUMORS

PLANNED STUDY DESIGN

PHASE 1: 3 + 3 Safety Evaluation

Dose-escalation of AB154 Monotherapy



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)

- Head and Neck Squamous Cell Carcinoma
- Non-Small Cell Lung Cancer
- Triple Negative Breast

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

CLINICAL STUDY SUMMARY

Significant advancement is being made with our clinical assets

1. **AB928 ($A_{2a}R/A_{2b}R$ dual antagonist):**
   - Confirmed PK & PK/PD correlation from Healthy Volunteer study in oncology patients
   - Established early favorable safety profile in multiple combination backbones, including chemotherapies and our own anti-PD-1 antibody (AB122)
   - Recommended doses for expansion have been established in 3 of our first 4 combinations, and enrollment in the Ph1b clinical signal phases will start in early 2H of 2019
   - Initial clinical combination signals expected to emerge during the 2H of 2019/early 1H of 2020
2. **AB680 (CD73 small molecule inhibitor):**
   - First combination study in 1L pancreatic cancer planned to start in the 2H of 2019
3. **AB122 (anti-PD-1 Antibody):**
   - Established Q2W and Q3W dose-schedules
   - Advancing into safety & signal-seeking combinations (with AB154 and AB928) starting in the 2H of 2019
   - Initiating monotherapy biomarker-targeted study in 2H of 2019
4. **AB154 (anti-TIGIT Antibody):**
   - Initial dose established to take into Ph1 safety-escalation evaluation in combination with AB122

EVOLUTION OF DISCOVERY PORTFOLIO

FIRST WAVE OF PROGRAMS
addressed important elements of tumor microenvironment-induced immunosuppression

- Adenosine pathway: $A_{2a}R/A_{2b}R$; CD73
- TIGIT
- PI3Kγ

SECOND WAVE OF TARGETS
aim to enhance immune activation; convert cold → hot tumors

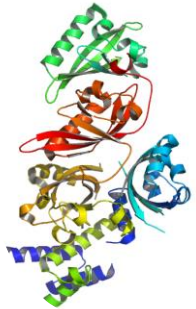
- PAK4

CELL-INTRINSIC PATHWAYS
with high intra-portfolio combinatorial potential

- HIF-2α
- Axl

HIF-2α PROGRAM UPDATE

HIF-2α



PDB=6E3S

Target Rationale:

- Constitutive activation of HIF-2α via gain-of-function mutations or defective pVHL induces expression of multiple pro-tumor genes (e.g., VEGF) and drives a variety of human cancers, including RCC
- High potential for intra-portfolio combinations
- Recent clinical POC generated by competitor compound

Program Status:

- Arcus team has extensive expertise in transcription factor drug discovery (Tularik) → extensive compound characterization pipeline
- Novel chemical series identified by Arcus chemists
- Goal is to identify a potentially best-in-class development candidate by YE2019 and advance into clinical trials by mid 2020

PI3Kγ PROGRAM UPDATE

PI3Kγ



PDB=4PS8

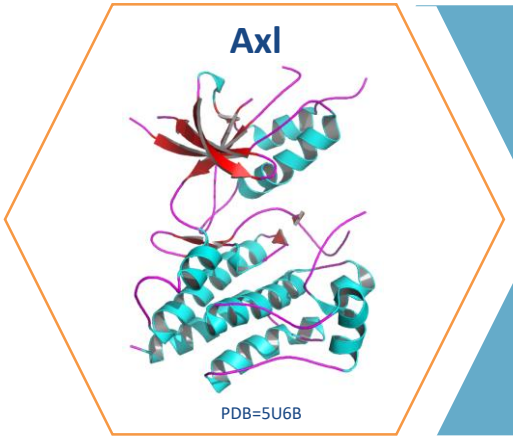
Target Rationale:

- Immunosuppressive tumor-infiltrating macrophages (TAM) require PI3Kγ
- Inhibition of this target is expected to diminish the number and suppressive activity of TAM in tumors with a significant myeloid infiltrate (e.g., PDAC, TNBC)

Program Status:

- Ongoing clinical collaboration with Infinity (AB928 + Doxil + IPI-549 in TNBC) may give us first glimpse at combinatorial potential of this pathway
- Anticipate selection of a high-quality development candidate in mid-2019
- Timing of FIH for Arcus compound will be linked to external data clinically validating the target

AXL PROGRAM UPDATE



Target Rationale:

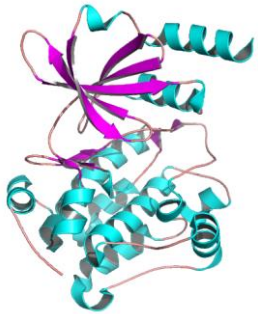
- Axl supports epithelial-mesenchymal transition (EMT), an important process in tumorigenesis
- Axl is a tyrosine kinase over-expressed by many cancers that have become resistant to chemotherapy and IO agents

Program Status:

- Novel, potent, chemical matter identified by Arcus chemists
- Sub-nM, selective molecules in hand
- Goal is to identify a potentially best-in-class development candidate in 1H2020
- Potential FIH in late 2020

PAK4 PROGRAM UPDATE

PAK4



PDB=5XVG

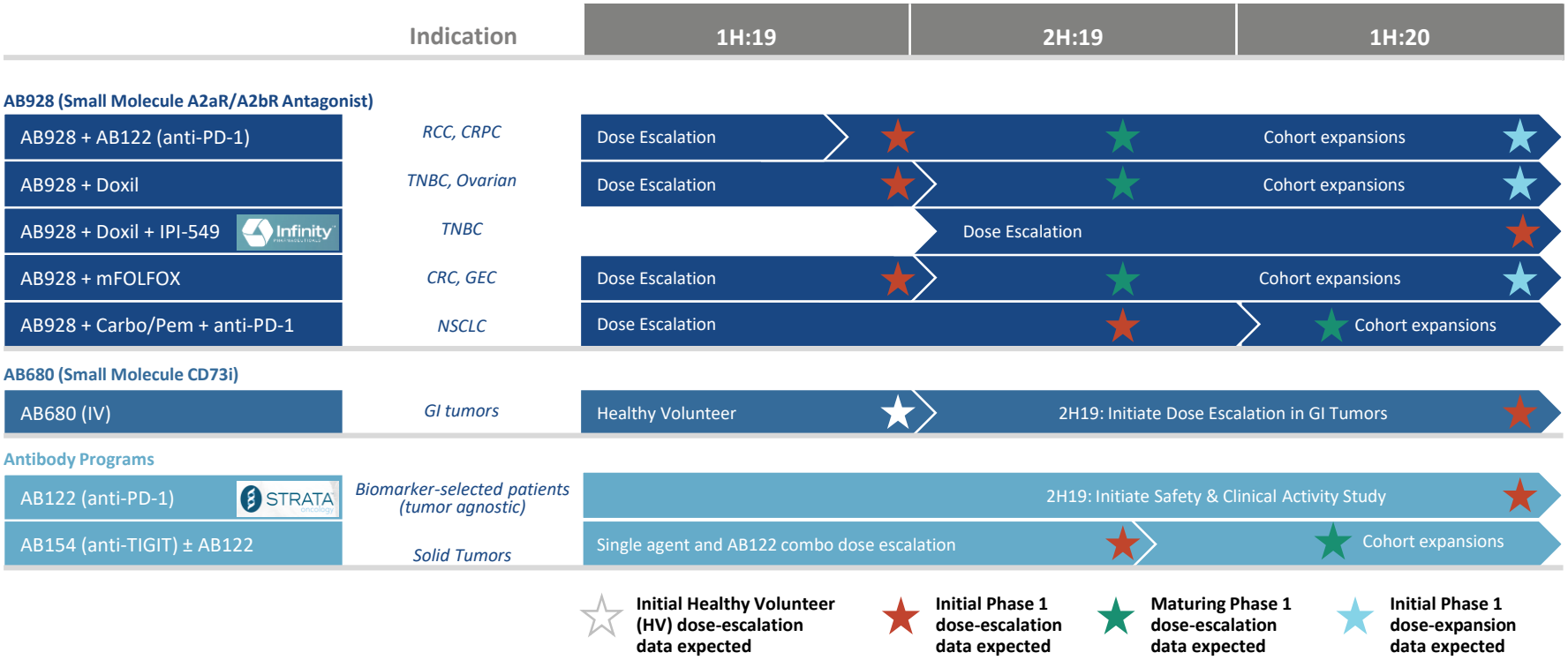
Target Rationale:

- PAK4 over-expression discovered by our advisor (Ribas) to be associated with T-cell exclusion (e.g., insensitivity to PD-1 therapy) in multiple solid tumor types
- PAK4 inhibition expected to result in enhanced responses to IO therapies (such as anti-PD-1) targeted at activating T cells

Program Status:

- Novel, potent, chemical matter identified by Arcus chemists
- Sub-nM, selective, molecules in hand
- Current emphasis is on confirming/expanding the preclinical observations made by Prof. Ribas's lab
- Depending on the confirmation of preclinical POC, we would aim for selection of a best-in-class development candidate during 1H2020

MULTIPLE DATA READOUTS IN THE NEXT 12 MONTHS



CREATING INNOVATIVE CANCER THERAPIES

Leverage Underexploited Biological Targets in Promising Pathways	*Initial focus on* ***ATP-adenosine pathway***
Clinical Stage Pipeline	*Four clinical compounds with* ***multiple data readouts in 2019***
Broad Portfolio	*Ability to* ***maximize development*** *and* ***commercial*** *potential of combinations*
World-class Drug Discovery Engine	***Small-molecule discovery engine*** *to enable pipeline expansion*
Proven Track Record	*Successful management team with* ***10+ years working together in multiple companies***