

CORPORATE PRESENTATION

JULY 09, 2018



NASDAQ: **APTO** TSX: **APS**

A P T O S E

B I O S C I E N C E S



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This presentation contains forward-looking statements, which reflect APTOSE Biosciences Inc.'s (the "Company") current expectations, estimates and projections regarding future events, including statements relating to our business strategy, our clinical development plans, our ability to obtain the substantial capital we require, our plans to secure strategic partnerships and to build our pipeline, our clinical trials and their projected timeline, the efficacy and toxicity of our product candidates, potential new intellectual property, our plans, objectives, expectations and intentions; and other statements including words such as "anticipate", "contemplate", "continue", "believe", "plan", "estimate", "expect", "intend", "will", "should", "may", and other similar expressions. Such statements constitute forward-looking statements within the meaning of securities laws.

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Aptose Corporate Snapshot

Clinical stage company employing a mechanism-driven approach to deliver safer, targeted, first-in-class cancer drugs

Public Company	NASDAQ: APTO / TSX: APS
Shares Outs. (6/30/2018)	Basic: 34.4 MM; FD: 38.8 MM <i>No Warrants / No Preferred Stock / No Debt</i>
3 Month ADTV	~400,000 Shares
Market Cap (6/30/2018)	~\$130 Million
Cash Position (3/31/18)	US\$16.2 Million / CA\$20.9 Million
Cash Runway	>12 Months
Executive Headquarters & Research Laboratories	San Diego, CA

Aptose Investment Highlights

Clinical stage **biotechnology** company developing first-in-class **targeted agents** to treat life-threatening **hematological malignancies** / orphan opportunities

Two differentiated targeted agents with Strong IP Protection

APTO-253 : MYC Inhibitor

FDA Orphan Drug Designation in AML

- Only clinical stage agent directly targeting MYC oncogene
- Currently at Phase Ib stage for acute myeloid leukemia (AML)

CG-806 : Oral Pan-FLT3 / Pan-BTK Inhibitor

FDA Orphan Drug Designation in AML

- Potent inhibitor of wild type & all mutant FLT3 >> AML
- Potent inhibitor of wild type & all mutant BTK >> B-cell Cancers
- IND planned 2018 to support AML and B-cell cancer FIH trials

\$1B+ commercial opportunity in lead indications (AML and CLL)

Strong leadership team of industry, financial and clinical research professionals

Aptose Leadership Team – See www.aptose.com

Dr. William G. Rice, PhD **Chairman, President & CEO**

Achillion Pharmaceuticals: Founder, CEO, President, CSO, Director
National Cancer Institute-FCRDC: Sr. Scientist, Drug Mechanism Lab
Cylene Pharmaceuticals: Chairman, CEO, President, CSO



Mr. Gregory Chow **Sr. Vice President & CFO**

RBC Capital Markets: Director, Led Life Sciences Private Placements
Wells Fargo: Led Private Capital Group
BDO Seidman, LLP: Senior Auditor, CPA (inactive), State of California



Dr. Hannah Zhang, MD, PhD **Sr. Director of Research**

Aangstrom Pharm: Project Mgr to Moores Cancer Center
Bio-Quant: Sr. Research Scientist
Guilin Medical College, Guilin, P.R. China: Ob.Gyn.



Dr. Stephen Howell, MD **Serves as Chief Medical Officer**

Distinguished Professor of Medicine, UCSD Moore's Cancer Center
Physician scientist conducting research to address drug resistance
Expertise in pharmacology and design and conduct of clinical trials



Mr. Ernest Kitt **VP, Dev't & Technical Operations**

Amgen/Onyx: Molecule Lead Director for Kyprolis in Clinical Operations
Oncosec Medical: Executive Director of Clinical Operations
Medicinova Inc: Associate Director of Clinical Operations

Aptose Scientific/Clinical Advisory Team



Dr. Daniel Von Hoff, MD, FACP
Serves as SVP of Medical Affairs

*Winner of 2010 **Karnofsky** Memorial Award*

Prior President of AACR

Board Member of ASCO

Appointed to President's National Cancer Advisory Board



Dr. Brian J. Druker, MD
Collaborator & Chair of SAB

Key Role in Dev't of Gleevec

Member, National Academy of Sciences

*Winner of Karnofsky Award and Lasker
"America's Nobel" Award*

*Leader of Inter-institutional **Beat AML Initiative***



Dr. Michael Andreeff, MD, PhD
Collaborator & Member of SAB

*Professor of Medicine, Chair in Genetics,
MD Anderson Cancer Center*

*Physician Scientist, expert in AML / drug resistance /
drug mechanisms, published over 450 peer-reviewed
papers / books / chapters*

Scientific Advisory Board Populated with KOLs – Domain Expertise

Aptose Program Pipeline

DRUG	TARGET	INDICATION	DISCOVERY	PRE-CLINICAL	PHASE 1	PHASE 2
APTO-253	MYC	AML / MDS	Completed	Completed	Ongoing	
CG-806	Pan-FLT3	AML	Completed	Ongoing		
CG-806	Pan-BTK (WT/C481S) Non-Covalent	B Cell Cancers (CLL/MCL/DLBCL)	Completed	Ongoing		
APL-581	BRD/Kinase	Hematologic Malignancies (Program Partnered with Ohm/LALS)	Completed			

Completed

Ongoing

APTO-253

Phase 1b Stage

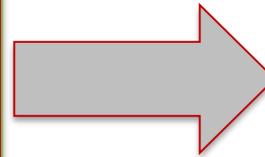
First-in-Class Inhibitor
of MYC Expression

APTO-253 Phase 1b Clinical Development Plan

Phase 1b Dose Escalation Trial Dosing Planned to Commence Shortly

R/R AML and High Risk MDS

- Planned up to 20 Patients
- 1^o Endpts: MTD, DLT, RP2D
- 2^o Endpts: PK, Biomarkers, Efficacy, Transfusions



Single Agent Expansions

AML – Up to 15 Patients

ORR, Efficacy, Biomarkers, Safety

Single Agent Expansions

MDS – Up to 15 Patients

ORR, Efficacy, Biomarkers, Safety

Drug Combination Trials

Selection/Design Underway

- Patient Populations: R/R-AML Aggressive Cancer of Blood/Bone Marrow and hr-MDS
- Dosing Levels Planned: 20 (1pt), 40 (1pt), 66 (3x3pts), 100, 140, 180, 220mg/m²
- Drug Product Employs Newly Modified Formulation/Manufacturing Procedures
- Dosing Schedule: Day 1 of Each Week on 28-day Cycle
- Clinical Sites: Up to 15 Elite Sites Planned to Participate
- Potential Other Indications: B Cell Malignancies

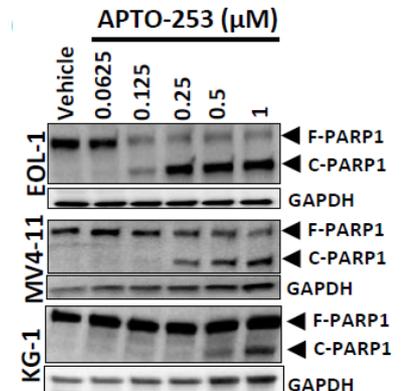
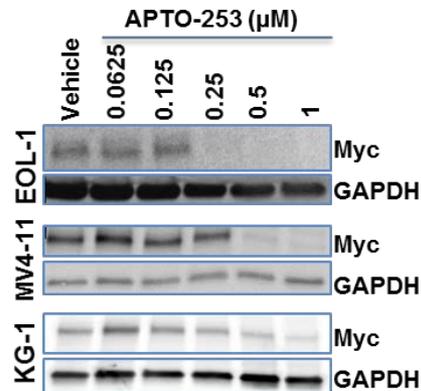
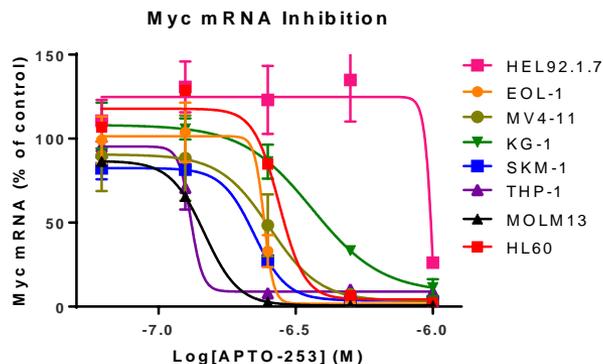
APTO-253 Inhibits Expression of MYC

MYC Oncogene Regulates cell growth, proliferation, apoptosis

- Dysregulated in numerous hematologic cancers, especially AML
- Notoriously difficult to inhibit MYC expression/signaling

APTO-253 Entirely new class of small molecule MYC inhibitor

- Targets a regulatory motif in the promoter region of MYC gene (NOT the MYC protein)
- Inhibits MYC gene expression (mRNA) → depletes cells of MYC protein → induces apoptosis



APTO-253 Value as Fresh Approach to Inhibit MYC

- APTO-253 is safe, combines well with other agents, and **not** myelosuppressive to date¹

APTO-253 Mechanism & Therapeutic Indications: AACR Publications and 2018 AACR Presentation

APTO-253 stabilizes G-quadruplex DNA, inhibits MYC expression and induces DNA damage in acute myeloid leukemia cells

Andrea Local, Hongying Zhang, Khalid D Benbatoul, Peter Folger, Xia Sheng, Cheng-Yu Tsai, Stephen B. Howell, and William G. Rice

AACR Journal: *Molecular Cancer Therapeutics*, June 2018 (Volume 17, Number 6)

Binding/Stabilizing G-quadruplex DNA (G4) motif in MYC promoter silences MYC gene expression

APTO-253 is a new addition to the repertoire of drugs that can exploit DNA BRCA1/2 deficiency

Cheng-Yu Tsai, Si Sun, Hongying Zhang, Andrea Local, Yongxuan Su, Larry A Gross, William Rice, and Stephen B. Howell

AACR Journal: *Molecular Cancer Therapeutics*, June 2018 (Volume 17, Number 6)

Binding of G4 can destabilize telomeres and stall replication forks resulting in DNA damage response

Cancer cells harboring BRCA1/2 mutations hypersensitive – new solid tumor path

APTO-253 is a new addition to the repertoire of drugs that can exploit DNA BRCA1/2 deficiency

Cheng-Yu Tsai, Si Sun, Hongying Zhang, Andrea Local, William Rice, and Stephen B. Howell

2018 AACR Abstract and Poster Presentation

Aptose Program Pipeline

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APL-581	BRD/Kinase	Hematologic Malignancies (Program Partnered with Ohm/LALS)	Completed			

Completed

Ongoing

CG-806

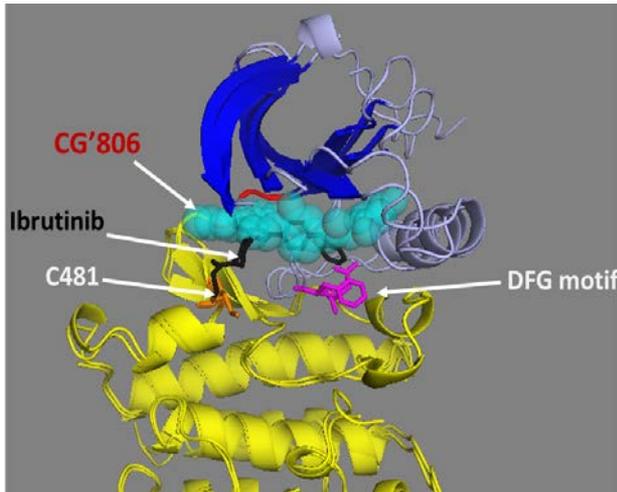
First-in-Class

Pan-FLT3 / Pan-BTK

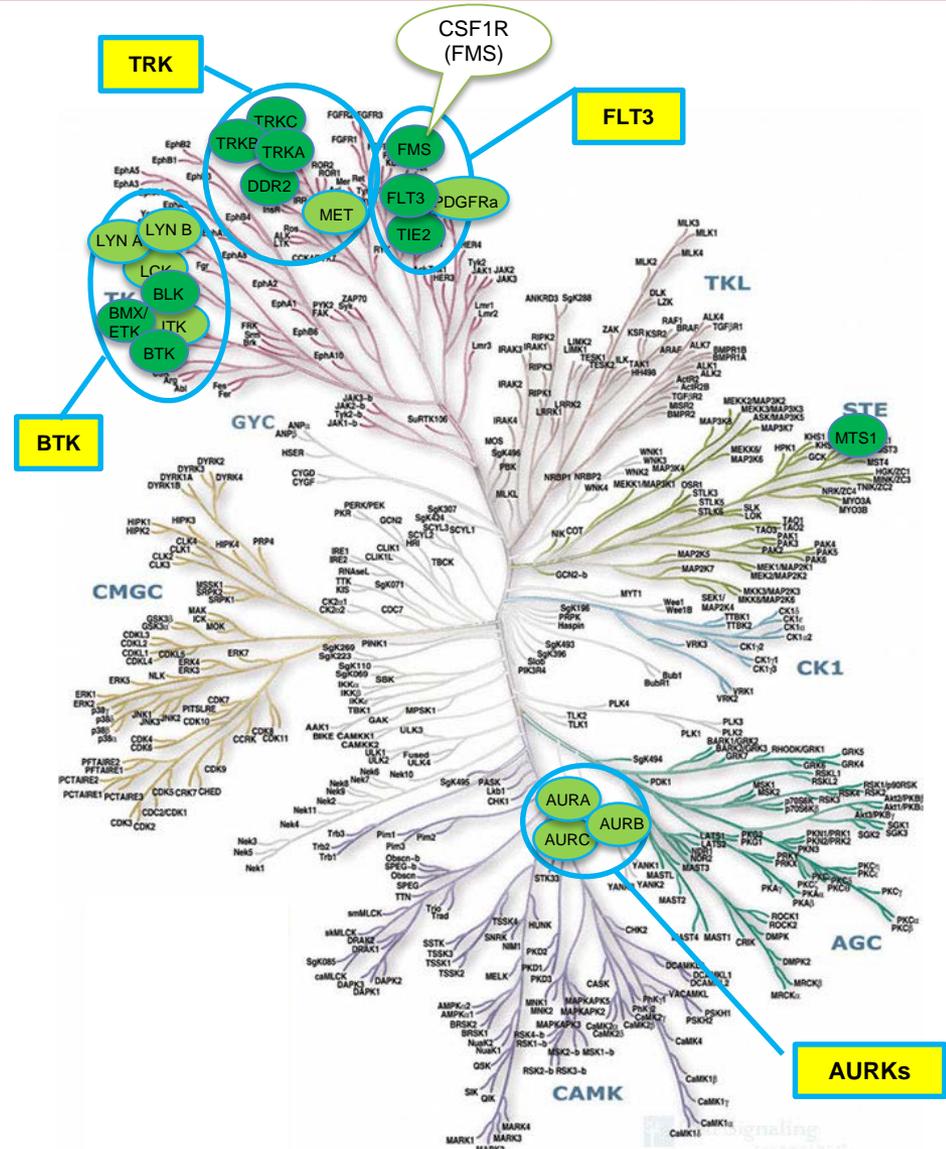
“Multi-Cluster” Kinase Inhibitor

CG-806 Selectively and Potently Targets “Clusters of Related Kinases”

- NOT a “Dirty Kinase Inhibitor”
- Targets Clusters of Oncogenic Kinases operative in Cancers Derived from Bone Marrow
- Selectivity for clusters linked to rigidity, functionalization, and “unique binding modes”



X-ray Crystal Structure CG-806 in BTK-C481S
Atypical Type II Binding Mode



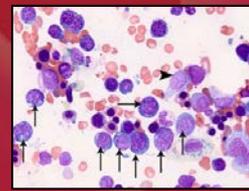
Aptose Program Pipeline

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Completed

Ongoing

CG-806 For the Treatment of Acute Myeloid Leukemia (AML)

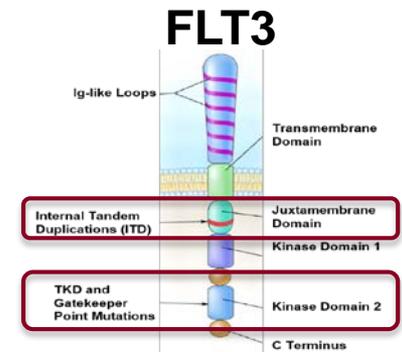


Aggressive & Heterogeneous Cancer of Blood and Bone Marrow

- 21,000 new cases estimated in US in 2016 and leading to 10,600 deaths¹
- **FLT3-ITD** mutation is key driver in **25-35% of AML patients**^{2,3}

Medical Need For Superior FLT3 Inhibitor

- Midostaurin (Rydapt®) approved; Quizartinib & others in development
- Current agents unable to control *all* mutant FLT3 forms → Resistance
- Need potent drug to inhibit *all* mutant forms of FLT3: ITD/TKD/GK/WT



Targeting Only FLT3 is Not Enough to Control AML

- Multiple pathways operative – compensate for loss of one or few
- Need potent drug to target FLT3 **plus** multiple other “rescue” pathways
- FLT3, CSF1R, ERK, AKT, BTK and AURK as key pathways to cripple

“Whac-a-mole”
Concept

CG-806: Only Known Pan-FLT3 Inhibitor for AML Plus, Targets Additional Rescue Pathways

CG-806 more potent FLT3-ITD inhibition relative to competitors

Drug	IC ₅₀ (nM)	
	FLT3-WT	FLT3-ITD
CG-806⁽¹⁾	8	0.8
Midostaurin⁽²⁾	11	11
Quizartinib⁽²⁾	4	8.8

CG-806 retains potency against all tested forms of FLT3:

	<u>Kd (nM)</u>
- FLT3-WT	0.2 nM
- FLT3-ITD	3.1 nM
- FLT3-D835Y (TKD Mutant)	4.2 nM
- FLT3-ITD/F691L (GK Mutant)	15 nM

CG-806 Differentiates as “More Than Just a FLT3 Inhibitor”

- Potent inhibitor of all forms of FLT3 operative in AML, plus.....
- Potent inhibitor of other oncogenic kinases/pathways operative in AML, including CSF1R (FMS), BTK, AURK, H3S10, ERK Pathway, AKT Pathway

CG-806 Induced Rapid and Sustained Tumor Eradication in Mouse Model of AML



ORAL



MV4-11 (FLT3-ITD Driven AML) in Balb/c Mice

EFFICACY

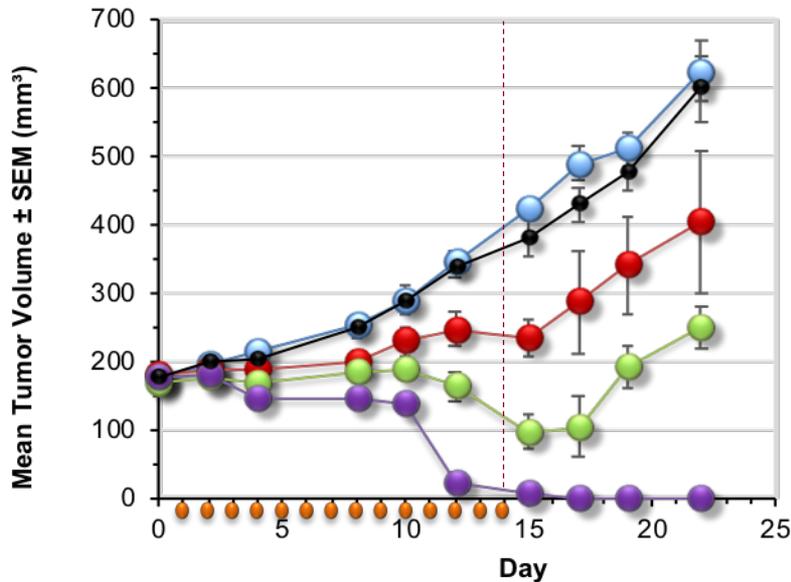


Treated Orally, Once Daily (QD) Dosing for 14 Days

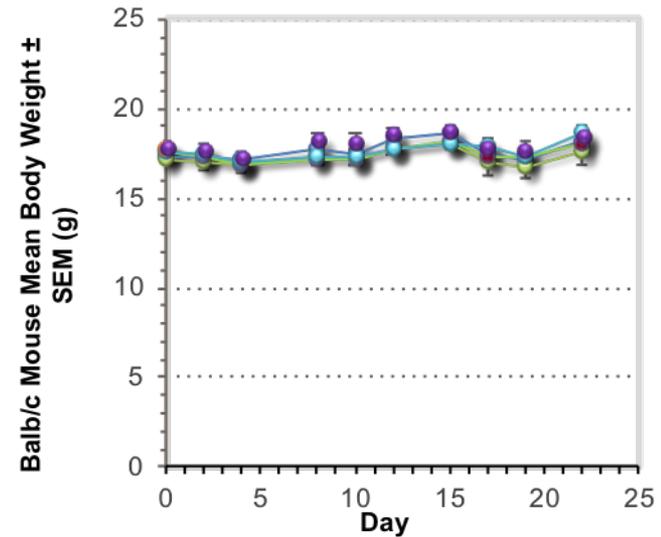
SAFETY



Complete Tumor Elimination with No Observed Toxicity at These Doses



● Vehicle Control ● CG026806, 2 mg/kg ● CG026806, 10 mg/kg
● CG026806, 100 mg/kg ● Ibrutinib, 12 mg/kg



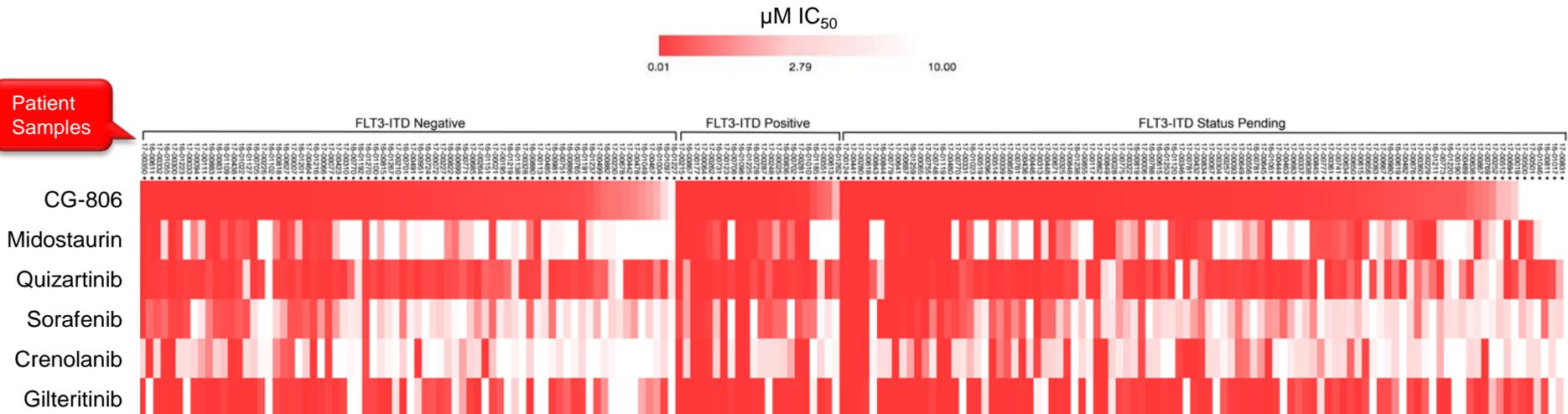
CG-806 Exerts Broad and Superior Potency Against AML Patient Samples

188 AML Patient Samples: Median IC₅₀ = 76nM

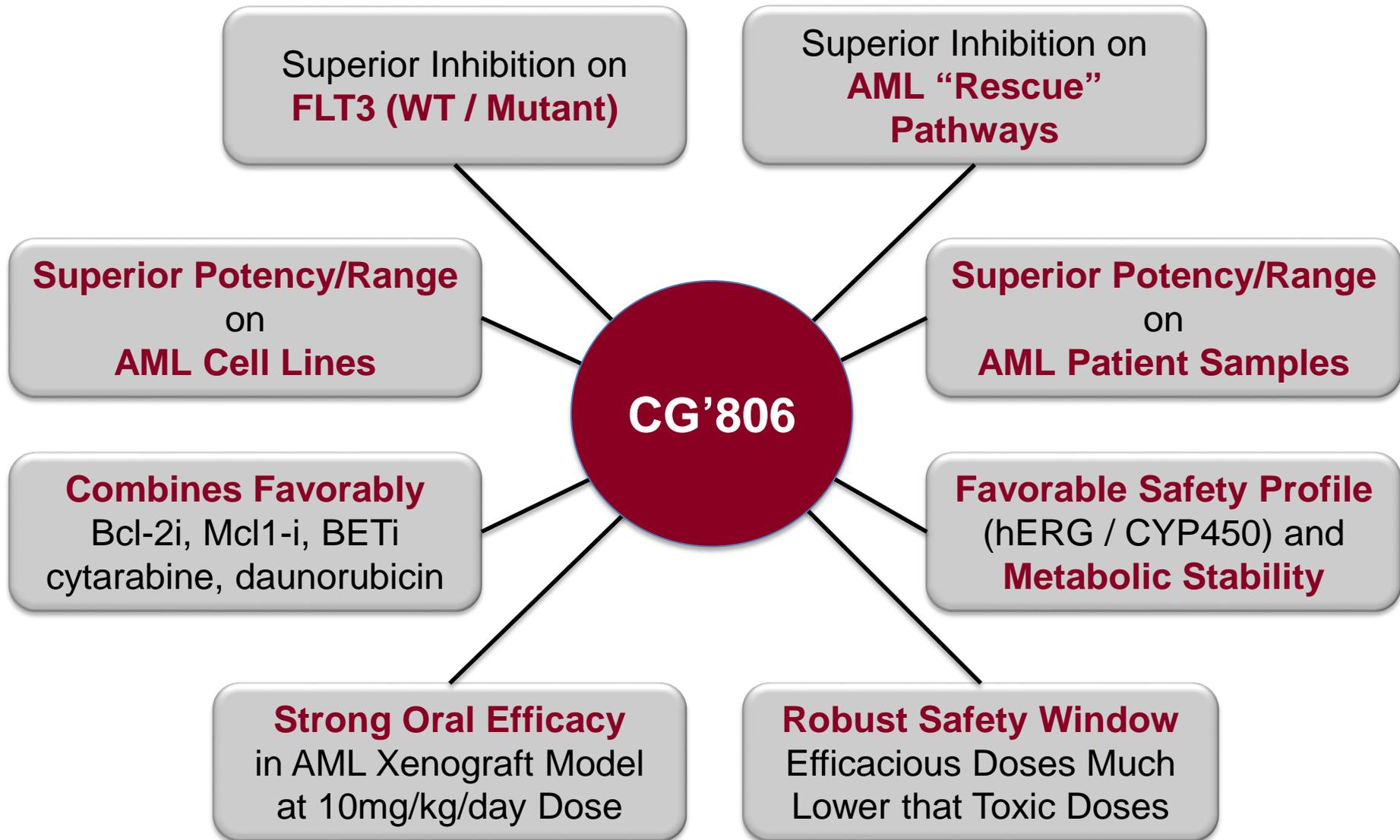
Ex Vivo Drug Sensitivity Assay

- Inhibitors assessed by ex vivo assay to determine sensitivities of **fresh bone marrow patient samples** to CG-806 and other FLT3 inhibitors.
- Cell viability was assessed after 72-hour culture using a tetrazolium-based MTS assay and **IC₅₀ values calculated** as a measure of drug sensitivity. Under the culture conditions used here, the cells retain viability (>90%), but do not proliferate.

Heatmap of CG-806 Versus Other FLT3 Inhibitors on Primary AML Samples



CG-806 Oral, Small Molecule, Multi-Cluster Inhibitor: Potential Best-In-Class Agent for AML

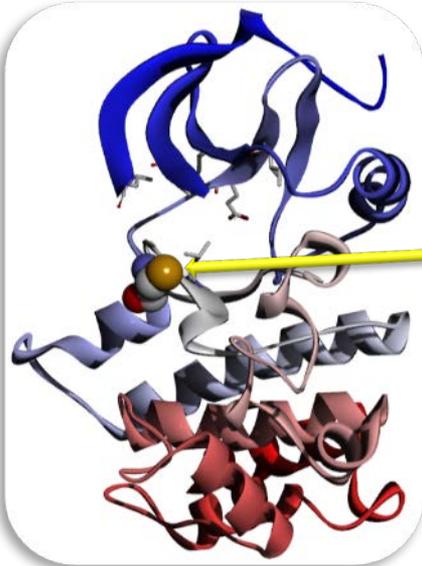


Aptose Program Pipeline

DRUG	TARGET	INDICATION	DISCOVERY	PRE-CLINICAL	PHASE 1	PHASE 2	
APTO-253	MYC	AML / MDS	Completed			Ongoing	
CG-806	Pan-FLT3	AML	Completed			Ongoing	
CG-806	Pan-BTK (WT/C481S) Non-Covalent	B Cell Cancers (CLL/MCL/DLBCL)	Completed			Ongoing	
APL-581	BRD/Kinase	Hematologic Malignancies (Program Partnered with Ohm/LALS)	Completed				

Completed Ongoing

Medical Need for Next Generation BTK Inhibitor



Overexpressed BTK Drives Signaling in B Cell Malignancies

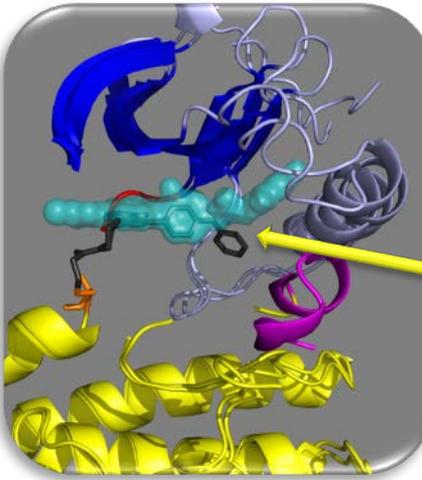
- CLL, MCL, DLBCL

Ibrutinib (Imbruvica®) is Current Standard of Care

- \$Multi-billion WW sales in 2017 (Bloomberg)

Ibrutinib Shortcomings – Patients Discontinuing

- 51% CLL Patients: Discontinue treatment with ibrutinib after 3.4yrs ⁽¹⁾
- 5-10% Patients: Resistant (C481S) to ibrutinib Covalent inhibitor
- 40-45% Patients: Intolerant or refractory to ibrutinib



CG-806 Overcomes Shortcomings of Ibrutinib

- “Non-covalent inhibitor” of BTK (WT & C481S)
- Well tolerated in animal toxicology studies
- Inhibits multiple “rescue” kinases/pathways
- Plan to treat all patients discontinuing ibrutinib

(1) Woyach et al. *J Clin Oncol.*; 2017; 35; 1-7

CG-806 Potently Inhibits Kinases in the BTK Cluster but NOT Kinases Related to Ibrutinib Side Effects

CG-806 Inhibits Kinases of BTK Cluster

Kinase	CG-806 IC50 (nM)
BTK-WT	5.0
BTK-C481S	2.5
BTK-P190K	6.5
BTK-E41K	14.5
BLK	0.7
ITK	4.3
LCK	0.7
LYNA	2.0
LYNB	6.9
BMX/ETK	14.5

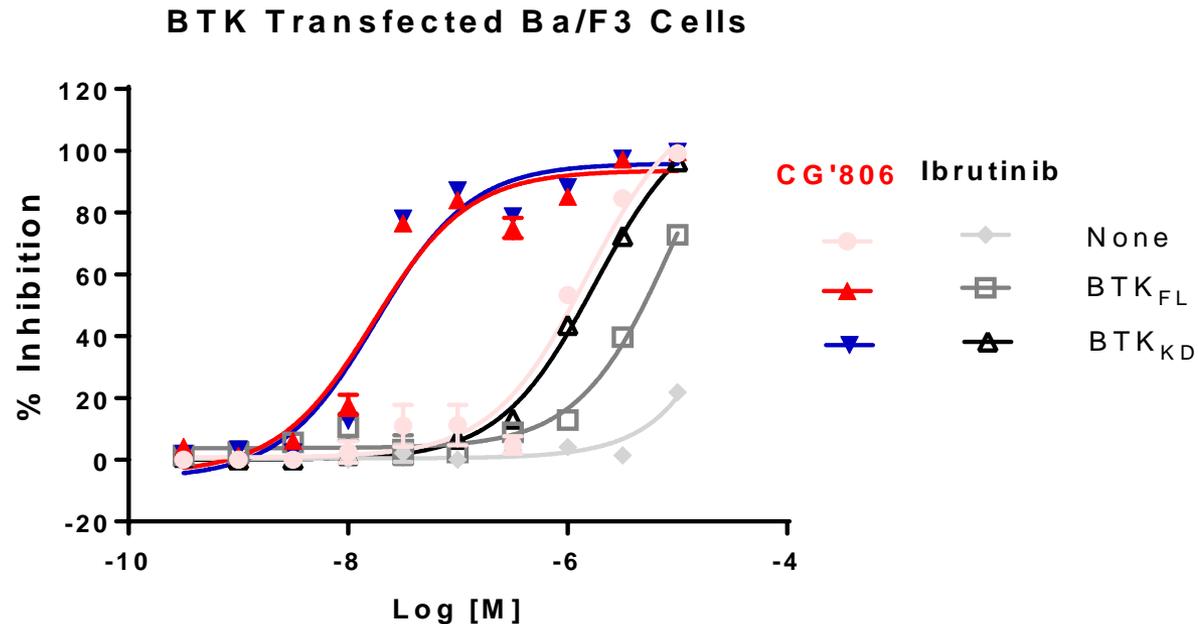
B Cell Cancer Rescue Pathways Potently Inhibited by CG-806

Kinase / Pathway
FLT3-WT / ITD / GK & TKD Mutants
CSF1R Receptor
AKT Pathway
ERK Pathway
AURK - A / B / C
H3S10 Epigenetic

CG-806 Does Not Inhibit Kinases Related to Ibrutinib Side Effects

	TEC	EGFR	ErbB2	ErbB4
CG-806	>1,000	>1,000	>1,000	>1,000
Ibrutinib	78	5.6	9.4	NA

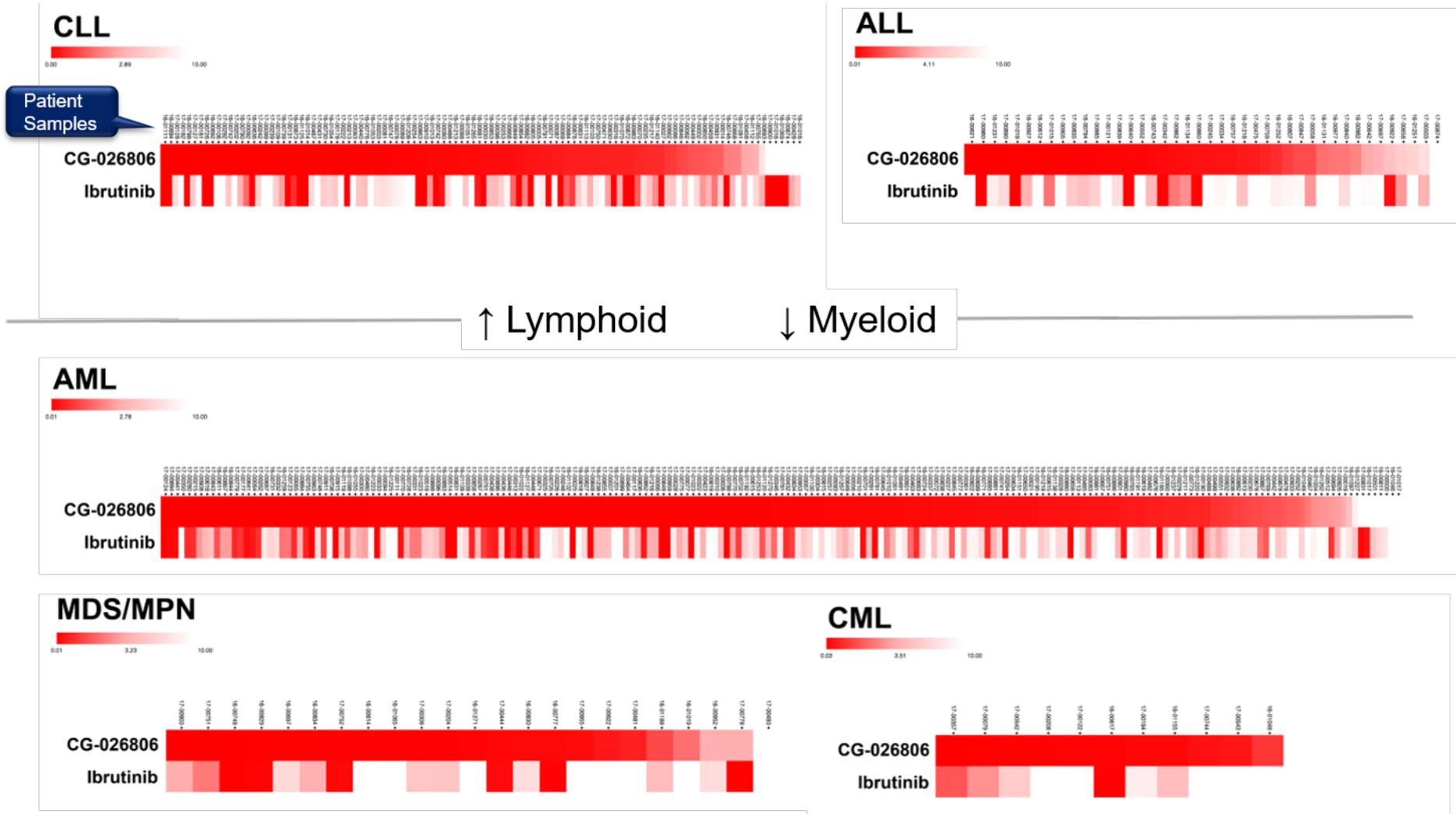
CG-806 Killing Potency Superior to Ibrutinib in Ba/F3 Cell Transfected with BTK



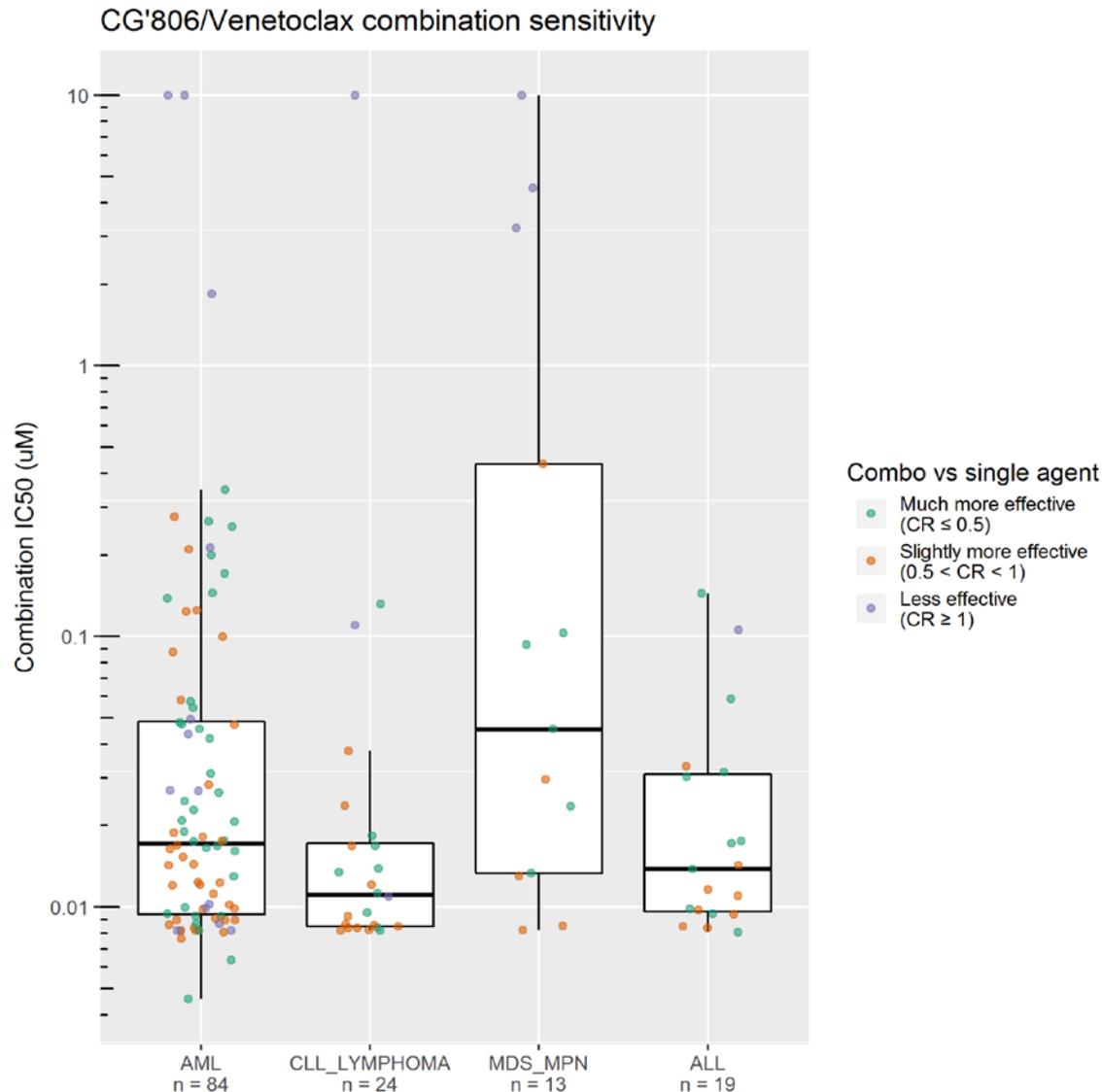
IC50 (nM)	CG'806	Ibrutinib
BTK _{FL}	22.8	4555.0
BTK _{KD}	23.2	1295.0
None	1001.0	> 10,000

Ba/F3 cells are murine lymphoma cells dependent upon exogenous IL-3 for survival. Isogenic Ba/F3 cells transfected with specific oncogenic kinases can be constructed so the only difference in the cells is the form of a particular kinase that is expressed and upon which cell survival is dependent (in the absence of IL-3). Ba/F3 cells were transfected with WT (Full Length of Kinase Domain only) forms of BTK. CG-806 effectiveness against isogenic murine Ba/F3 cells was compared to ibrutinib. CG-806 killed Ba/F3 cells transfected with BTK WT full length (WT-FL) or the WT kinase domain (WT-KD) at equal potency, while ibrutinib required higher concentrations to kill the cells. Note that CG-806 is more effective than ibrutinib at killing the non-transfected Ba/F3 lymphoma cells in the presence of IL-3.

CG-806 Exerts Broad and Superior Killing Potency Compared to Ibrutinib Against Patient Samples



CG-806 plus Venetoclax : Enhanced Killing of Bone Marrow Samples from Patients with Hematologic Malignancies



- CG-806 and Venetoclax individually are highly active cancer agents
- CG-806 + Venetoclax Combination Studies
 - Enhanced ex vivo killing of patient bone marrow cells in most samples (green and orange spheres)
- Suggests the combination of CG-806 and Venetoclax may become a preferred drug combination for patients with AML, MDS/MPN, CLL, ALL and other hematologic malignancies

CG-806 Differentiates from Other BTK Inhibitors (Covalent and Non-Covalent)

CG-806 and Other Non-Covalent Agents

Potent Inhibitors of **Wild Type** and **Mutant C481S-BTK**, but **not EGFR**

Agent	Company	Binding	BTK IC ₅₀ (nM)		Key Off-Targets	
			WT	C481S	ITK	EGFR
Ibrutinib ⁽¹⁾	Abbvie	Covalent	0.5	R	10.7	5.6
Acalabrutinib ⁽²⁾	AZ / Acerta	Covalent	5.1	R	>1000	>1000
CG-806	APTOSE	Non-Covalent	5.0	2.5	4.3	>1000
SNS-062 ⁽³⁾	Sunesis	Non-Covalent	4.6	1.1	14	>1000
ARQ 531 ⁽⁴⁾	ArQule	Non-Covalent	4.2	NA	>1000	290

CG-806 is “More than Just a Non-covalent BTK Inhibitor”

- Inhibits clusters of oncogenic kinases operative in B cell malignancies
- Results in greater potency than ibrutinib in killing B-cell cancer cells
- Does NOT inhibit TEC, EGFR or ErbB2/4 kinases associated with bleeding disorders, rash/diarrhea and atrial fibrillation, respectively

References

(1) Proc Natl Acad Sci U S A. 2010 Jul 20;107(29):13075-80.

(3) Sunesis Corporate Presentation, September 2017

(2) N Engl J Med. 2016 Jan 28;374(4):323-32

(4) Eathiraj et al, Pan Pacific Lymphoma Conference 2016

CG-806: Steps Toward the Clinic

✓ **Completed manufacture of GLP API and formulation of drug product**



✓ **Completed dose range finding studies for pre-IND meeting with FDA**



➤ **IND-enabling GLP toxicology studies in two species ongoing**



➤ **Target IND Submission to FDA during 2018**



- **Planned Clinical Trials Following IND**
- Acute Myeloid Leukemia (AML)
 - B Cell Malignancies (MCL, CLL and DLBCL)
-

Aptose Executive Summary

Developing Highly Differentiated / Targeted Drugs for Blood Cancers

APTO-253 First-in-Class MYC Expression Inhibitor in Phase Ib for AML

- Expect to commence screening and dosing of R/R-AML / hr-MDS patients soon
- Potential to expand into B cell malignancy patients (role of MYC)
- New modified formulation creates potential for new IP

CG-806 First-in-Class Pan-FLT3 / Pan-BTK Multi-Cluster Inhibitor

- FLT3 inhibitor to treat sizable segment of AML population
- BTK inhibitor to treat B cell cancer patients resistant to / discontinuing Imbruvica
- Exercised Exclusive License Agreement and Captured China Rights in 2018
- Expect to file IND for AML and CLL clinical trials in 2018

Announced Licensing Deal for Our Dual BET/Kinase Program

Strong Leadership and KOL Support

Strengthened Financial Foundation

- Cash runway >12 months

Thank You!

A P T O S E
BIOSCIENCES