Key Opinion Leader Breakfast:
Novel Treatment for AML and B-cell Cancers
Hosted by Aptose Biosciences (Nasdaq: APTO)

8:00 – 9:30 am ET
December 12, 2018
Lotte New York Palace Hotel, New York, NY

Live Webcast: Aptose KOL Presentation Webcast Link

APTOSE BIOSCIENCES

NASDAQ: APTO TSX: APS

Brian Druker, M.D.
The Featured Key Opinion Leader (KOL)

- **Academic Positions**
  - Director of the Knight Cancer Institute & Associate Dean for Oncology of the OHSU School of Medicine
  - JELD-WEN Chair of Leukemia Research & Howard Hughes Medical Institute Investigator
- **Member of Prestigious Scientific and Medical Societies**

NATIONAL ACADEMY OF SCIENCES

NATIONAL ACADEMY OF MEDICINE

TANG PRIZE

- **Recipient of Numerous Awards**
  - Lasker-DeBakey Laureate in Clinical Medical Research Award – 2009
  - Japan Prize Laureate in Healthcare and Medical Technology – 2012
  - Tang Prize Laureate in Biopharmaceutical Science – 2018

ALBERT AND MARY LASKER FOUNDATION

gleevec™ imatinib mesylate

- **Notable Scientific and Medical Contributions**
  - His research translated knowledge of the molecular pathogenesis of cancer into specific cancer therapies
  - Spearheaded development of imatinib (Gleevec) for chronic myeloid leukemia (CML) and FDA approval in record time
  - His work changed the life expectancy of patients with CML from an average of 3 to 5 years to a 95% five-year survival
  - His work led to approval of first kinase inhibitor in history and piloted a paradigm-shift in cancer treatment from non-specific chemotherapy to highly targeted cancer therapies
- **He Altered the Course of Cancer Treatment and the Lives of our Families**

Today's Agenda

- **Introduction to CG-806**
  - William G. Rice, Ph.D., Chairman, President and CEO of Aptose Biosciences
  - Overview of efficacy and GLP animal toxicology & toxicokinetic studies
  - Review preclinical profile of this highly atypical kinase inhibitor
  - Development plans for Tx of AML, CLL and other B-cell cancers
- **Dr. Druker's Presentation**
  - Discuss the evolution of kinase inhibitors as anticancer drugs
  - Highlight the medical needs for AML and B-cell cancer patient populations
  - Note his experience with CG-806, an oral first-in-class pan-FLT3/ pan-BTK multi-cluster kinase inhibitor, to potentially address these medical needs
- **Dr. Stephen Howell, M.D.**
  - CG-806 Phase 1 Development Plan – Strategy to Streamline the Plan
- **Dr. Druker Available to Answer Questions**

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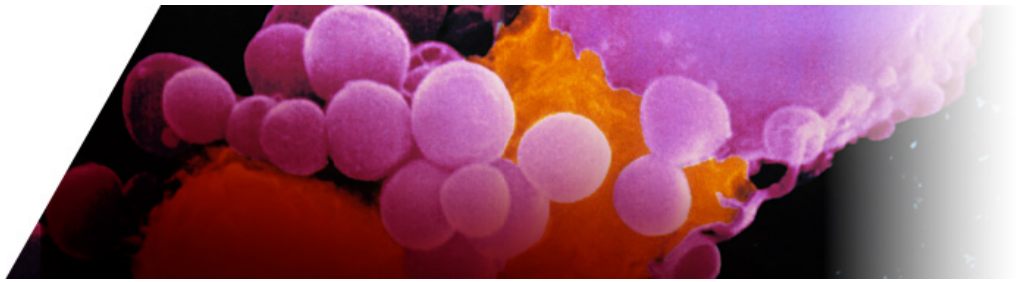

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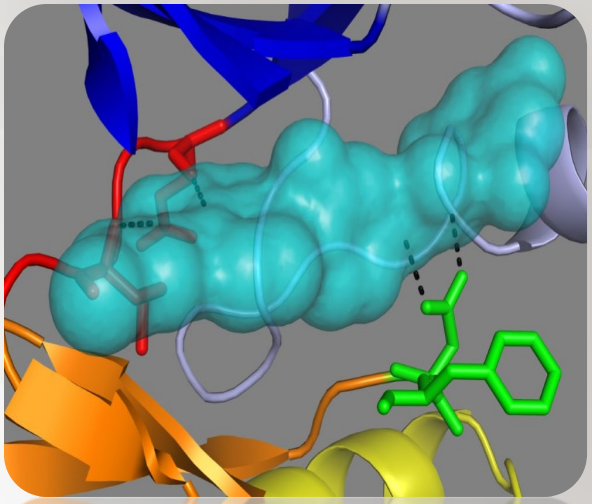


CG-806

Preclinical Agent Approaching IND

Pan-FLT3 / Pan-BTK Multi-Cluster Kinase Inhibitor

APTOSE BIOSCIENCES

William G. Rice Ph.D.

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

- **Oral, Small Molecule, Kinase Inhibitor**
- **Well-Differentiated MofA and Superiority to Competitor Agents**
  - Improved Profile : Over competitor FLT3i for AML patients
  - Improved Profile : Over competitor BTKi for B-cell cancer patients
  - More than FLT3i and BTKi : Targets "Driver" and "Rescue" pathways
- **Long Term : Plan to Develop Broadly for Many Blood Cancers**
- **Near Term : Target Emerging AML and B-Cell Cancer Patients with Unmet Needs and Potential for Rapid Approval ("Low Hanging Fruit")**
  - AML: FLT3i-R (Emerging resistance to FLT3 inhibitors)
  - AML: IDH1-M (Sensitive or resistant to IDH1 inhibitors)
  - AML: Elderly/fragile (Unable to tolerate other regimens)
  - AML/CLL/SLL: Venetoclax-R (Emerging resistance to venetoclax)
  - CLL/SLL/MCL: R/R/I to BTKi (Failed covalent &/or non-covalent BTKi)
  - CLL/SLL: Richter's (Richter's Transformation/Richter's Syndrome)

1. CG-806 Highlights

- Highly Efficacious
- Yet, Well Tolerated
- Atypical Kinase Inhibitory Profile

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

AML MODEL

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

ORAL DOSING

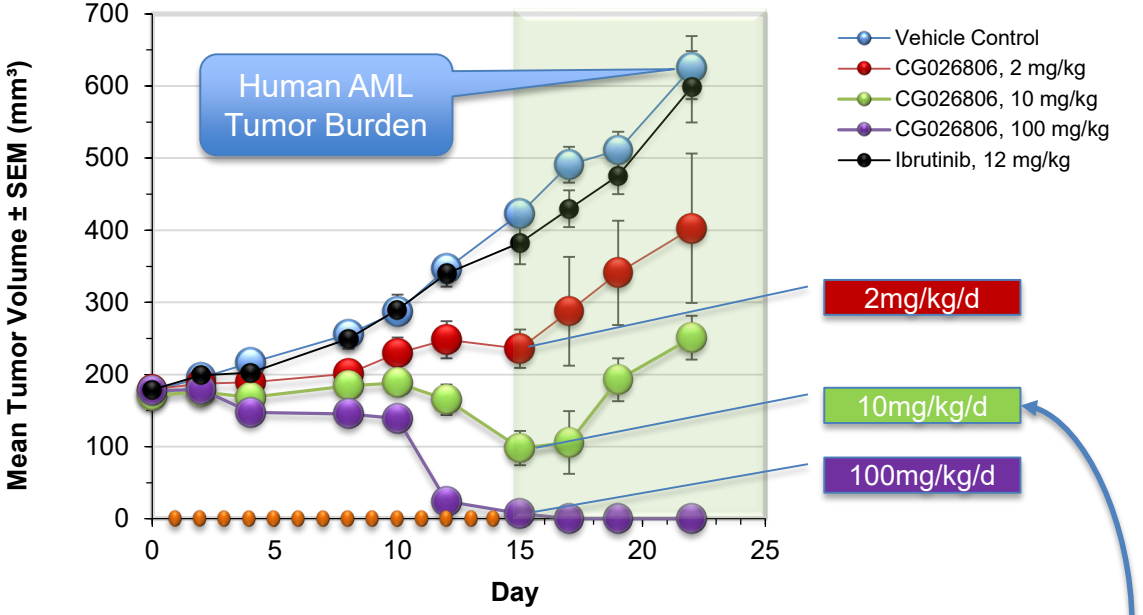
Treated Orally, **Once Daily** (QD) Dosing for 14 Days

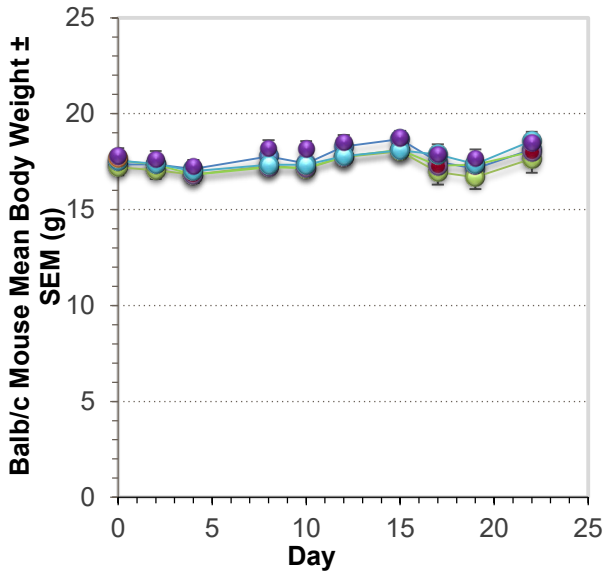
EFFICACY

Strong Anti-Tumor Activity with No Observed Adverse Events

SAFETY

Higher Doses Well Tolerated In GLP Toxicology Studies





Note that 10mg/kg once daily in a mouse is equivalent to a 50mg dose in humans

CG-806 Exhibits Favorable Safety Profile In Extensive GLP Toxicity & Toxicokinetic Program

GLP 28-Day (Twice Daily) Oral Gavage Toxicity and TK Study in Mice or Dogs with a 2-Week Recovery

Mouse:

Doses Tested:	60, 200, 600 mg/kg/day
Adverse findings:	**NONE**
Clinical Signs	None
Food Consumption:	None
Clinical Pathology:	None
Anatomic Pathology:	None

All doses achieved µM plasma levels

NOAEL: **600** mg/kg/day (highest dose tested)

Dog:

Doses Tested:	60, 120, 240 mg/kg/day
Adverse findings:	**NONE**
Clinical Signs	None
Food Consumption:	None
Clinical Pathology:	None
Anatomic Pathology:	None
Electrocardiogram	None

NOAEL **240** mg/kg/day (highest dose tested)

Secondary Safety Evaluations:

Ames Genotoxicity Assay	Clean
Mouse Respiratory Safety Study	Clean
Mouse CNS Safety Study	Clean
Dog Cardiovascular Safety Study	Clean

Anticipate bone marrow suppression as DLT after long term dosing

Calculated Human Starting Dose

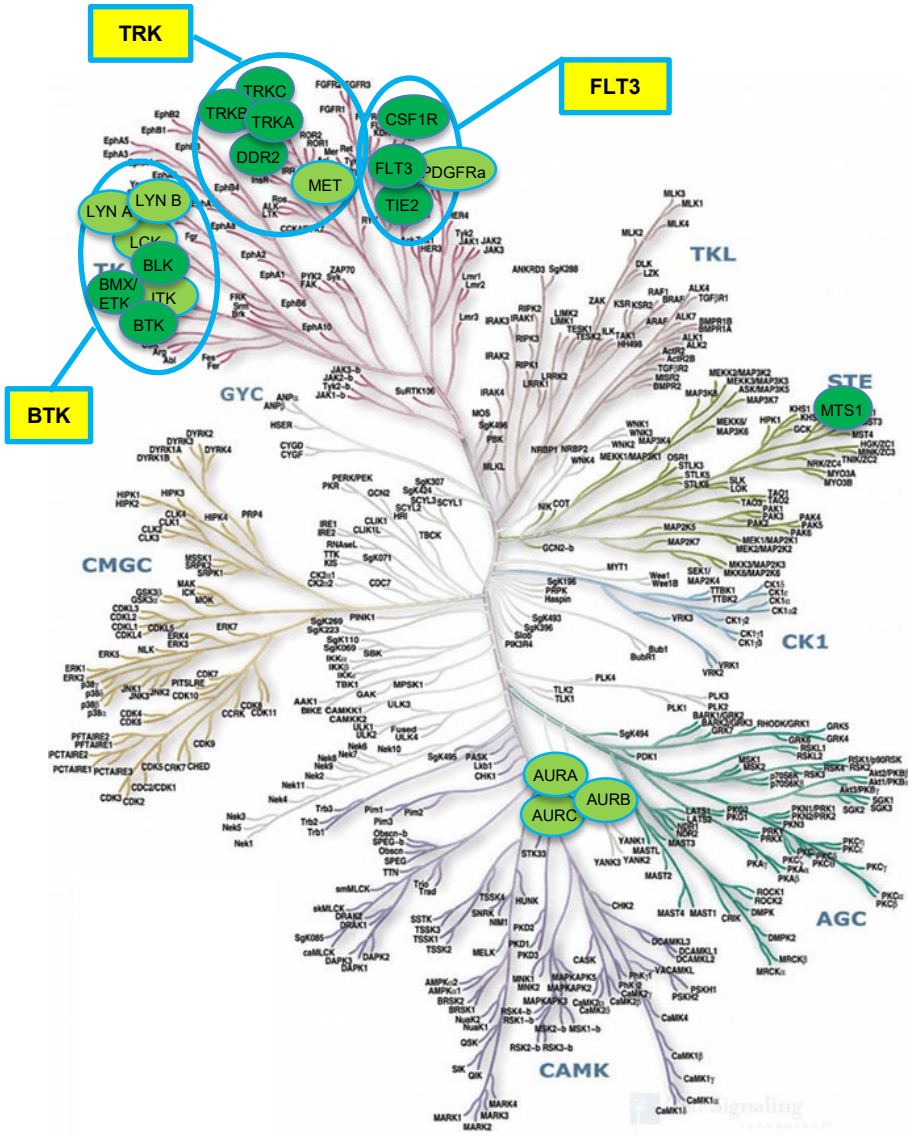
Mouse NOAEL ÷ 12.3 → HED
HED ÷ 10 (S.F.) x 60kg = 300mg/day
150mg BID Predicted

What Does This Mean?

If absorption and PK in humans are similar to mouse, then may achieve therapeutic exposures early in dose escalation

"Multi-Cluster Kinase Inhibitor": CG-806 Potently and Selectively Inhibits Clusters of Related Kinases

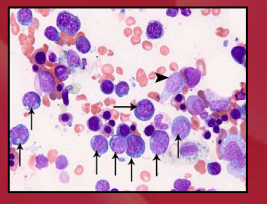
- **Atypical inhibition profile of kinase clusters**
  - FLT3 cluster
  - BTK cluster
  - TRK/AURK clusters
- **Avoids other kinase clusters associated with toxicity**
- **NOT a "dirty" kinase inhibitor**
- **NOT "single-hit" kinase inhibitor**
- **Inhibits Multiple Kinases Operative in Blood Cancers**
  - FLT3 cluster → AML
  - BTK cluster → B-cell cancers
  - Kinases of Rescue Pathways



2. CG-806 Highlights

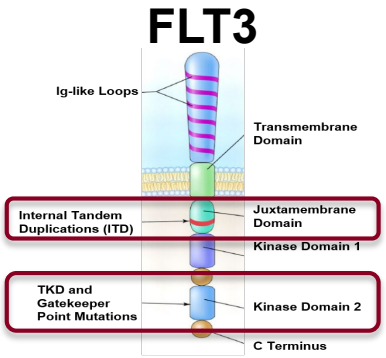
- Focus on AML
- Targets/Pathways Disrupted
- Superior to Other FLT3 Inhibitors
- PDX Model of FLT3i-Relapsed AML

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



Aggressive Cancer of Blood and Bone Marrow (Orphan Disease)

- **FLT3-ITD mutation** is key driver in **25-35% of AML patients**[2,3]
- Approved: Midostaurin (Rydapt®) 2017; Gilteritinib (Xospata®) 2018
- Development Stage: Quizartinib, Crenolanib, other FLT3 inhibitors



Medical Need For a Superior FLT3 Inhibitor

- "Dirty" agents (Midostaurin, Sorafenib, etc.) are limited ➔ Toxicity
- "Single-hit" agents don't provide durable responses ➔ Resistance
- Need potent drug to inhibit *all* mutant forms of FLT3: ITD/TKD/GK/WT

"Whac-a-mole"

Inhibiting FLT3 is Not Enough to Control AML

- Also need to target multiple other "rescue" pathways that compensate

CG-806 Potently Inhibits All FLT3 + "Rescue" Pathways

- FLT3, CSF1R, ERK/MYC, AKT, BTK and H3S10 key pathways crippled

(1) American Cancer Society : [2] *Cancer*. 2014 July 15; 120(14): 2142-2149 : [3] *Blood* 2016;128(5);686-698.

CG-806 Pan-FLT3 Inhibitor: Potent Inhibitor of ITD, WT and All Clinically Relevant Mutant Forms of FLT3

Potent Inhibitor of FLT3-ITD (800pM IC_{50} Comparison)

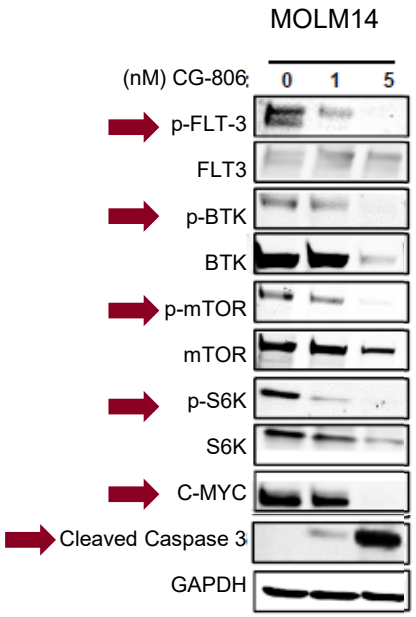
	IC_{50} (nM)
Drug	**FLT3-ITD**
CG-806(1)	**0.8**
Quizartinib (AC220)(2)	8.8
Gilteritinib (ASP2215)(3)	0.9
Crenolanib(4) (CP-868596)	2
Midostaurin(2)	11
Nexavar(2)	79
Sutent(2)	1

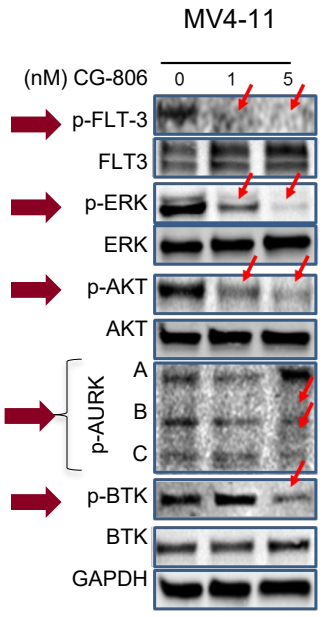
Potent (Kd) Binding to WT and FLT3 Mutants (ITD/TKD/GK)

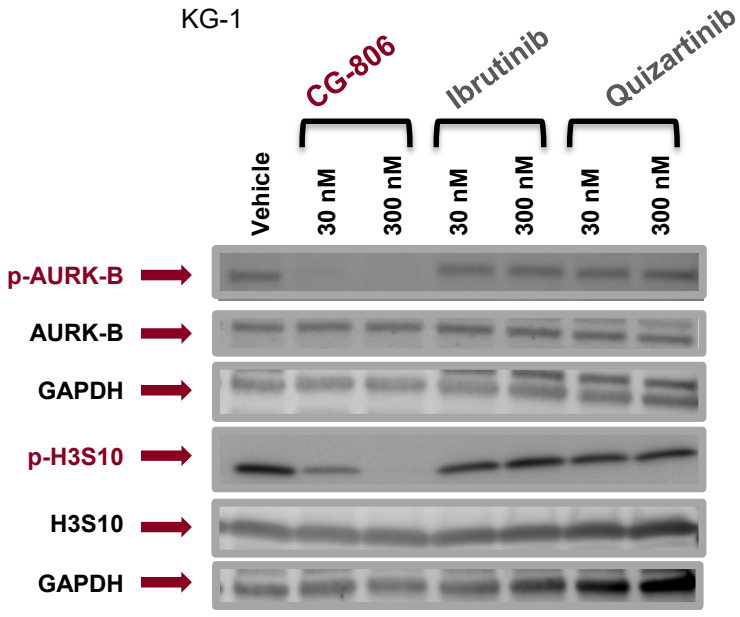
FLT3 Proteins (Fragments)	CG-806 Kd (nM)
FLT3 WT	0.24
FLT3 ITD	3.1
FLT3 D835Y	4.2
D835H	2.2
D835V	7.9
R834Q	6.4
N841I	0.8
K663Q	0.55
ITD / F691L	16

(1) Reaction Biology Corp.
(2) Blood. 2009 Oct 1; 114(14): 2984–2992
(3) J Clin Oncol 32:5s, 2014 (suppl; abstr 7070)
(4) Blood 2014 Jan 2; 123(1): 94-100 ; AACR Poster 2012
(5) ASH Oral Presentation 2016
N/A – Data not available / Not Applicable.

CG-806 Inhibits Key Oncogenic Pathways in AML Cells that Utilize Multiple Pathways to Survive







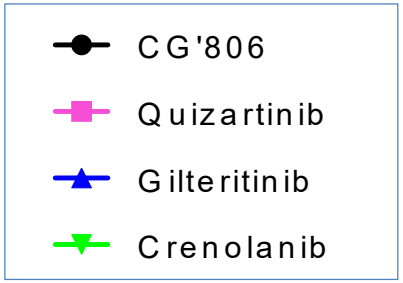
CG-806 Potently Inhibits:

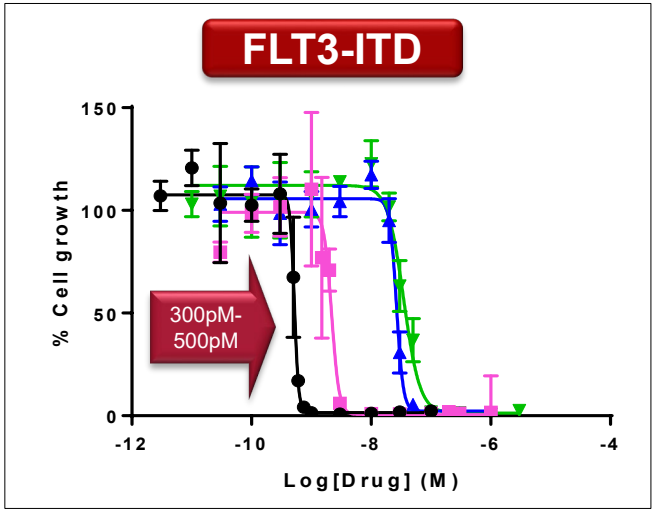
- **FLT3 Driver Kinases**
- **And Rescue Pathways**

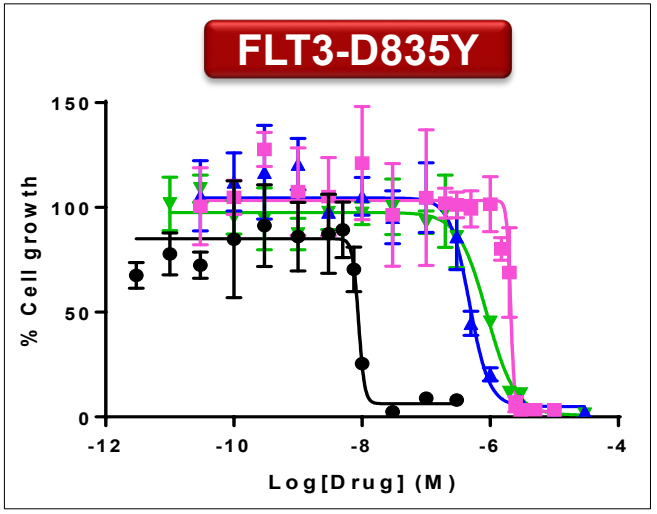
FLT3-WT / ITD / GK & TKD Mutants
CSF1R / PDGFRα Receptors
AKT/mTOR/S6K Pathway
ERK Pathway
MYC Pathway
H3S10 Histone
BTK and BCR Pathway

CG-806 Kills Ba/F3 Isogenic Cells with FLT3 Mutations More Potently than Other Flt3 Inhibitors

- **Ba/F3 Cells[1] with Clinically Relevant FLT3 Mutations**
  - ITD
  - D835Y (TKD)
  - ITD + F691L (Gatekeeper)
- **Compared Effectiveness of CG-806 to Competitor Agents**
- **CG-806 Distinguished as Superior to Other FLT3 Inhibitors**







[1]Ba/F3 cells kindly provided by Dr. Michael Andreeff at MDACC

CG-806 Efficacy in PDX Model Against AML Patient Cells with FLT3 ITD + D835 Mutations

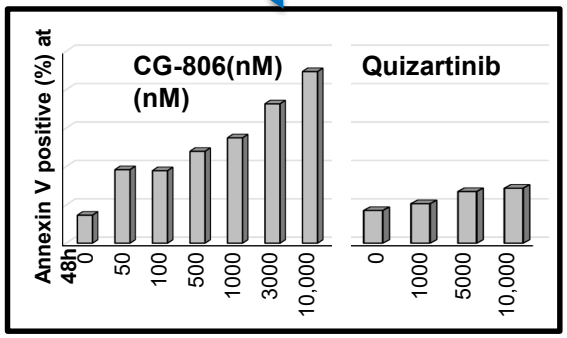
Dr. Andreeff
MDACC

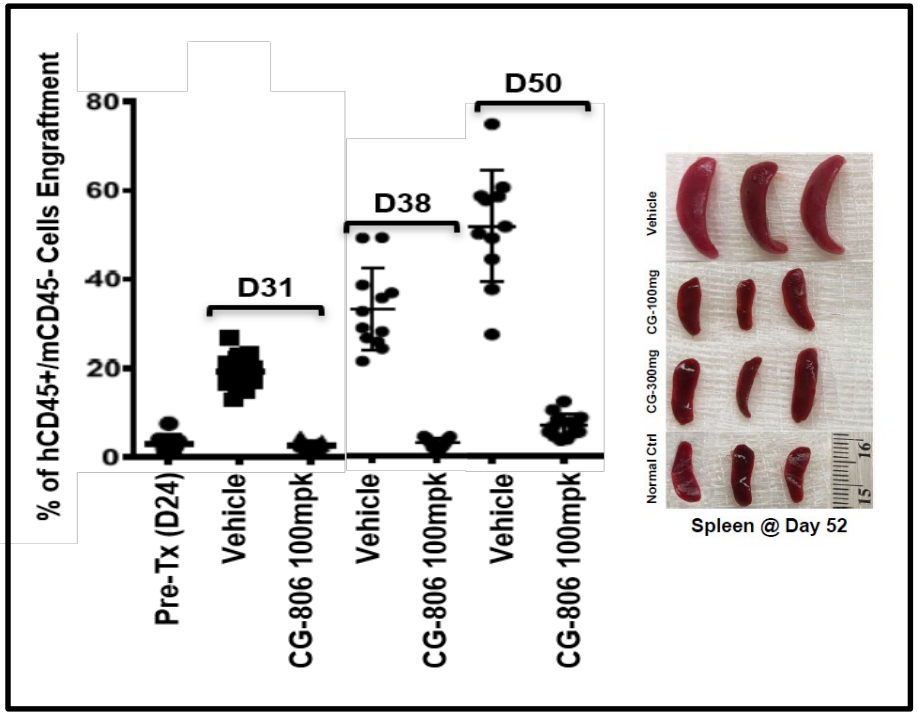
Patient information: AML patient (FLT3-ITD) received Sorafenib+Azacitidine Tx and experienced CR after one cycle therapy; relapsed after 3 cycles of treatment and acquired a D835 mutation (now FLT3-ITD/D835)

Patient Derived Xenograft (PDX) Model

CG-806

- **Reduced leukemia cell burden**
- **Reduced splenomegaly**





Tx In initiated D27

CG-806

- Active against patient-derived FLT3-ITD / D835 AML
- Potential to treat emerging FLT3i-resistant AML patients

Model implanted with FLT3 ITD+D835 mutated primary AML cells CG-806 (QDx5/wk Orally). hCD45+/mCD45- leukemic cells in peripheral blood were quantitated with flow cytometry.

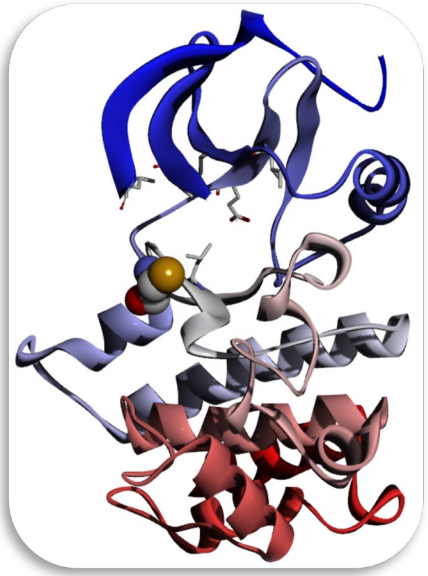
CG-806 :
Potential Best-In-Class Agent for AML

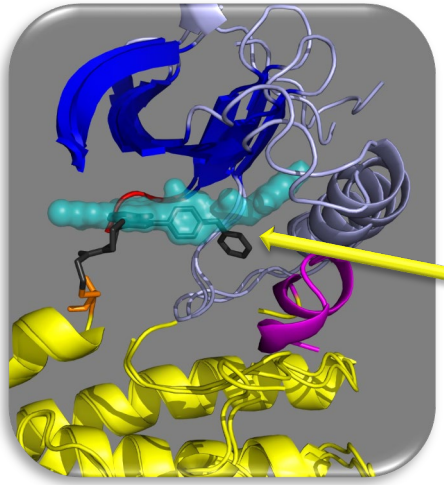
- **Well-Differentiated MoA and Superiority to Other FLT3i**
  - Superior inhibition of FLT3 (WT and mutant forms) driver kinases
  - Superior inhibition of “rescue” pathways to cripple cells
  - Potently kills cells resistant to other FLT3i
  - Potent efficacy with tumor elimination
  - Favorable safety profile and well tolerated
- **Profile Supports Plan to Pursue Rapid Development for AML Patients with Unmet Medical Needs**
  - FLT3i-Resistant
  - IDH1-Mutant
  - Elderly/fragile
- **Dr. Druker Will Present Data : CG-806 is Superior to Other FLT3i at Killing Malignant Cells from the Bone Marrow of AML Patients**

3. CG-806 Highlights

- Focus on CLL & B-Cell Cancers
- Targets/Pathways Disrupted
- Superior to Ibrutinib / BTK Inhibitors

Medical Need for Next Generation BTK Inhibitor





Overexpressed BTK Drives Signaling in B Cell Malignancies

- CLL, MCL, DLBCL

Ibrutinib (Imbruvica®) BTKi 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 May Overcome 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 BTK Enzymes, but NOT Kinases Related to Ibrutinib Side Effects

CG-806 Potently Inhibits All Available Forms of BTK

Kinase	CG-806 IC_{50} (nM)
BTK-WT	8.4 (0.1 - 12nM)
BTK-C481S	2.5

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

IC_{50} (nM)	TEC	EGFR	ErbB2
Ibrutinib	78	5.6	9.4
CG-806	>1,000	>1,000	>1,000

CG-806 Potently Inhibits Driver Kinases and Rescue Pathways

- FLT3-WT / ITD / GK & TKD Mutants
- CSF1R / PDGFRα Receptors
- AKT/mTOR/S6K Pathway
- ERK Pathway
- MYC Pathway
- H3S10 Histone
- **BTK and BCR Pathway**

CG-806 Kills Malignant B-Cells More Potently than Ibrutinib, Including Ibrutinib-Insensitive Cells

CG-806 on average 1000X more potent than ibrutinib at killing B-cell lines

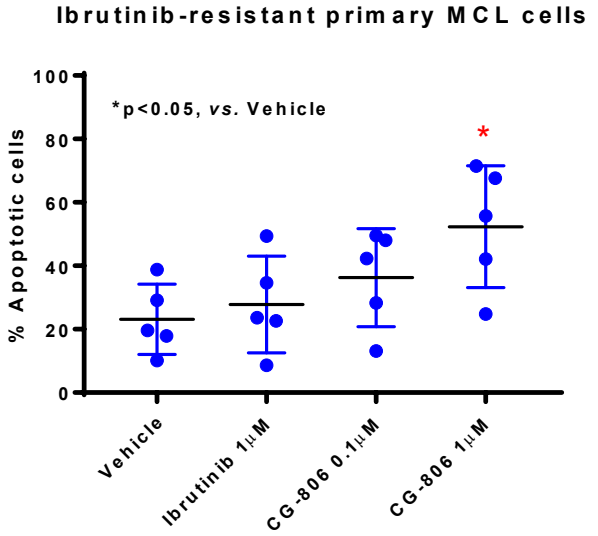
Disease Type	Cell Line	IC_{50} (μM)		Fold difference
		CG-806	Ibrutinib	
MCL	Mino	0.006	18.2	3033
	Granta-519	0.020	29.9	1495
	Jeko-1	0.197	23.6	120
B-ALL	RS411	0.002	12.4	6200
	MHH-Call4	0.026	22.8	877
Burkitt's	Ramos	0.014	22.0	1571
	Daudi	0.236	23.9	101
ABC-DLBCL	OCI-Ly3	0.830	29.0	35
	U2932	0.632	8.9	14
	SU-DHL2	0.744	27.0	36
GCB-DLBCL	BJAB	0.882	1.8	2
	SU-DHL6	0.083	1.2	14
	RL	0.667	17.0	25
FL	DOHH2	0.003	0.441	147

CG-806 kills (induces apoptosis) ibrutinib-resistant primary MCL cells

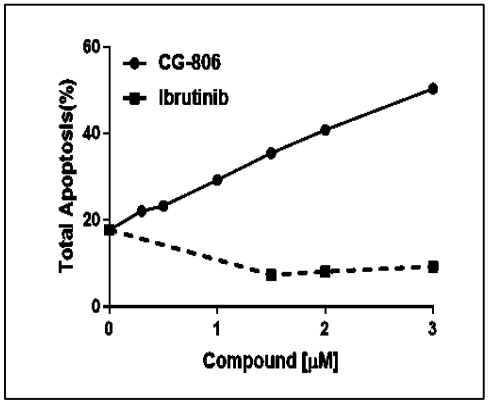
ASH 2018 Abstract #3503

CG-806, a first-in-class pan-FLT3/pan-BTK inhibitor, Exhibits Broader and Greater Potency Than Ibrutinib Against Primary and Cultured Malignant B Cells

Hongying Zhang, Andrea Local, Khalid Benbatoul[1], Peter Folger, Susan Sheng, Taryn McLaughlin, Alexey Danilov, Stephen E. Kurtz, Jeffrey W. Tyner, Stephen B. Howell, and William G. Rice



CG-806 kills DLBCL lines insensitive to ibrutinib



Dr. Druker will present OHSU data showing CG-806 superior to ibrutinib in killing malignant cells from the bone marrow of patients with CLL and ALL B-cell cancers

CG-806 :
Potential Best-In-Class Agent for B-cell Cancers

- **CG-806 "Directly" Kills B-Cell Cancer Cells**
  - Ibrutinib inhibits BTK at low nM levels, but does not kill until uM levels
  - Demonstrates that just hitting BTK alone does not effectively kill the cells
  - CG-806 hits BTK driver and "rescue" pathways to kill cells at nM levels
- **Well-Differentiated MoA and Superiority to Ibrutinib**
  - Potently kills ibrutinib-resistant cells
  - Inhibits B-cell migration more effectively
  - Overcomes stromal cell protection better
  - More potently and directly kills B-cell cancer cells
- **Profile Supports Plan to Pursue B-cell Cancer Patients R/R/I to BTKi (Covalent or Non-covalent) for Rapid Development**

4. CG-806

- Development Status
- Summary

CG-806: Steps Toward the Clinic

- ✓ **Completed pre-IND meeting with FDA**
- ✓ **Completed dose range finding studies (rodents and dogs)**
- ✓ **Completed two batches of GMP drug substance (multiple kg)**
- ✓ **Completed IND-enabling GLP toxicology studies**
- ✓ **Completed Genotoxicity, Respiratory, CNS, CV safety studies**
- ➢ **Placed two capsule strengths on stability testing**
- ➢ **Collecting reports and writing IND for submission to FDA**

- ➢ **Planned Clinical Trials with Fastest Path to Clinical POC**
  - B Cell Malignancies
  - AML/MDS Patients

CG-806: First-in-Class Pan-FLT3 / Pan-BTK Inhibitor
Summary

- **Multi-Cluster Kinase Inhibitor**
  - Targets multiple driver kinases & rescue pathways
  - Does not inhibit kinases linked to toxicities of other KI's
- **Strong Efficacy and Well Tolerated**
  - Extensive safety program and animal models
  - May achieve therapeutic exposures early in clinical dose escalation
- **Planned Clinical Development**
  - AML, MDS/MPN, CLL/SLL, DLBCL, MCL, FL, Others
  - Near Term: Patients R/R/I to other drugs and high unmet medical need

Key Opinion Leader Breakfast:
Novel Treatment for AML and B-cell Cancers
Hosted by Aptose Biosciences (Nasdaq: APTO)

8:00 – 9:30 am ET
December 12, 2018
Lotte New York Palace Hotel, New York, NY

Live Webcast: Aptose KOL Presentation Webcast Link

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NASDAQ: APTO TSX: APS

1. History of Kinase Inhibitors

2. Needs of AML and of B-Cell Cancer Patients

Brian Druker, M.D.

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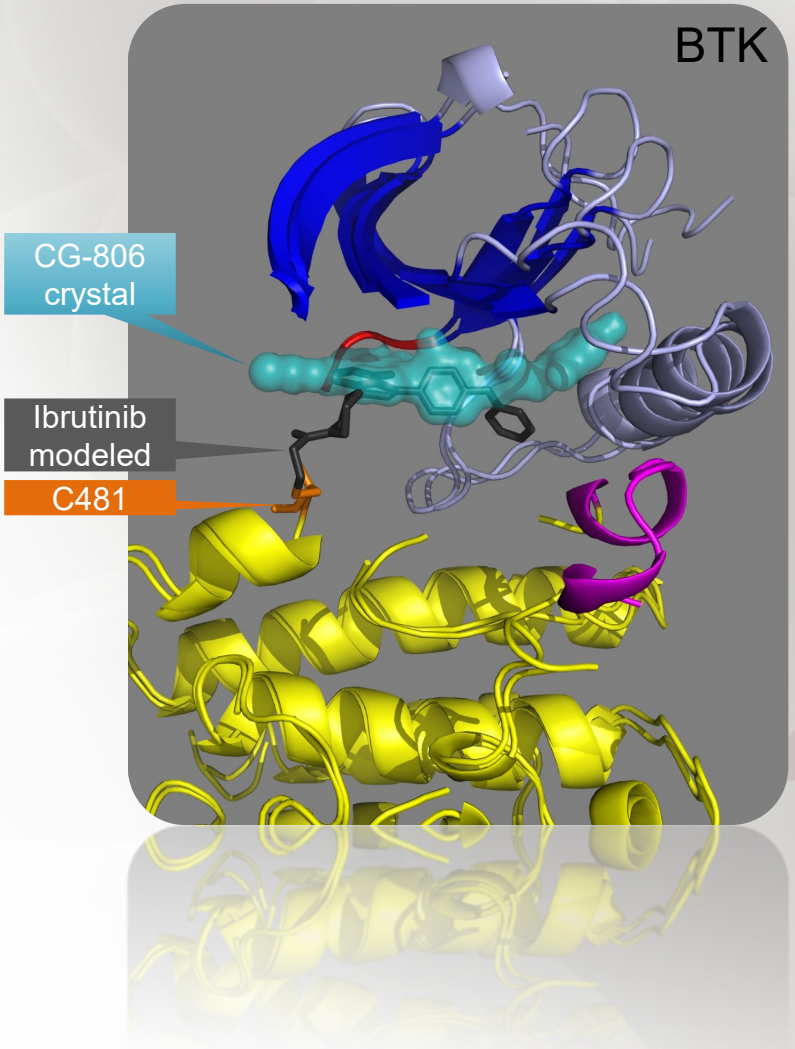

CG-806

Pan-FLT3 / Pan-BTK Kinase Inhibitor

Activity Against Patient Samples OHSU Data

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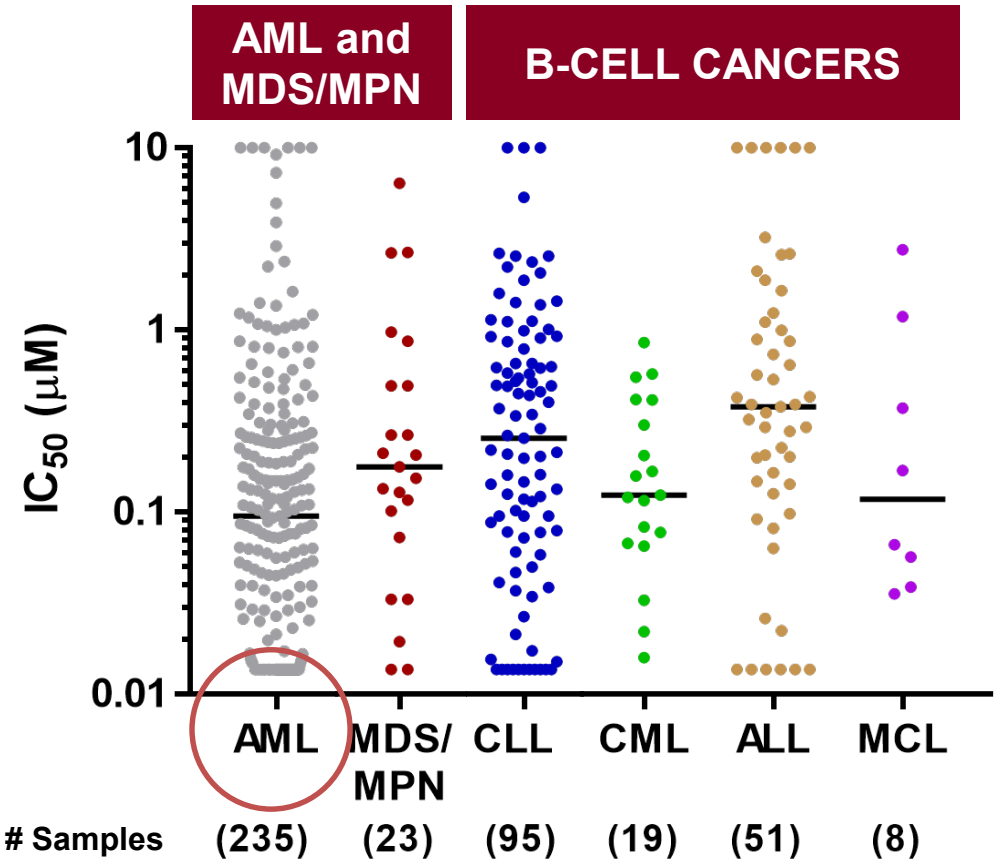
CG-806: First-in-Class Pan-FLT3 / Pan-BTK Multi-Cluster Kinase Inhibitor

- **Orally Bioavailable Small Molecule**
- **ATP-Competitive, Non-Covalent Kinase Inhibitor**
- **Targets Clusters of Related Kinases Active in Heme Cancers**
  - **FLT3 Cluster**: Potently inhibits WT and all mutant forms of FLT3 + CSF1R, PDGFα
  - **BTK Cluster**: Potently inhibits WT and all mutant forms of BTK + BLK, LCK, LYN, c-SRC
  - **TRK/AURK Clusters**: Plus potently inhibits TRK-A/B/C, DDR2, c-MET
  - Inhibits signaling pathways: FLT3, BTK/BCR, AKT/mTOR/S6K, MYC, ERK, H3S10
- **Well Tolerated with Robust Safety Profile in Animals**
- **Strong Efficacy in AML Xenograft and PDX Models**
- **Being Developed for Multiple Populations of AML**
- **Being Developed for CLL / Other B-Cell Cancers**

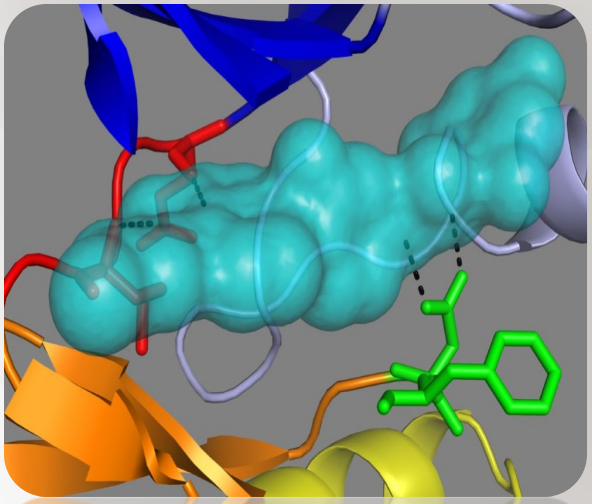
CG-806 Broadly and Potently Kills Primary Malignant Cells from Patients with Diverse Hematologic Cancers



Determined Cell Killing IC_{50} Against Bone Marrow Malignant Cells from Patient with Various Hematologic Cancers

Ex Vivo Drug Sensitivity Assay Performed at Knight Cancer Institute / OHSU

- Inhibitors assessed by ex vivo assay to determine sensitivities of fresh bone marrow patient samples to CG-806.
- Cell viability was assessed after 72-hour culture using a tetrazolium-based MTS assay and IC_{50} values calculated as a measure of drug sensitivity. Under the culture conditions used here, the cells retain viability (>90%), but do not proliferate.



CG-806

Focus on Cells from **Patients with AML**

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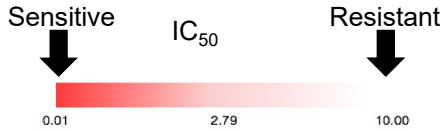
CG-806 Exerts Broad & Superior Killing Potency Compared to FLT3i on AML Patient Samples

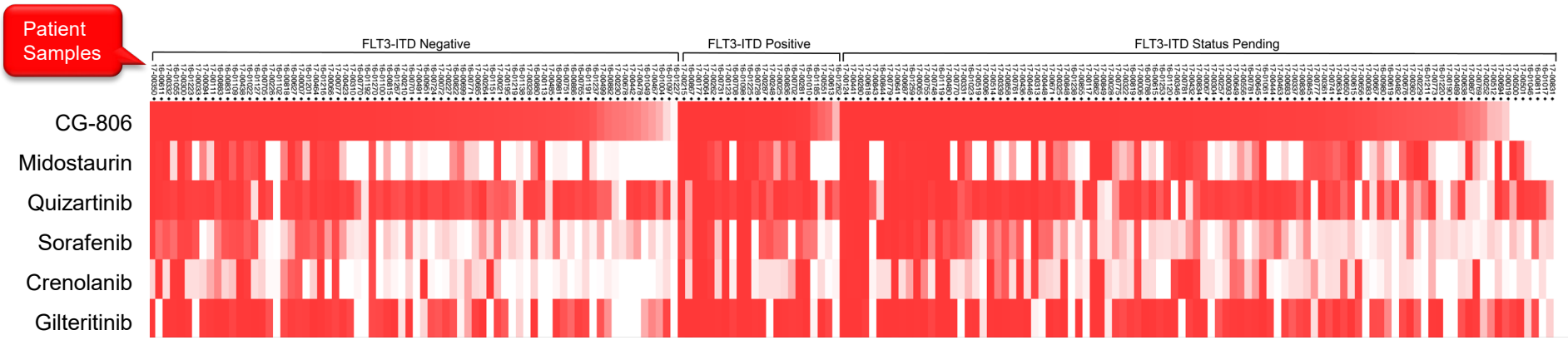
188 AML Patient Samples: Determined Cell Killing IC_{50}

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 **IC_{50} values calculated** as a measure of drug sensitivity. Under the culture conditions used here, the cells retain viability (>90%), but do not proliferate.

IC_{50} for each drug against each patient sample: Expressed as a Heatmap

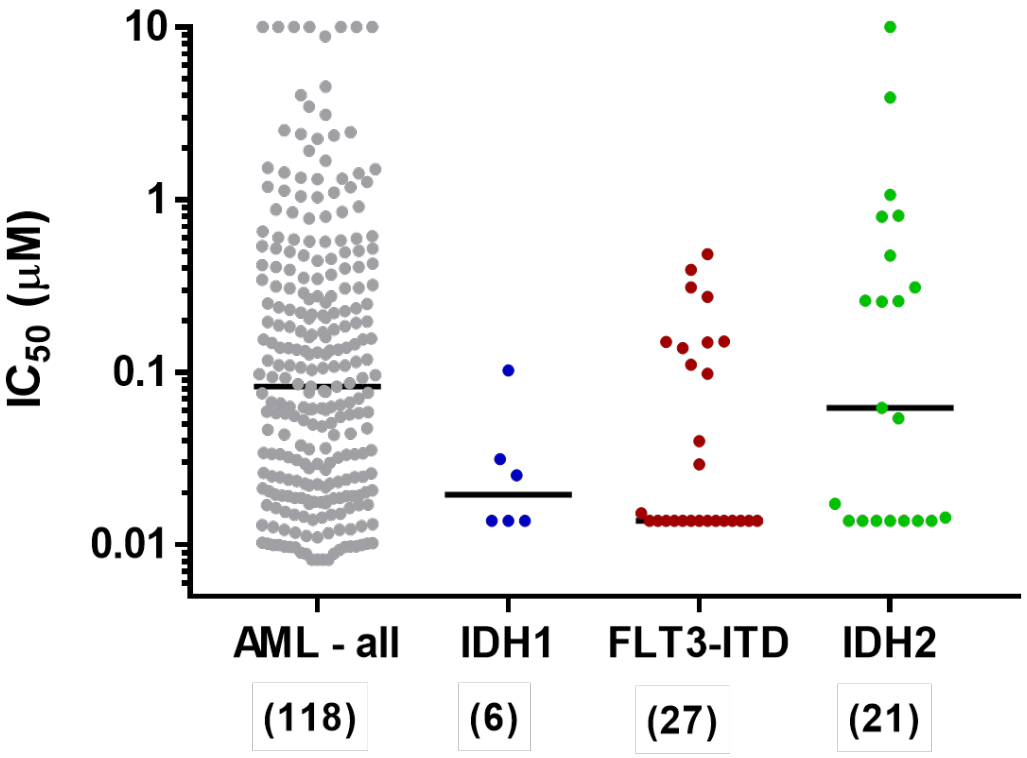




CG-806 Targets Driver (FLT3) and Bypass Pathways in AML

"More Than Just a FLT3 Inhibitor"

Primary Cells from AML Patients with IDH-1 Mutation or FLT3-ITD Mutation Hypersensitive to CG-806



AML Patient Samples

- IC_{50}
- RNAseq
- Mutational Status
- Bioinformatic Analysis

Identified Hypersensitive Populations as Potential Paths for Rapid Development

- FLT3-ITD AML
- IDH1 Mutant AML

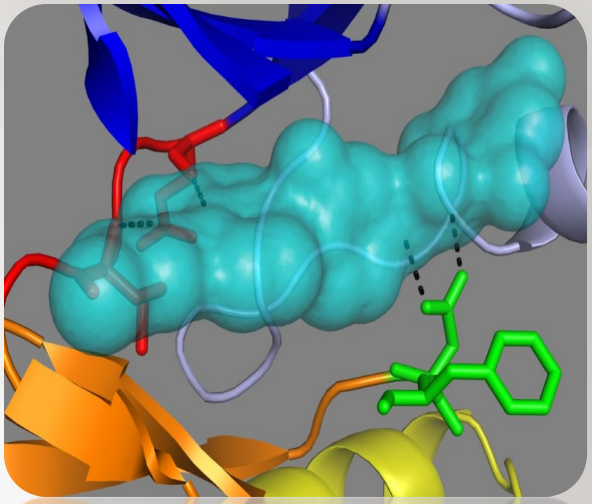
Determined Cell Killing IC_{50} Against Bone Marrow Malignant Cells from Patient with Various Hematologic Cancers

Ex Vivo Drug Sensitivity Assay Performed at Knight Cancer Institute / OHSU

- Inhibitors assessed by ex vivo assay to determine sensitivities of fresh bone marrow patient samples to CG-806.
- Cell viability was assessed after 72-hour culture using a tetrazolium-based MTS assay and IC_{50} values calculated as a measure of drug sensitivity. Under the culture conditions used here, the cells retain viability (>90%), but do not proliferate.

CG-806: Application to AML Patients

- **Observed potent killing of malignant cells from AML patients**
- **Observed superior potency relative to other FLT3 inhibitors**
  - Due to ability to inhibit all WT and mutant forms of FLT3
  - Plus, activity on other pathways
- **Identified FLT3-ITD AML populations as hyper-sensitive**
- **Identified IDH1-mutant AML population as hyper-sensitive**
- **What does this tell us about CG-806?**
  - Potential to out-compete other FLT3 inhibitors
  - Potential to treat patients resistant to other FLT3 inhibitors
  - Potential to treat patients with IDH1 mutations even if failed IDH1 inhibitors
  - Potential to treat patients that are elderly and cannot tolerate other drugs
  - Potential to treat a broad pool of AML patients
  - Stands in a class of its own



CG-806

Focus on Cells from

Patients with B-Cell Cancers

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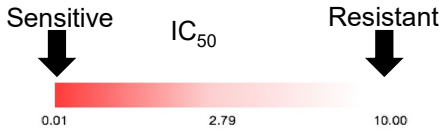
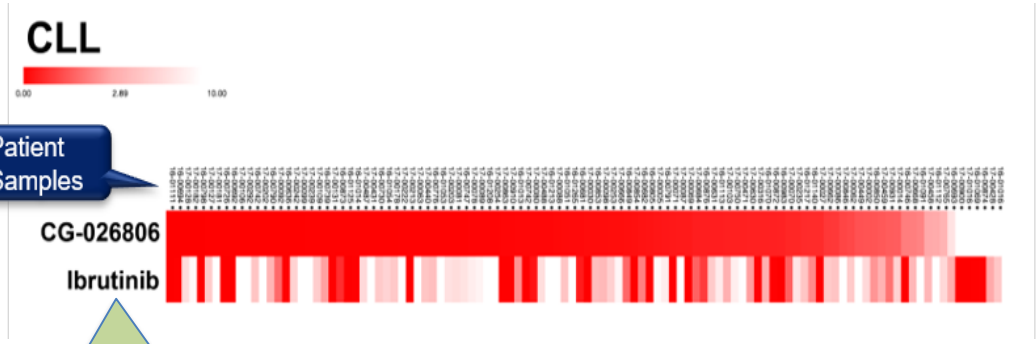
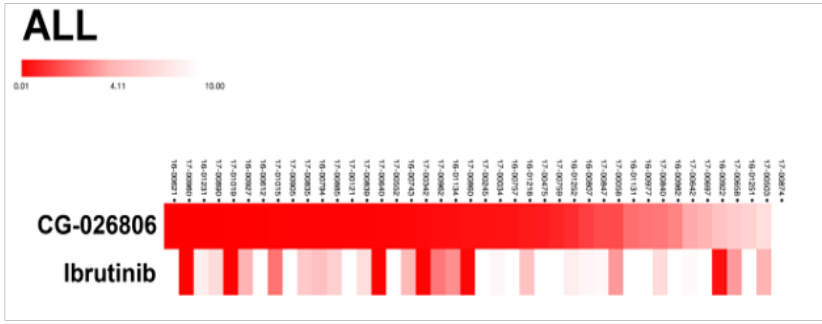
CG-806 Exerts Broad & Superior Killing Potency Compared to Ibrutinib on Patient Samples

CLL and ALL Patient Samples: Determined Cell Killing IC_{50}

IC_{50} for each drug against each patient sample: Expressed as a Heatmap







CG-806 Superior Killing to Standard-of-Care Ibrutinib Covalent BTK Inhibitor

CG-806 Targets Driver (BTK) and Bypass Pathways in B Cell Cancers: "More Than Just a BTK Inhibitor"

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

CG-806 Targets Driver (BTK) and Rescue Pathways in B Cell Cancers

			BTK IC_{50} (nM)		Key Off-Targets	
Agent	**Company**	**Binding**	**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
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	**APTOSE**	**Non-Covalent**	**5.0**	**2.5**	**4.3**	**>1000**

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

- **Inhibits clusters of oncogenic kinases operative in B cell malignancies**
- **Yet, 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.

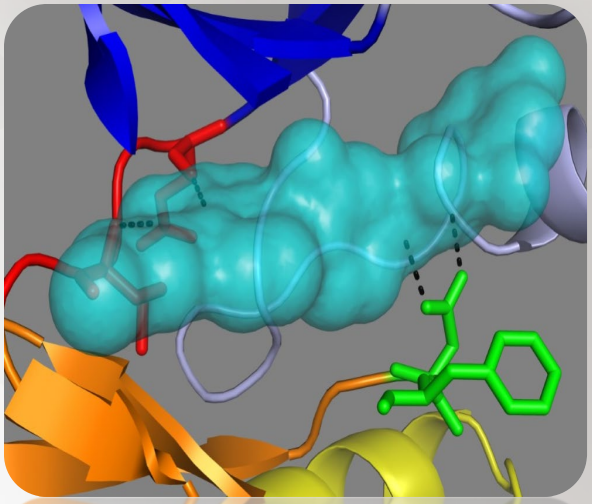
(2) N Engl J Med. 2016 Jan 28;374(4):323-32

(3) Sunesis Corporate Presentation, September 2017

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

CG-806: Application to B-Cell Cancer Patients

- **Observed potent killing of malignant cells from B-cell cancer patients**
- **Observed superior potency relative to Ibrutinib *covalent* BTK inhibitor**
  - Does not inhibit kinases that cause toxicity to ibrutinib
  - Expect superior potency to extend to other covalent BTK inhibitors
- **Distinct kinase inhibition profile from *non-covalent* BTK inhibitors**
  - Potent activity against WT and C481S mutant BTK
  - Plus, activities on other pathways enable potent cell killing
- **What does this tell us about CG-806?**
  - Distinct from Covalent and from other Non-covalent BTK inhibitors
  - Potential to treat patients resistant to Covalent BTK inhibitors
  - Potential to treat patients resistant to Non-Covalent BTK inhibitors
  - Potential to treat a broad pool of B-cell cancer patients
  - Stands in a class of its own



CG-806

Drugs Combination Studies on Bone Marrow Cell from Patients with Various Hematologic Cancers

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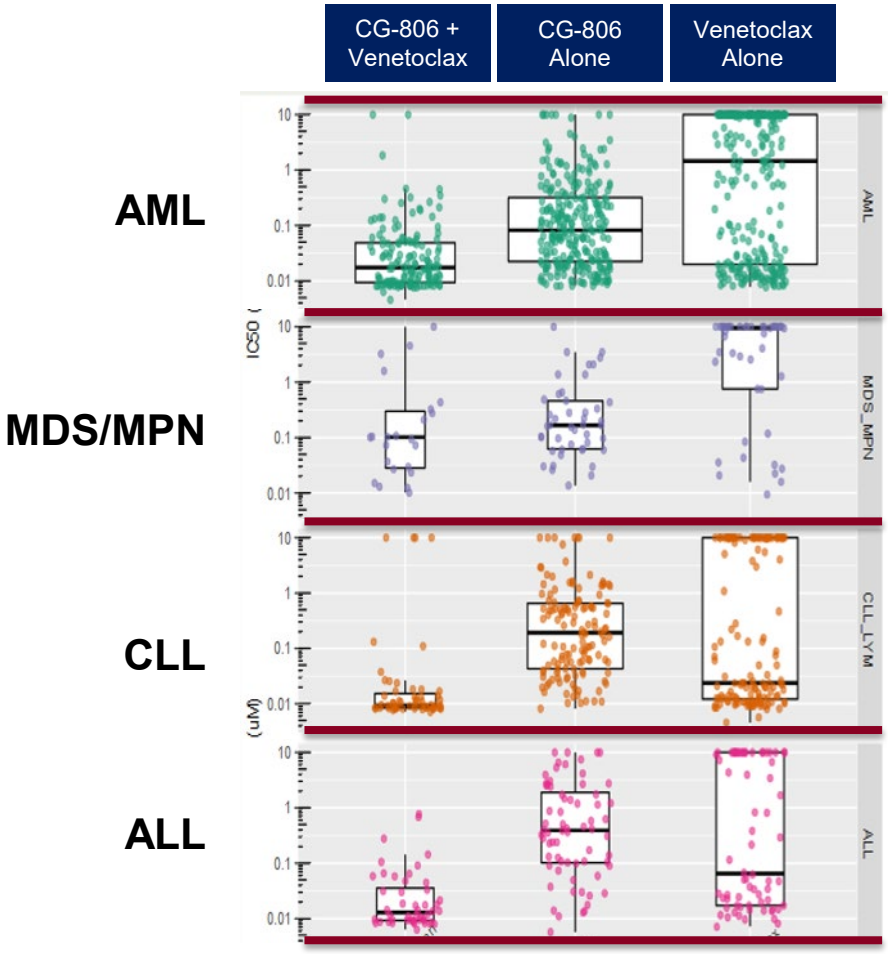
Impressive Combination of CG-806 with Venetoclax on Patient Samples from Hematologic Cancers



- CG-806 and Venetoclax (Bcl2i):
  - Individually highly active agents
- Combination Studies:
  - Enhanced ex vivo killing of patient bone marrow cells in most samples
- **<u>CG-806 + Venetoclax:</u>**
  - Combination may become the preferred drug combination for patients with AML, MDS/MPN, CLL, ALL and other hematologic malignancies

Box plots show median and IQR; width is proportional to number of samples
Drugs are ordered from left to right by increasing median IC_{50} across all diagnoses

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

- **Oral, Small Molecule, Non-covalent Kinase Inhibitor**
  - Well tolerated with robust safety profile and considerable therapeutic window
- **Targets Clusters of Related Kinases Active in Heme Cancers**
  - Inhibits FLT3, BTK, TRK/AURK Clusters
  - Inhibits WT and all mutant forms of FLT3 and BTK Driver Kinases
  - Inhibits “Rescue / Accessory” Pathways that Provide for Drug Resistance
- **Being Developed for AML**
  - Plan to treat sizable segment of AML population → More than just FLT3 inhibitor
  - Develop for 1) elderly 2) FLT3i-resistant and 3) IDH-1 mutant AML populations
- **Being Developed for CLL and Other B Cell Malignancies**
  - Plan to treat B cell cancer patients discontinuing Imbruvica (resistant / refractory / intolerant)
  - Inhibits driver BTK (WT/Mutant) and “rescue” pathways → More than just BTK inhibitor
  - But, does not inhibit TEC, EGFR, ErbB2/4 toxicity-related kinases
- **Combination with Venetoclax May Emerge as Preferred Regimen**

Key Opinion Leader Breakfast:
Novel Treatment for AML and B-cell Cancers
Hosted by Aptose Biosciences (Nasdaq: APTO)

8:00 – 9:30 am ET
December 12, 2018
Lotte New York Palace Hotel, New York, NY

Live Webcast: Aptose KOL Presentation Webcast Link

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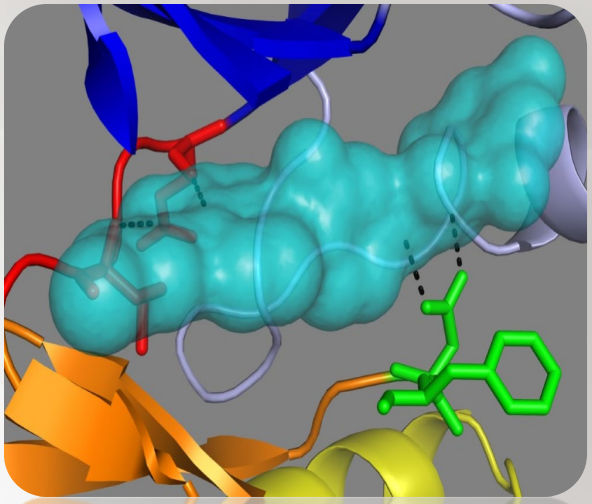
NASDAQ: APTO TSX: APS

Stephen B. Howell, M.D. Serves as Acting Chief Medical Officer

- **Distinguished Professor of Medicine**
  - University of California, San Diego
  - Past Director, Cancer Therapeutics Training Program
  - Past Leader, Solid Tumor Therapeutics Program, Moores UCSD Cancer Center
- **Research Programs**
  - Extensive M of Action and M of Resistance studies with APTO-253 and CG-806
  - Development of novel drugs and delivery systems for the treatment of cancer
  - Molecular and genetic mechanisms underlying drug resistance
  - >40 years of experience in experimental therapeutics
  - Authored more than 360 papers in peer-reviewed journals
- **Training**
  - Medical Degree - Harvard Medical School
    Intern/Resident - Massachusetts General Hospital
    Research Associate - Laboratory of Cell Biology, NCI
    Resident - University of California Hospitals
    Fellow - Oncology, Dana Farber Cancer Institute



CG-806

Pan-FLT3 / Pan-BTK Kinase Inhibitor

Phase I Plan

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Stephen Howell, M.D.

CG-806 Early Phase I clinical Development Plan

GLP Toxicology/Safety Studies
Drug Product Capsule Stability
IND Submission

IND Allowance

Relapsed/Refractory B-cell Lymphoma Patients

- Less acutely ill than AML patients
  - CLL/SLL, DLBCL, MCL, FL, others
- Dose escalating Phase Ib trial - daily oral dosing; 28 day cycles
- Collect PK and PD data – Seek a dose that delivers a "**therapeutic exposure**"
- Continue dose escalation to define RP2D
- Define safety and tolerance
- Expand into sensitive subpopulations

Healthy Volunteers

- Single Ascending Dose Study
- Collect PK and PD data over 1 week
- Identify a dose that delivers "**therapeutic exposure**"

Relapsed/Refractory AML

- Define safety and tolerance
- Measure PK / biomarkers / Identify RP2D
- Expand into sensitive subpopulations
  - $FLT3i^{R}$, $IDH1^{M}$, elderly, other

(1) Cancer. 2014 July 15; 120(14): 2142-2149.

Thank You!

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