Lunch & Corporate Update

Hosted by Aptose Biosciences Inc.
During the 61st ASH Annual Meeting

APTOSE BIOSCIENCES

Saturday, December 07, 2019
11:00 AM-Noon ET

Stephen B. Howell, MD

Distinguished Professor of Medicine
Moores Cancer Center, University of California, San Diego

Acting Chief Medical Officer of Aptose Biosciences

MEETING HOST

APTOSE BIOSCIENCES

Meeting Participants

Subject Matter Experts

Rafael Bejar MD, PhD
Associate Professor of Medicine
Director, MDS Center of Excellence
Moores Cancer Center
University of California, San Diego
Joining Aptose as **Chief Medical Officer** Jan 2020

Stephen B. Howell, MD
Distinguished Professor of Medicine
Moores Cancer Center
University of California
Acting Chief Medical Officer

Participating Telephonically

Brian J. Druker MD
Professor of Medicine
Division of Hematology/Medical Oncology
Director, Knight Cancer Institute
Oregon Health & Science University
Chair, Aptose Scientific Advisory Board

Management Team

Mr. Gregory Chow
Exec. Vice President and Chief
Financial Officer
Aptose Biosciences Inc.

William G. Rice, PhD
Chairman, President and Chief
Executive Officer
Aptose Biosciences Inc.

Jotin Marango, MD, PhD
Sr. Vice President and Chief
Business Officer
Aptose Biosciences Inc.

William G. Rice, PhD
Chairman, President and Chief Executive Officer
Aptose Biosciences Inc.

Corporate Highlights & Introduction to CG-806

First-in-Class Oral FLT3 / BTK Inhibitor

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Company Highlights

APTOSE…..Serving Patients and Market Opportunities

Developing first-in-class, targeted agents to treat hematologic malignancies

Potential to serve broadly CLL and AML patient needs : $1B+ commercial opportunity

CG-806 Oral FLT3 / BTK Inhibitor

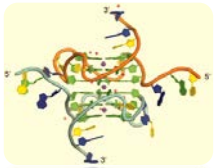
Inhibits wild type and all mutant forms of FLT3 : Driver of AML & MDS

Inhibits wild type and all mutant forms of BTK : Driver of CLL & NHL

Precision suppresses multiple oncogenic pathways yet spares safety targets

Potential to treat broadly hematologic malignancies and avoid drug resistance

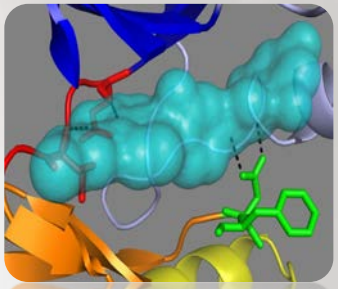
Phase 1a/b trial ongoing for CLL & NHL and Phase 1 is planned for AML & MDS



APTO-253 MYC Inhibitor

Only clinical stage agent directly targeting G-Quadruplex of notable MYC oncogene

Phase 1b trial ongoing for AML & MDS demonstrating safety and MYC inhibition



CG-806

Oral FLT3 / BTK Inhibitor

(Selectively Inhibits Clusters of Key Kinases)

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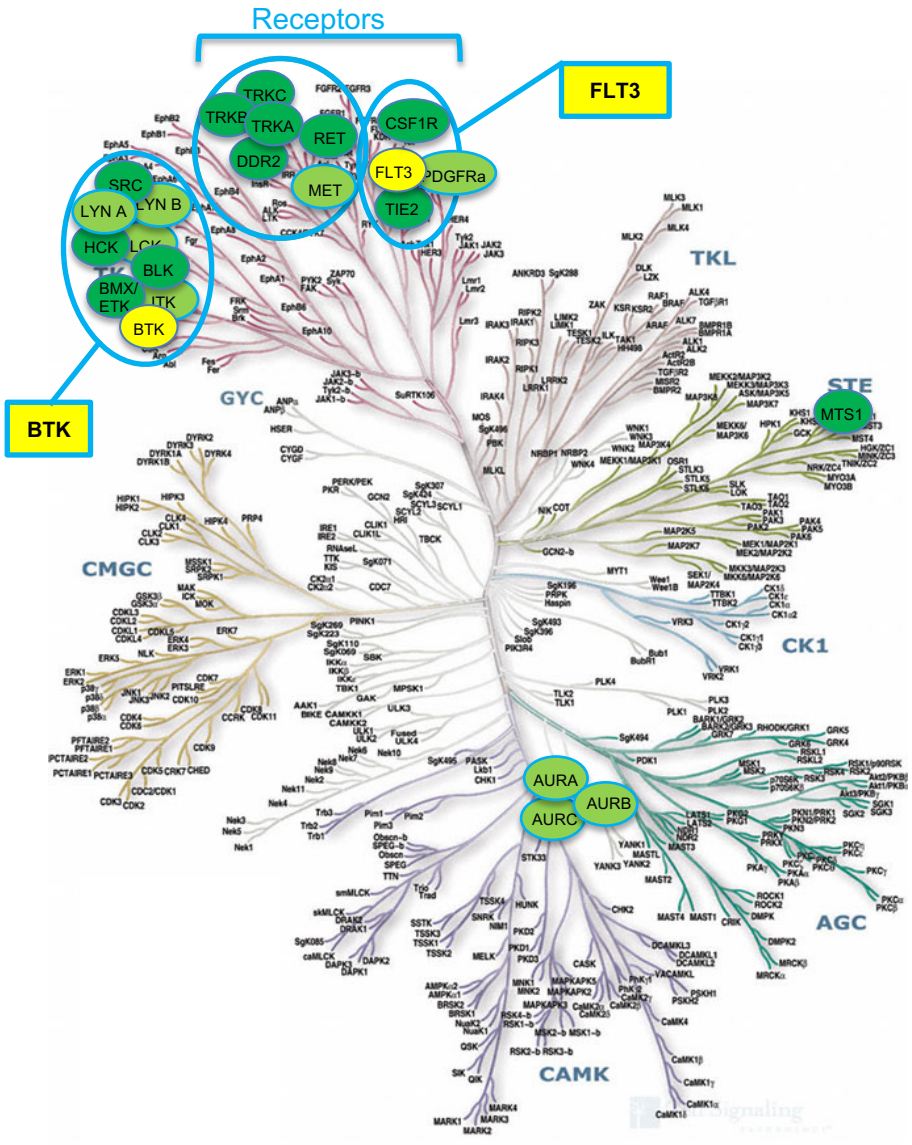
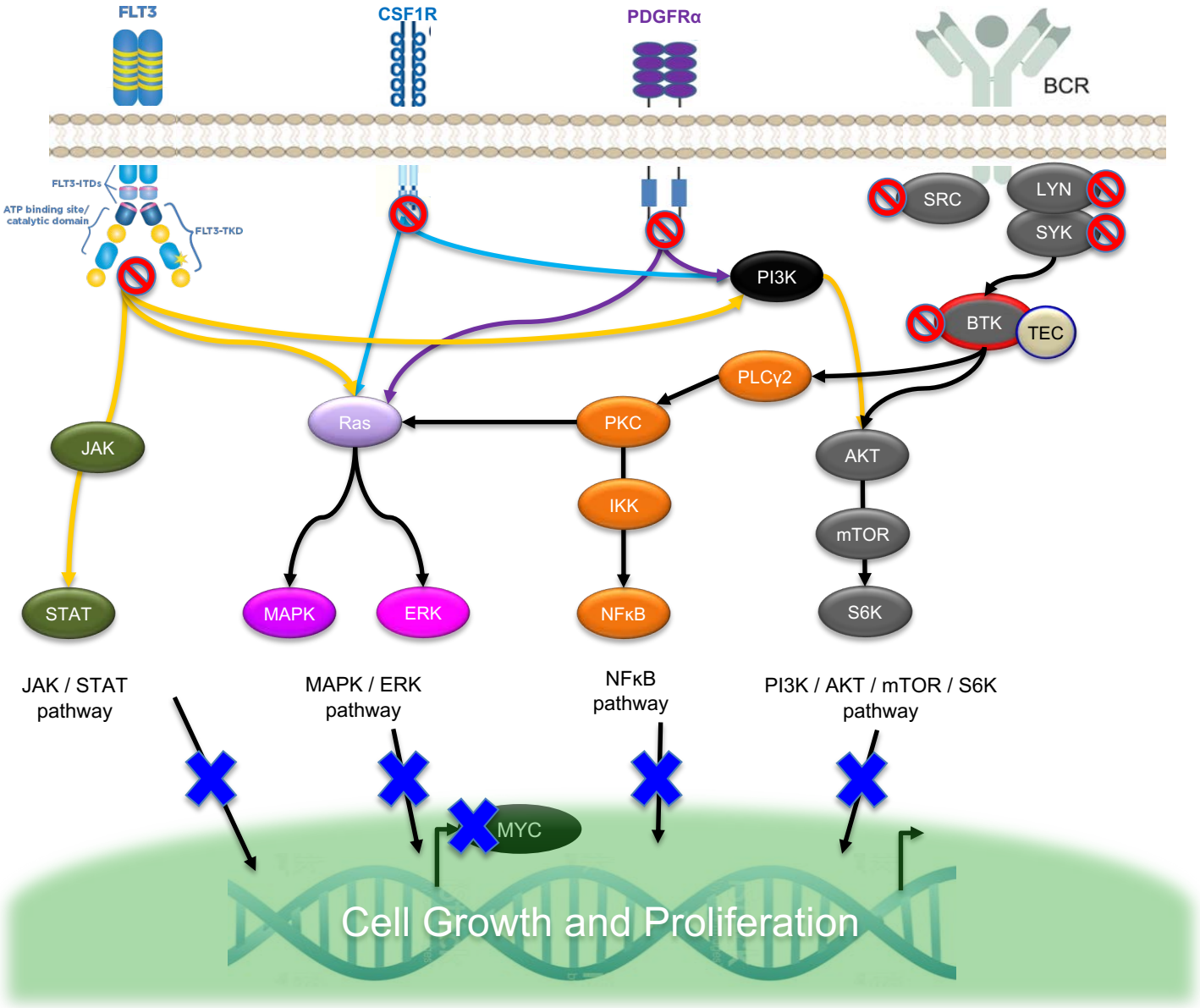
CG-806 Potently& Selectively Inhibits Clusters of Kinases That Drive Hematologic Malignancies

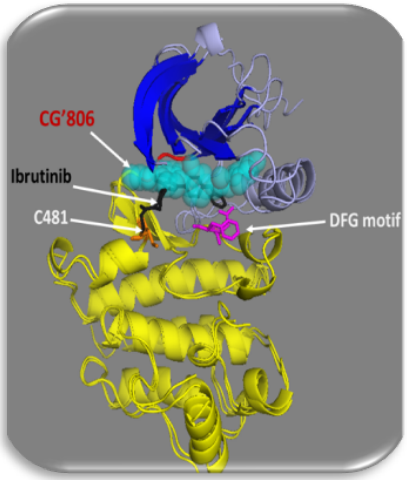


- **Mutation Agnostic**
  - Inhibits WT and all mutant FLT3
  - Inhibits WT and all mutant BTK
- **Robust Safety Profile**
  - NOT a “dirty” kinase inhibitor
  - Avoids kinases that impact safety
- **Inhibits Clusters of Driver Kinases Operative in Heme Cancers**
  - FLT3 cluster → AML & MDS
  - BTK cluster → CLL & NHL
  - Simultaneously suppresses multiple signaling pathways

CG-806 Suppresses Key Oncogenic Targets and Pathways in Myeloid & Lymphoid Malignancies



CG-806 Non-Covalent BTK Inhibitor for CLL & NHL: Potent Against WT-BTK and C481S-BTK



- **BTK kinase dysregulation** drives CLL & NHL cancers
- **Ibrutinib** (covalent WT-BTKi) ineffective on C481S-BTK
- **CG-806**
  - Binds non-covalently to **WT**-BTK *and* **C481S**-BTK
  - Retains potency (IC_{50} = 2.5nM) against C481S-BTK
  - 1000x more potent than ibrutinib killing CLL/NHL cells

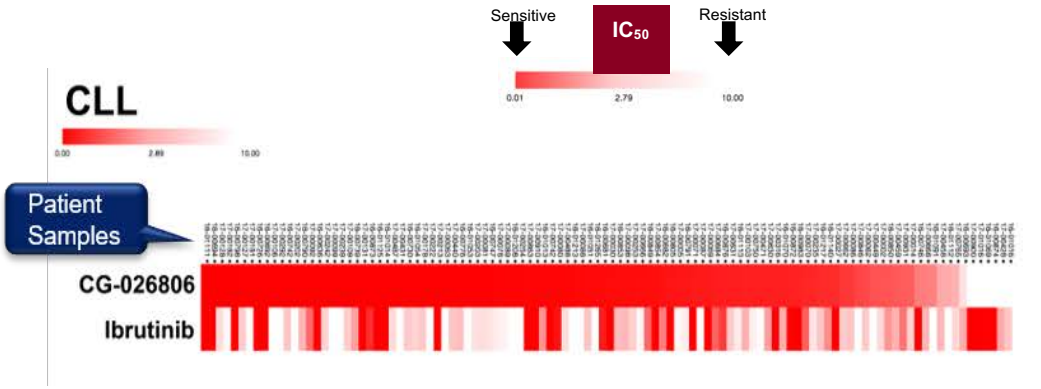
But, does **NOT** inhibit TEC, EGFR or ErbB2 kinases linked to **ibrutinib** related toxicities; including bleeding disorders, gut and skin toxicity and atrial fibrillation, respectively

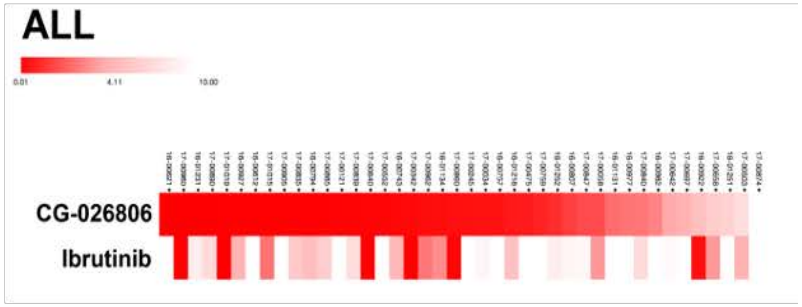
IC_{50} (nM)	TEC	EGFR	ErbB2
Ibrutinib	78	5.6	9.4
CG-806	>1,000	>1,000	>1,000

CG-806 Exceptionally Well Tolerated in Preclinical Studies

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

- **OHSU Measured the Ability of CG-806 or Ibrutinib to Kill Primary Cells from Patients with CLL or B-cell ALL Ex Vivo : IC_{50} transformed into a Heatmap of Sensitivity**



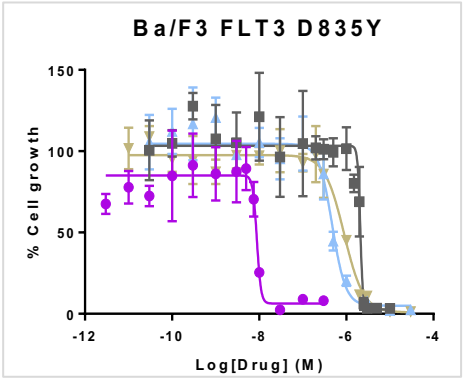


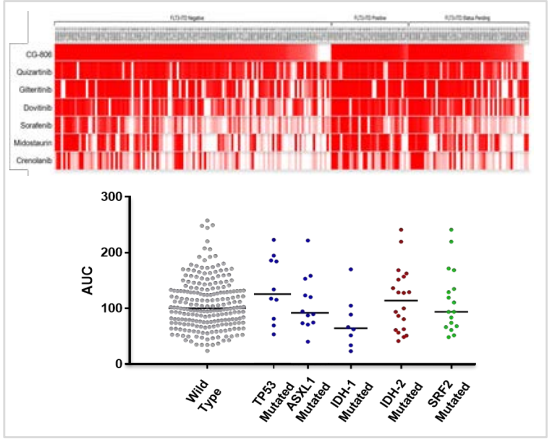
"CG-806 is More Than Just a BTK Inhibitor"

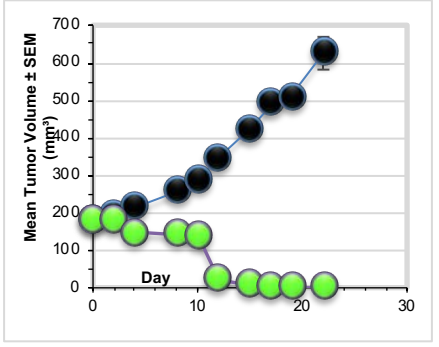
- **Targets driver (BTK-WT/Mutant) and rescue pathways operative in B-cell cancers**
- **1000x more potent than ibrutinib (SOC covalent BTKi) at killing malignant B-cells**

CG-806 Potent FLT3 Inhibitor for AML (Myeloid Cancers): Potent Against WT-FLT3, Mutant-FLT3, Other Mutations

- **IC_{50} = 0.8nM on FLT3-ITD**
  - Low nM IC_{50} on WT and all other FLT3 mutants (including D835)
  - 100x potency of gilteritinib / quizartinib / crenolanib on FLT3-D835Y
- **Broad & Superior Killing of Samples from Patient with AML Compared to All Other FLT3i**
  - Retains sensitivity to samples from patients with FLT3-WT, FLT3-ITD, FLT3-TKD, or mutant p53, IDH-1, IDH-2, SRF2 or ASXL1
- **Safe / Tumor Elimination / Cures in Animal Models**
  - FLT3-ITD AML in murine xenograft
  - FLT3-ITD+D835 AML in PDX models
- **Planning Development for Patients with R/R AML**
  - Patients with mutant FLT3 and failing other FLT3i
  - Patients with FLT3-WT or with mutant p53 or mutant IDH1







CG-806 Phase 1 Clinical Development Activities

Planning a Phase 1 Study for Relapsed/Refractory AML/MDS

Dose escalating Phase I trial – Define safety, tolerance, PK, PD and RP2D

We do not wish to administer sub-therapeutic doses to R/R AML patients, as they are acutely ill

So, first

Conducting Ongoing Phase 1 Study in R/R CLL and NHL Patients

Dose escalating Phase I trial – Define safety, tolerance, PK, PD and RP2D
Collecting serum and characterizing steady-state PK properties
Seek to identify a dose that could deliver a "therapeutic exposure" for AML

Plan to advance CG-806 into AML study early 2020

Stephen B. Howell, MD
Distinguished Professor of Medicine
Moores Cancer Center, University of California, San Diego
Acting Chief Medical Officer of Aptose Biosciences

CG-806 Oral FLT3/BTK Inhibitor

Clinical Findings from Active Phase 1a/b Trial in CLL & NHL

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CG-806: Key Messages from Phase 1 a/b CLL/NHL Trial Findings Through Dose Levels 1 and 2 (Accelerated Titration)

- **Safety: No Unexpected Toxicities Have Emerged To Date**
  - No Myelosuppression, No Drug-related SAE or DLT
- **Evidence of BTK Target Engagement**
  - PIA Assay: Inhibition of P-BTK, P-SYK, P-ERK and P-PDGFRα in Dose 2
  - Lymphocytosis in Dose 2
- **Early Evidence of Clinical Response**
  - Lymphocytosis and Platelet Stabilization
- **Significant Oral Absorption and Predictable PK Profile**
  - Achieving Approximately 1μM Levels at Steady State in Dose Level 2
- **Exposures Likely Therapeutic for AML Patients**
- **Hematology KOL Support : Dr. Druker and Dr. Bejar**

CG-806 PHASE 1a/b CLINICAL TRIAL UNDERWAY IN PATIENTS WITH R/R CLL/SLL OR NHL

PATIENT POPULATION

Relapsed or refractory CLL/SLL & NHL who **failed or are intolerant** to 2 or more lines of established therapy, or for whom no other treatment options are available

TRIAL DESIGN

Continuous oral administration, 28 day cycles

Dose level 150 mg BID: one patient
Dose level 300 mg BID: one patient
Dose level 450 mg BID and higher: 3 + 3

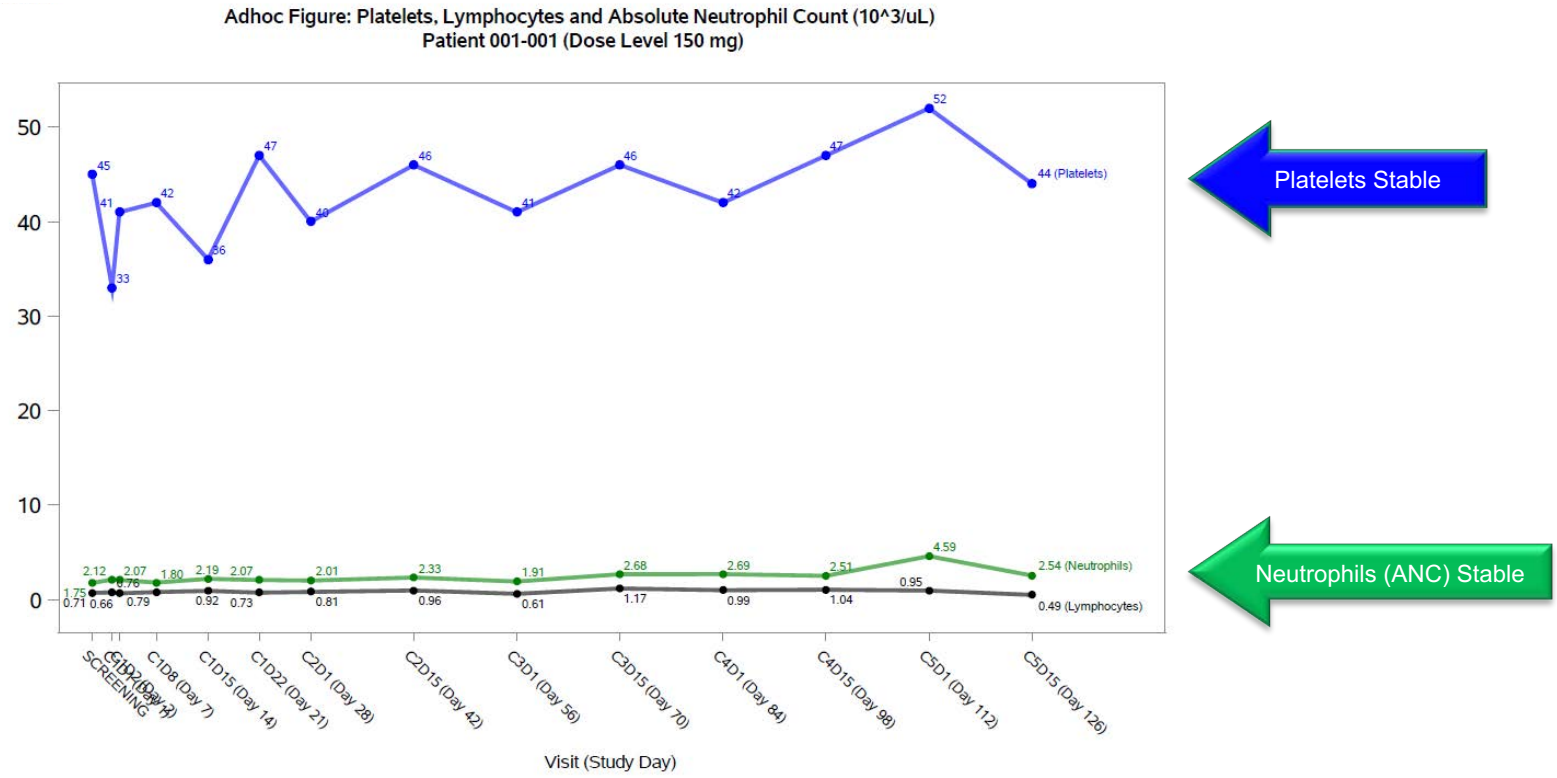
CURRENT STATUS

Dose level 150 mg BID: Completed, no dose-limiting toxicities
Dose level 300 mg BID: Completed, no dose-limiting toxicities
Dose level 450 mg BID: Open for enrollment; patients in screening

Dose Expansion will occur once MTD or Therapeutic Dose is Reached to Define RP2D

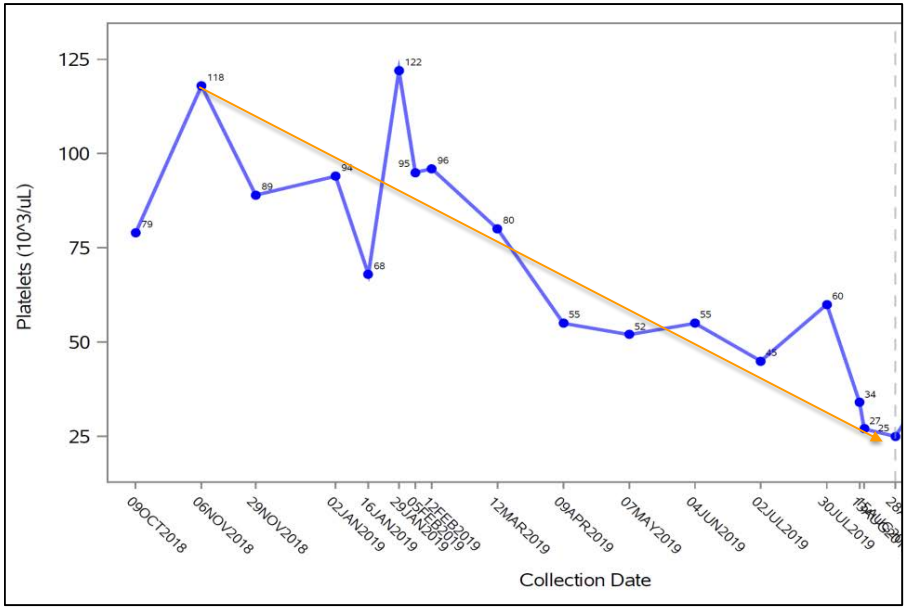
DOSE LEVEL 1 (150 MG BID)

- **One patient with R/R CLL**
- **Heavily pretreated**
  - Failed fludarabine, cytoxan, radiation, ibrutinib, venetoclax, rituximab, idelalisib
- **No DLTs : Patient remains on study currently in Cycle 6**



DOSE LEVEL 2 (300 MG BID)

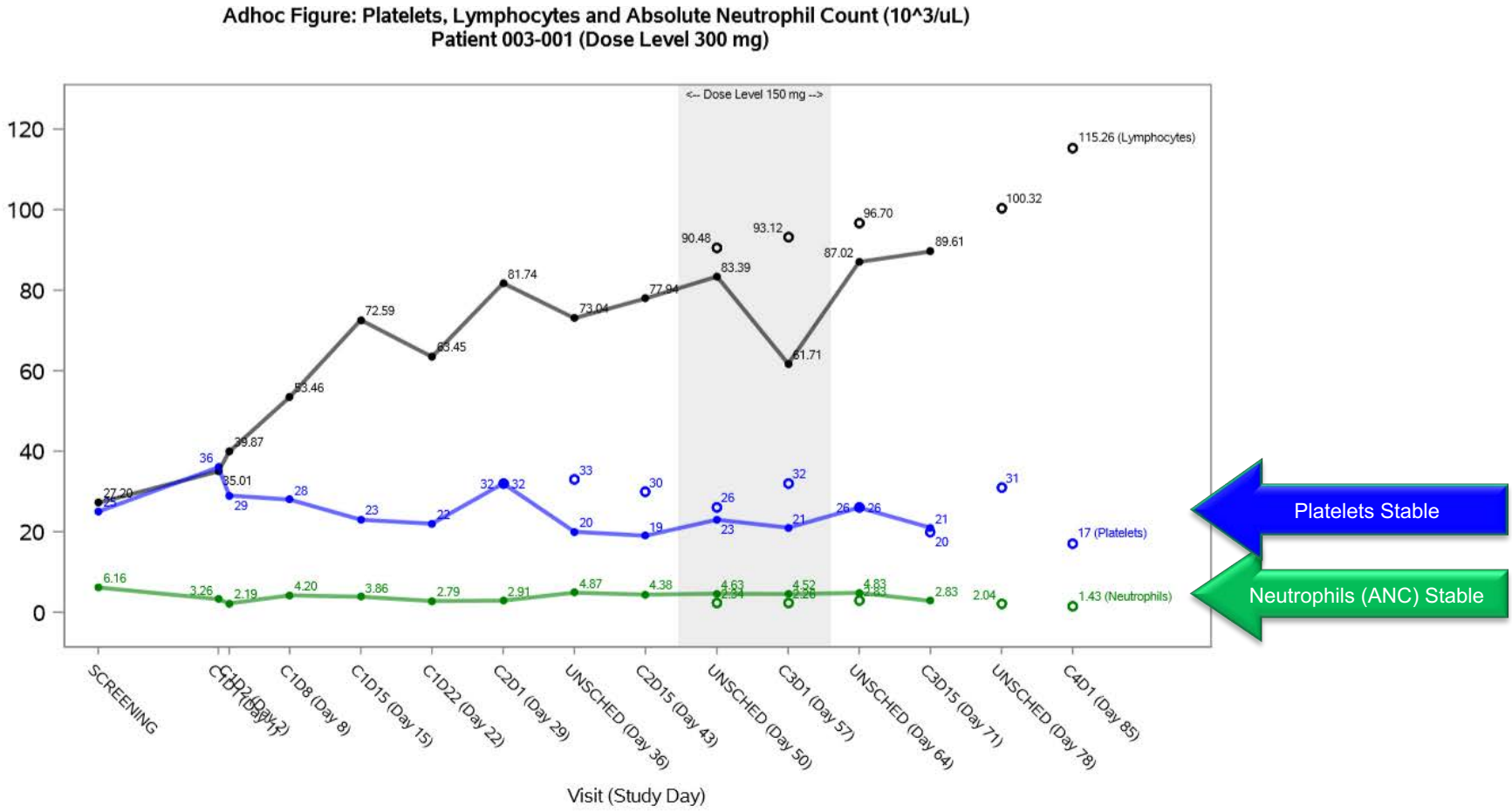
- **One Patient with R/R CLL**
- **Heavily pretreated**
  - Failed fludarabine, rituximab, obinutuzumab & ofatumumab and refused ibrutinib
- **Marrow involvement with severe thrombocytopenia**
  - Acutely ill with need for agent that spares bone marrow and unlikely to cause bleeding



- **Completed Cycle 3 with no DLTs**
- **No drug-related SAEs**
- **Currently in Cycle 4**

Platelet count 25,000/mm^3 at screening

PATIENT #2: SAFE, WELL TOLERATED AND NO EVIDENCE OF MYELOSUPPRESSION



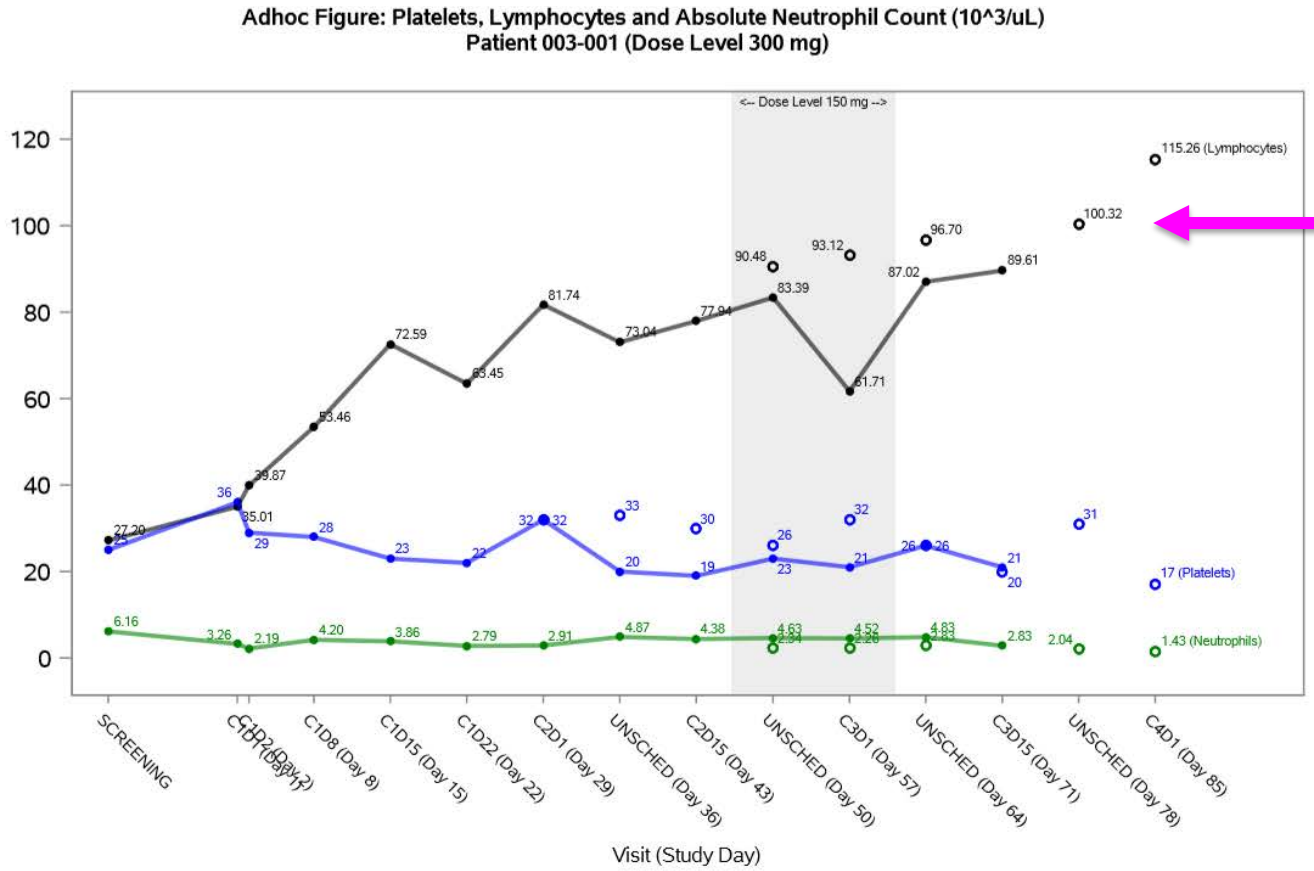
No myelosuppression after 3 cycles of treatment:

- Neutrophils (ANC) stable
- Platelet count stable

PATIENT #2 PHARMACODYNAMICS - TARGET ENGAGEMENT

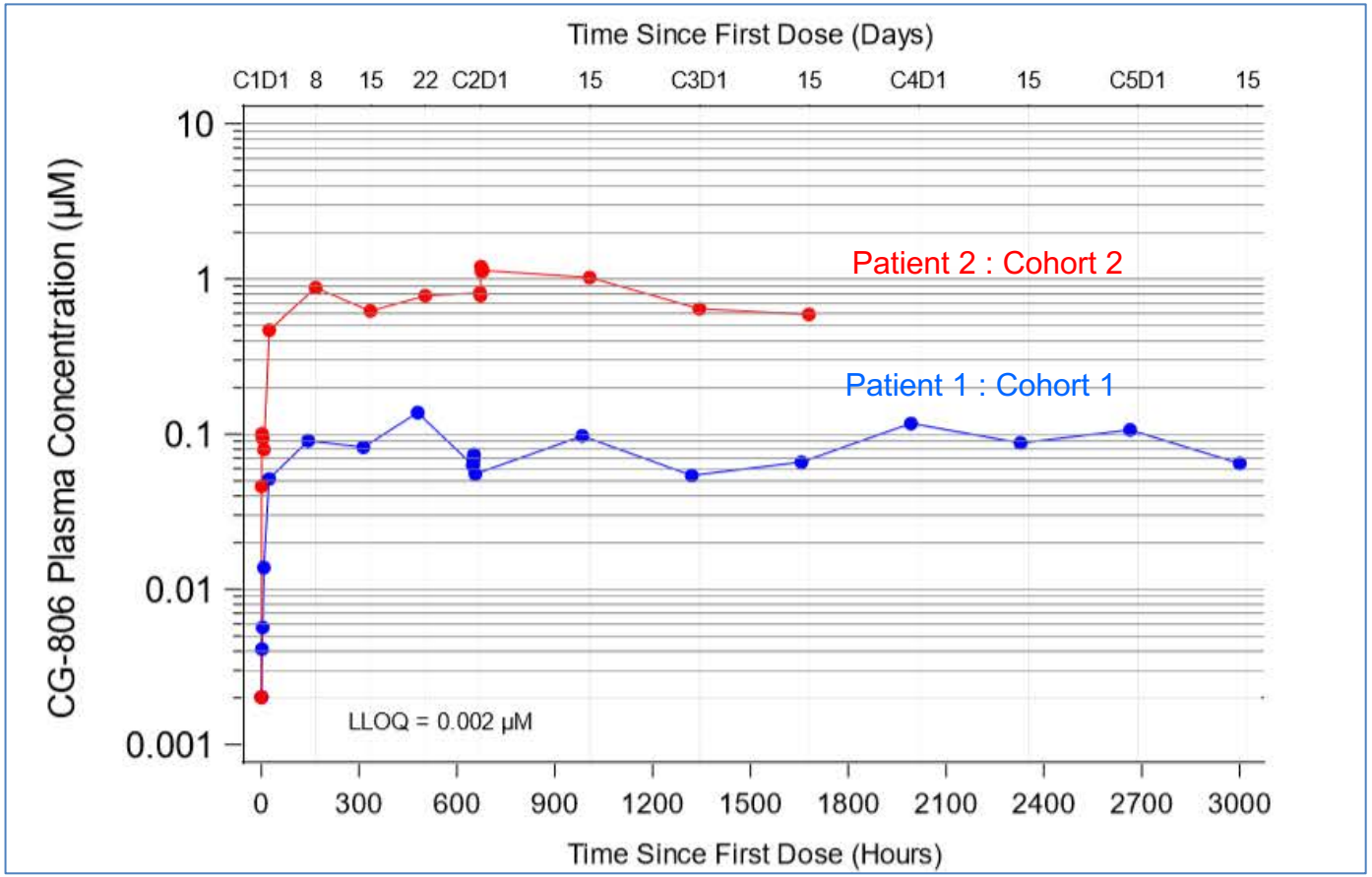
Evidence of response:

- Marked lymphocytosis: indicator of target engagement by BTK inhibitors
- Stabilization of platelet count without transfusion



Marked and ongoing lymphocytosis

CG-806 PHARMACOKINETICS: STEADY-STATE C_{MIN}



- **CG-806 level is ~ 10 times high at 300 mg BID than at 150 mg BID**
- **At 300 BID level approaches that know to be effective in xenograft models**

CG-806 SUMMARY CLL/NHS

- **Evidence of Safety and Tolerance to Date**
  - No drug-related or dose-limiting toxicities
  - No drug-related SAEs
  - No myelosuppression

- **Evidence of Response in R/R CLL Patient #2**
  - Lymphocytosis observed (BTK Target Engagement)
    - Observed in Cycle 1 and continuing through Cycle 3 in Patient #2
    - Well accepted indicator of response to BTK inhibition in CLL patients

- **Platelet Stabilization**

CG-806 DEVELOPMENTAL GOALS CLL/NHS

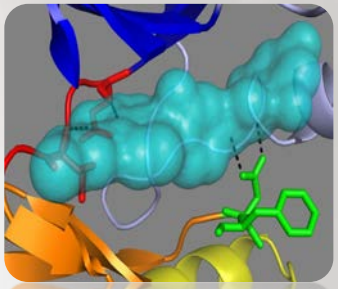
Address Major Unmet Needs in B Cell Tumors

CLL: Seek to treat patients resistant or intolerant to all:

- Covalent BTK inhibitors
- BCL2 inhibitors
- Anti-CD20 therapy
- PI3K inhibitors
- Cytotoxins, Other Agents

NHL: Seek to treat patients with relapsed or refractory DLBCL, MCL, FL, and other indolent lymphomas

Dose Expansion will occur once MTD or Therapeutic Dose is Reached to Define RP2D



CG-806

Oral FLT3/BTK Inhibitor

Phase 1a/b in AML & MDS

(in preparation)

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Developing CG-806 for the Treatment of AML

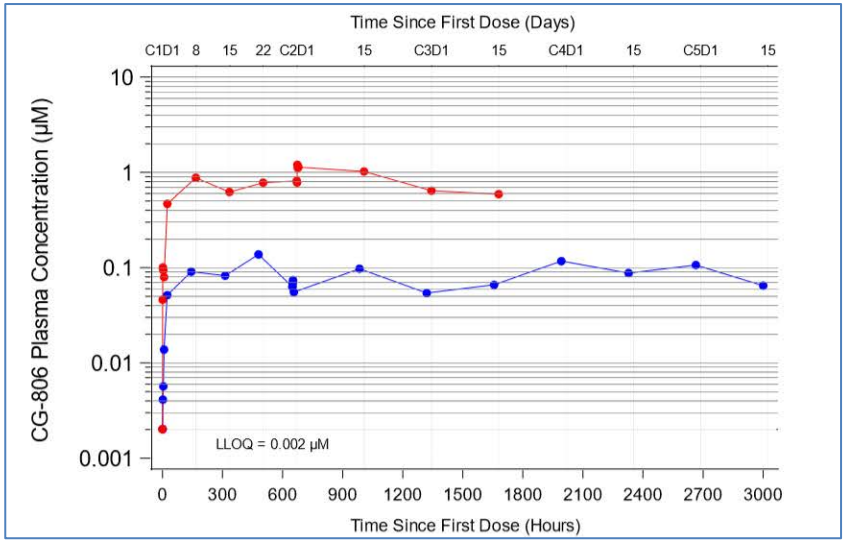
- **Strong Rationale:**
  - Broadly potent against AML cells
    - Wild type FLT3 and mutated FLT3, TP53, IDH1, IDH2, SRF2 and ASXL1
  - More potent than other FLT3 inhibitors on >200 AML patient samples
  - Delivers cures in xenograft models of human AML without toxicity
  - High “value creation impact”
- **Phase 1 Plan: Treat R/R AML Patients with Unmet Needs:**
  - Patients who failed other FLT3 inhibitors
  - Patients who failed IDH-1 inhibitors
  - Patients who failed venetoclax
  - Patients with mutated p53
  - Patients with wild type-FLT3

- Rapidly differentiate CG-806 from other FLT3i’s
- Plan to initiate dosing with an active dose level

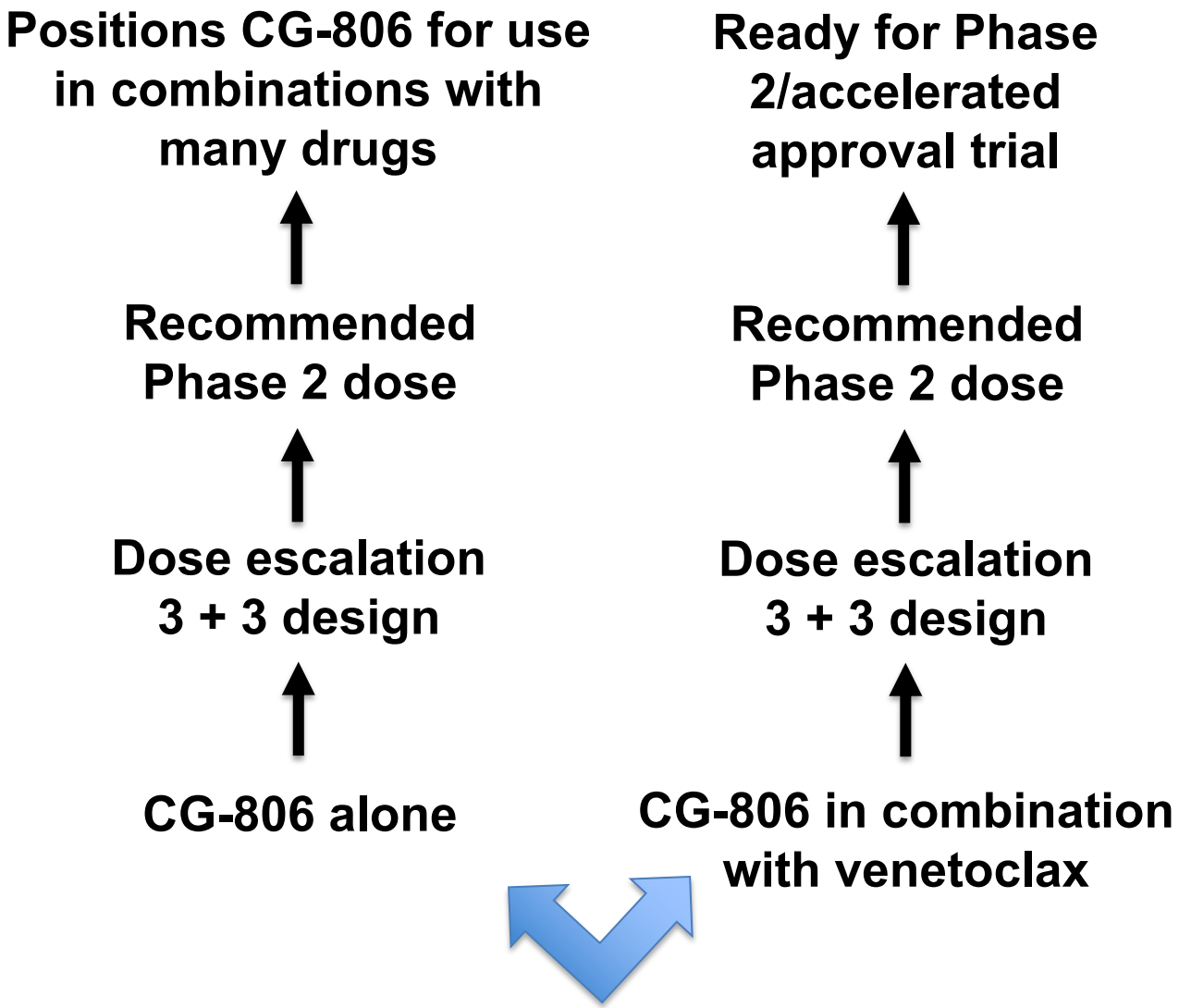
CG-806 CLINICAL DEVELOPMENT PLAN FOR AML/MDS

Approach:

- Identify dose in CLL/NHL patients that produces a steady-state C_{min} known from animal studies to produce response in human AML xenografts
- Current PK data in two patients are compelling
- C_{min} plasma concentration 0.8 – 1.0 μM at 300 mg BID likely sufficient for activity in AML patients
- Desire PK data from additional patients to confidently claim dose-related PK exposures can be predicted



PHASE 1 a/b CG-806 ALONE AND IN COMBINATION WITH VENETOCLAX IN AML PATIENTS



Rafael Bejar MD, PhD
Chief Medical Officer, Aptose
Formerly: Associate Professor of Medicine
Division of Hematology and Oncology
Director, MDS Center of Excellence
Moores Cancer Center, University of California, San Diego

Introduction as Chief Medical Officer

Analysis of CG-806 Findings to Date

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Rafael Bejar, MD, PhD

BS, Physics	**Massachusetts Institute of Technology**
MD	**Univ. of California, San Diego School of Medicine**
PhD, Neuroscience	**Univ. of California, San Diego School of Medicine**
Internship	**Internal Medicine Univ. of Chicago Hospital**
Residency, Chief	**Internal Medicine Brigham and Women's Hospital**
Fellowship	**Hematology/Oncology Dana Farber Cancer Institute & Massachusetts General Hospital**
Assoc. Professor	**Univ. of California, San Diego Moores Cancer Center**
Consultancy	**Foundation Medicine, Genoptix, Celgene, Astex, Daiichi-Sankyo, AbbVie, FortySeven**

Brian J. Druker MD
Professor of Medicine
Division of Hematology/Medical Oncology
Director, Knight Cancer Institute
Oregon Health & Science University

Perspectives on CG-806 in the Context of Kinase Inhibitors

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CG-806 in the Context of Kinase Inhibitors

- **Development of Imatinib (Gleevec) as First Kinase Inhibitor**
  - Kinases (>500 in humans) transmit signals to regulate proliferation, death, other processes
  - Controversial to attempt selective targeting of a kinase active site at that time
  - Imatinib set stage for all future kinase inhibitors
- **Over 50 Kinase Inhibitors (KIs) Approved in the US**
  - Saved numerous lives and generated tremendous revenues
- **Multiple Generations of KIs Have Been Developed**
  - Trailblazer: Imatinib highly selective for Bcr-Abl
  - First Generation: Non-selective with off-target toxicities
  - Second Generation: More selective to reduce toxicities - resistance problematic

CG-806 in the Context of Kinase Inhibitors

- **Next Generation KI**
  - Desire strong efficacy and safety while avoiding drug resistance
  - Must hit multiple “operative” targets/pathways simultaneously but avoid targets that compromise safety
- **CG-806 Preclinical Profile Meets this Profile**
  - If the preclinical safety profile of CG-806 continues in humans, CG-806 has the potential to be among the very best KI I’ve seen
- **CG-806 Clinical Data Delivering the Desired Profile in Humans**
- **Expect CG-806 Can Become a Highly Differentiated Agent for the Treatment of CLL / NHL and for AML / MDS**

CG-806

Q&A Session

APTO-253

Small Molecule MYC Inhibitor

Ongoing Phase 1b in AML & MDS

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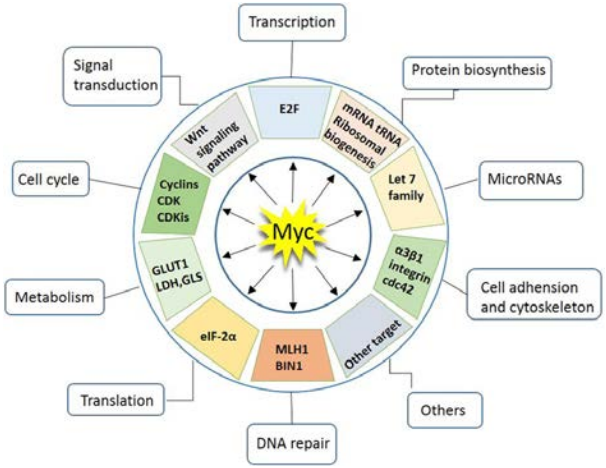
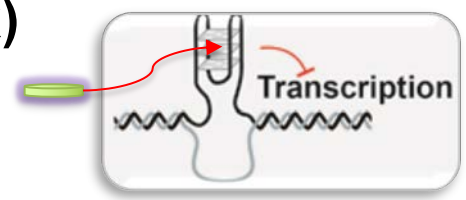
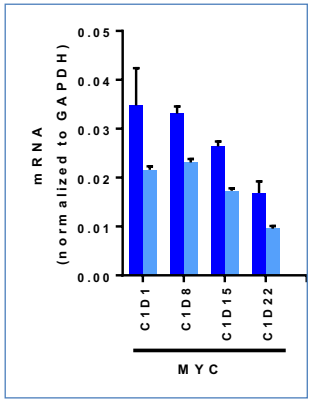
RATIONALE: APTO-253 REDUCES THE EXPRESSION OF MYC

- **MYC protein regulates multitude of key biological processes**
  - **Transcription factor binds to hundreds of genes**
- **Dysregulated in >50% of all human cancers**
  - **Reprograms signaling pathways to support survival**
- **Direct targeting of MYC *protein* is challenging**
  - **Generally considered "undruggable" – no active site**
- **Targets DNA regulatory motif (G-Quadruplex) in promoter of MYC gene**
  - **Does NOT bind to MYC protein**
- **Inhibits MYC gene expression (mRNA)**
  - **Depletes cells of MYC protein**
  - **Induces cell cycle arrest and apoptosis**

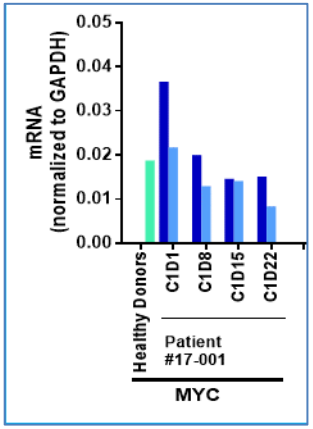




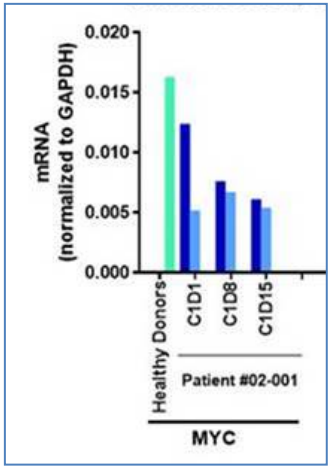
APTO-253 Phase 1 Trial First Three Dose Levels:
Safely Inhibits MYC Expression in AML & MDS Patients



- **AML Patient: Dose Level 1 (20mg/m2)**
  - Sampled pre-dose and 24 hr post-dose day 1, 8, 15, 22
- **MYC Suppression & Well Tolerated**
  - Observed inhibition of MYC expression in PBMC



- **MDS Patient: Dose Level 2 (40 mg/m2)**
  - Sampled pre-dose and 24 hr post-dose day 1, 8, 15, 22
- **MYC Suppression & Well Tolerated**
  - Observed inhibition of MYC expression in PBMC



- **AML Patient: Dose Level 3 (66 mg/m2)**
  - Sampled pre-dose and 24 hr post-dose day 1, 8, 15, 22
- **MYC Suppression & Well Tolerated**
  - Observed inhibition of MYC expression in PBMC

APTO-253 Ongoing Phase 1 a/b Dose Escalating Clinical Trial

✓ Dose Level 1 (20 mg/m^2)	Completed	1 AML Patient
✓ Dose Level 2 (40 mg/m^2)	Completed	1 MDS Patient
✓ Dose Level 3 (66 mg/m^2)	Completed	3 AML Patients

- 3 AML patients completed 28-day cycle
- To Date, Well-Tolerated & No Drug-Related SAEs

Dose Level 4 (100mg/m2): Now Screening for 3 Patients

APTO-253

Q&A Session

Thank You!

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