Lunch & Corporate Update

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

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
Meeting Participants

Subject Matter Experts

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

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

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.
Corporate Highlights &
Introduction to CG-806
First-in-Class Oral FLT3 / BTK Inhibitor
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)
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

<table>
<thead>
<tr>
<th>IC$_{50}$ (nM)</th>
<th>TEC</th>
<th>EGFR</th>
<th>ErbB2</th>
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<tbody>
<tr>
<td>Ibrutinib</td>
<td>78</td>
<td>5.6</td>
<td>9.4</td>
</tr>
<tr>
<td>CG-806</td>
<td>&gt;1,000</td>
<td>&gt;1,000</td>
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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

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

So, first

Plan to advance CG-806 into AML study early 2020
CG-806 Oral FLT3/BTK Inhibitor
Clinical Findings from Active Phase 1a/b Trial in CLL & NHL
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

<table>
<thead>
<tr>
<th>PATIENT POPULATION</th>
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<tbody>
<tr>
<td>Relapsed or refractory CLL/SLL &amp; NHL who failed or are intolerant to 2 or more lines of established therapy, or for whom no other treatment options are available</td>
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<tr>
<th>TRIAL DESIGN</th>
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<tr>
<td>Continuous oral administration, 28 day cycles</td>
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<tr>
<td>Dose level 150 mg BID: one patient</td>
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<tr>
<td>Dose level 300 mg BID: one patient</td>
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<tr>
<td>Dose level 450 mg BID and higher: 3 + 3</td>
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<table>
<thead>
<tr>
<th>CURRENT STATUS</th>
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<tbody>
<tr>
<td>Dose level 150 mg BID: Completed, no dose-limiting toxicities</td>
</tr>
<tr>
<td>Dose level 300 mg BID: Completed, no dose-limiting toxicities</td>
</tr>
<tr>
<td>Dose level 450 mg BID: Open for enrollment; patients in screening</td>
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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/mm³ 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
Evidence of response:
• Marked lymphocytosis: indicator of target engagement by BTK inhibitors
• Stabilization of platelet count without transfusion
CG-806 PHARMACOKINETICS: STEADY-STATE C\textsubscript{MIN}

- CG-806 level is \(~ 10\) times high at 300 mg BID than at 150 mg BID
- At 300 BID level approaches that known to be effective in xenograft models
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)
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
Approach:

- Identify dose in CLL/NHL patients that produces a steady-state $C_{\text{min}}$ known from animal studies to produce response in human AML xenografts.
- Current PK data in two patients are compelling.
- $C_{\text{min}}$ 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

Positions CG-806 for use in combinations with many drugs

- Recommended Phase 2 dose
- Dose escalation 3 + 3 design
- CG-806 alone

Ready for Phase 2/accelerated approval trial

- Recommended Phase 2 dose
- Dose escalation 3 + 3 design
- CG-806 in combination with venetoclax
Introduction as Chief Medical Officer

Analysis of CG-806 Findings to Date
<table>
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<tr>
<th>Education</th>
<th>Institution</th>
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<tr>
<td>BS, Physics</td>
<td>Massachusetts Institute of Technology</td>
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<tr>
<td>MD</td>
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<td>PhD, Neuroscience</td>
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<td>Hematology/Oncology Dana Farber Cancer Institute &amp;</td>
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<td></td>
<td>Massachusetts General Hospital</td>
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<tr>
<td>Assoc. Professor</td>
<td>Univ. of California, San Diego Moores Cancer Center</td>
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<tr>
<td>Consultancy</td>
<td>Foundation Medicine, Genoptix, Celgene, Astex, Daiichi-</td>
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<td>Sankyo, AbbVie, FortySeven</td>
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Perspectives on 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
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
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 (100 mg/m^2): Now Screening for 3 Patients
APTO-253

Q&A Session
Thank You!