Jefferies 2019
Global Healthcare Conference
JUNE 2019

NASDAQ: APTO  TSX: APS
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Investment Highlights

**APTOSE**

**Clinical stage biotech company** developing first-in-class targeted agents

**Treating hematologic malignancies** life-threatening / orphan diseases

**Two clinical-stage targeted agents** with strong IP protection

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**CG-806** Oral pan-FLT3 / pan-BTK Inhibitor

**All wild type & mutant forms of BTK and FLT3** potently inhibited

**Simultaneously targets** multiple essential pathways to kill cancer cells

**Phase 1a/b stage** for the treatment of CLL/SLL/NHL and planned for AML/MDS

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**APTO-253** MYC Inhibitor

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

**Phase 1B stage** for AML/MDS demonstrating clinical safety and MYC inhibition

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**Market**

**$1B+ commercial opportunity** in AML and CLL lead indications with two agents

**Rapid clinical POC and value creation** when treating hematologic malignancies
Strong Leadership Team and Financial Foundation

**Dr. William G. Rice, PhD**  
Chairman, President &  
Chief Executive Officer

**Mr. Gregory Chow**  
Executive Vice President &  
Chief Financial Officer

**Dr. Jotin Marango, MD, PhD**  
Senior Vice President &  
Chief Business Officer

- *Announced This Week*
  - Former Research Analyst

**Completed Public Offering of Common Shares**

- Oversubscribed with aftermarket support by validating Institutional Funds

**Availability of nearly $100 million**  
Comfortable cash position into 3Q2020

Ability to advance clinical assets without need to use ATM or CEFF at this time
Dr. Brian J. Druker, MD
Collaborator & Chair of SAB
Key Role in Dev’t of Gleevec
Member, National Academy of Medicine, National Academy of Sciences & American Academy of Arts & Sciences
Winner of Karnofsky Award, Lasker “America’s Nobel” Award
Winner of Japan Prize in Healthcare and Medical Technology and the Tang Prize in Biopharmaceutical Science
Winner of the prestigious Sjöberg Prize
Leader of Inter-institutional Beat AML Initiative

Dr. Michael Andreeff, MD, PhD
Collaborator & Member of SAB
Professor of Medicine
Paul and Mary Haas Chair in Genetics
Director, Flow Cytometry and Cellular Imaging Facility
Director, Bone Marrow Aspiration Clinic
Chief, Section of Molecular Hematology and Therapy
MD Anderson Cancer Center
Physician Scientist
Expert in AML and other hematologic malignancies
Expert in drug resistance and drug mechanisms
Published over 450 peer-reviewed papers
Published multiple books and chapters

Distinguished KOLs with Domain Expertise in the Hematology/Oncology Space
CG-806
Phase 1a/b Stage
Oral, First-in-Class
Pan-FLT3 / Pan-BTK Inhibitor

1. Potently inhibits all known forms of FLT3 and BTK driver kinases
2. Suppresses other signaling pathways essential for cancer cell survival
3. Precision that spares targets and pathways associated with toxicity
CG-806

- Inhibits WT/mutant “Driver” BTK & FLT3
- Suppresses oncogenic “Rescue” Pathways
- Avoids many of kinases that cause toxicity
- Hope avoid rapid emergence of drug resistance

B-Cell Cancers

AML

**BTK “Driver” Intracellular**

Ibrutinib
Acalabrutinib
Zanabrutinib
ARQ 531
SNS-062

**FLT3 “Driver” Surface Receptor**

Midostaurin
Sorafenib
Gilteritinib
Quizartinib
Crenolanib

**“Rescue” Pathways**

FLT3, BTK, SYK, BCR, CSF1R, PDGFRα, RET, MET, ERK, MYC, AKT, H3S10

**CG-806**

- Inhibits WT/mutant “Driver” BTK & FLT3
- Suppresses oncogenic “Rescue” Pathways
- Avoids many of kinases that cause toxicity
- Hope avoid rapid emergence of drug resistance

**pan-FLT3/pan-BTK Multi-Cluster Kinase Inhibitor**

**Intolerance**

**Resistance**

**Refractory**
Medical Need for Next Generation BTK Inhibitor (BTKi)

Overexpressed BTK (Bruton’s Tyrosine Kinase)
- Drives B-cell cancers: CLL/SLL and NHL (FL, MCL, DLBCL, others)

Ibrutinib Covalent BTKi: SOC with >$6B Annual Sales
- Chemically targets Cys481 residue in the active site of BTK
- Disrupts signaling among CLL cells and lymphoid microenvironment
- Promotes egress of CLL cells from lymphoid tissues and cells die

Ibrutinib Shortcomings: Patients Discontinuing
- 54% CLL Patients Discontinue treatment by 44 months\(^{(1,2)}\)
- Patients resistant (C481S mutant), intolerant or refractory to ibrutinib

CG-806 May Overcome Shortcomings of Ibrutinib
- “Non-covalent”: Retains activity against WT and C481S-BTK enzyme
- Well tolerated and inhibits “oncogenic rescue” pathways
- Potently and directly kills CLL and other B-cell cancer cells

CG-806 Non-Covalent Inhibitor Retains Potency Against C481S-BTK

Retains potency against C481S-BTK

Does not inhibit TEC, EGFR, ErbB2 kinases that are linked to ibrutinib related toxicities, including bleeding disorders, gut and skin toxicity and atrial fibrillation, respectively

CG-806 Binds Non-Covalently and Productively to BTK

X-ray Crystallographic Analysis:
• Binds to WT-BTK and C481S-BTK Active Sites
• Atypical Binding Mode Not Reported with Other Drugs
• Chemical Structure Distinct from Ibrutinib/Other BTKi’s

<table>
<thead>
<tr>
<th>Kinase</th>
<th>CG-806 IC₅₀ (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTK-WT</td>
<td>8.4</td>
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<tr>
<td>BTK-C481S</td>
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<tr>
<th>IC₅₀ (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>
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</table>
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

Sensitive down arrow IC$_{50}$ Resistant down arrow

“CG-806 More Than Just a BTK Inhibitor”

- Superior killing relative to ibrutinib (SOC covalent BTK inhibitor)
- **1000x more potent than ibrutinib** at killing malignant B-cells
- Targets driver (BTK) and rescue pathways in B-cell cancers
Impressive Combination of CG-806 with Venetoclax on Primary Samples from CLL or ALL Patients

- **CG-806 and Venetoclax (Bcl2i):**
  - Individually highly active agents

- **Combination Studies:**
  - Enhanced ex vivo killing of patient bone marrow cells in most samples

- **CG-806 + Venetoclax:**
  - 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 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: Sorafenib (Nexavar®); Midostaurin (Rydapt®); Gilteritinib (Xospata®)
- Development Stage: Quizartinib, Crenolanib, other FLT3 inhibitors

**Medical Need For a Superior FLT3 Inhibitor**

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

**Inhibiting FLT3 Only 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, PDGFR\(\alpha\), CSF1R, MET, RET, ERK/MYC, AKT/mTOR, BTK, SYK, SRC, MYC and H3S10 key pathways suppressed

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\(^1\) American Cancer Society : \(^2\) Cancer. 2014 July 15; 120(14): 2142-2149 : \(^3\) Blood 2016;128(5);686-698.
CG-806 Inhibits FLT3-ITD and Kills Cells with FLT3-ITD Mutation More Potently than Other FLT3 Inhibitors

CG-806 Superior to Other FLT3-ITD Inhibitor

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<tr>
<th>Drug</th>
<th>IC$_{50}$ (nM)</th>
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<tr>
<td>CG-806$^{(1)}$</td>
<td>0.8</td>
</tr>
<tr>
<td>Quizartinib$^{(2)}$</td>
<td>8.8</td>
</tr>
<tr>
<td>Gilteritinib$^{(3)}$</td>
<td>0.9</td>
</tr>
<tr>
<td>Crenolanib$^{(4)}$</td>
<td>2</td>
</tr>
<tr>
<td>Midostaurin$^{(2)}$</td>
<td>11</td>
</tr>
<tr>
<td>Nexavar$^{(2)}$</td>
<td>79</td>
</tr>
<tr>
<td>Sutent$^{(2)}$</td>
<td>1</td>
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(1) Reaction Biology Corp.
(2) Blood. 2009 Oct 1; 114(14): 2984–2992
(3) J Clin Oncol 32;5a, 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.

(1) Ba/F3 isogenic cells kindly provided by Dr. Michael Andreeff at MDACC
CG-806 Rapid and Sustained Antitumor Activity in Mouse Model of FLT3-ITD AML After Oral Dosing for 28 Days

- Observed no weight loss or any sign of toxicity at any dose level
- Tumor growth inhibition observed at all dose levels over 28 days of dosing
- Significant cure rates at two highest dose levels through 120 days
CG-806 Inhibits All Forms of FLT3 and Kills Cells with FLT3-D835Y Mutation More Potently than Other FLT3 Inhibitors

<table>
<thead>
<tr>
<th>FLT3 Proteins (Fragments)</th>
<th>CG-806 Potent (Kd)</th>
<th>FLR3 WT/Mutants</th>
</tr>
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<tbody>
<tr>
<td>FLT3 WT</td>
<td>0.24 nM</td>
<td></td>
</tr>
<tr>
<td>FLT3 ITD</td>
<td>3.1 nM</td>
<td></td>
</tr>
<tr>
<td>FLT3 D835Y</td>
<td>4.2 nM</td>
<td></td>
</tr>
<tr>
<td>D835H</td>
<td>2.2 nM</td>
<td></td>
</tr>
<tr>
<td>D835V</td>
<td>7.9 nM</td>
<td></td>
</tr>
<tr>
<td>R834Q</td>
<td>6.4 nM</td>
<td></td>
</tr>
<tr>
<td>N841I</td>
<td>0.8 nM</td>
<td></td>
</tr>
<tr>
<td>K663Q</td>
<td>0.55 nM</td>
<td></td>
</tr>
<tr>
<td>ITD / F691L</td>
<td>16 nM</td>
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</tr>
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CG-806 Superior to Other FLT3 Inhibitors on AML Cells with FLT3-D835Y Mutation

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

(1) Ba/F3 isogenic cells kindly provided by Dr. Michael Andreeff at MDACC

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(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 Efficacy in PDX Model Against AML Patient Cells with FLT3 ITD + D835 Mutations

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

Model implanted with FLT3 ITD+D835 mutated primary AML cells. CG-806 Tx initiated d27 (QDx5/wk Orally). hCD45+/mCD45- leukemic cells in peripheral blood were quantitated with flow cytometry.

CG-806
- Reduced leukemia cell burden
- Reduced splenomegaly
- Extended survival
- Active against patient-derived FLT3-ITD / D835 AML
- Potential to treat emerging FLT3i-resistant AML patients
More than 200 AML Patient Samples: Determined Cell Killing (Ex Vivo IC₅₀)

- **Determined IC₅₀ for FLT3i’s**: CG-806, Quizartinib, Gilteritinib, Dovitinib, Sorafenib, Midostaurin, Crenolanib

- **CG-806 demonstrated greater potency in killing primary AML cells bearing wild-type FLT3 or FLT3-ITD**

IC₅₀ for each drug against each patient sample: Expressed as a Heatmap
Impressive Combination of CG-806 with Venetoclax on Primary Samples from AML and MDS/MPN Patients

Box plots show median and IQR; width is proportional to number of samples
Drugs are ordered from left to right by increasing median IC₅₀ across all diagnoses

• CG-806 and Venetoclax (Bcl2i):
  — Individually highly active agents

• Combination Studies:
  — Enhanced ex vivo killing of patient bone marrow cells in most samples

• CG-806 + Venetoclax:
  — Combination may become the preferred drug combination for patients with AML, MDS/MPN, and other hematologic malignancies
Potential Best-in-Class FLT3i
Potential Best-In-Class Non-Covalent BTKi

CG-806

Superior Inhibition of key “Oncogenic” Pathways

- Strong Inhibition on BTK (WT / Mutant)
- Superior Potency/Range on Cell Lines
- Combines Favorably: Venetoclax (Bcl-2 inh), Mcl-1 inh, BETi, cytarabine, daunorubicin

Superior Inhibition on FLT3 (WT / Mutant)

- Superior Potency/Range on Patient Samples
- Strong Oral Efficacy and Safety Profile: Standard & PDX Models

Developing Broadly Among B-Cell Malignancies & AML/MDS

Rapid Approval Paths: FLT3iResistant, IDH-1Mutant, Unfit/Fragile, VenetoclaxResistant

Combines Favorably: Venetoclax (Bcl-2 inh), Mcl-1 inh, BETi, cytarabine, daunorubicin
CG-806 Phase 1a/b Clinical Trial: Patients with R/R CLL/SLL or NHL

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

- Includes Patients with WT or C481S BTK

### Dose Escalation Phase

- Patients administered oral capsules
- Every 12 hours on a 28-day cycle
- Dose Level 1: 150mg every 12 hours
- Planned 6 dose levels

**Expansion Phase**

25 Patients Each

- Diffuse Large B-Cell Lymphomas
- Mantle Cell Lymphomas
- Indolent Lymphomas
- CLL/SLL

*Dose Expansion will occur once MTD or Therapeutic Dose is Reached to Define RP2D*
CG-806 Phase I Clinical Development Plan: B-Cell Cancers AND AML/MDS

R/R B-Cell Cancer Patients: CLL/SLL and NHL

- Begin with B-cell cancer patients – Less acutely ill than AML patients
- Dose escalating Phase I a/b trial – Define safety, tolerance, PK and PD profiles
- Continue dose escalation to define RP2D – Expand to sensitive subpopulations
- Seek a dose in B-cell cancer patients that delivers a “therapeutic exposure” for AML

Relapsed/Refractory AML/MDS

- AML patients are acutely ill and do not wish to dose sub-therapeutically
- Dose escalating Phase I a/b trial – Define safety, tolerance, PK and PD profiles
- Continue dose escalation to define RP2D
- Expand to sensitive subpopulations: FLT3iR, IDH1M, Unfit/elderly, other

Excited to move CG-806 into the clinic – Provide updates throughout the year
APTO-253

Phase 1b Stage

Treatment of AML

Small Molecule

MYC Inhibitor
Tremendous Interest in Targeting MYC as a Cancer Treatment

- **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**
  - NOT the MYC protein

- **Inhibits MYC gene expression (mRNA)**
  - Depletes cells of MYC protein → induces apoptosis

- **APTO-253 inhibits MYC expression**
  - Causes induction of p21
  - Triggers cell cycle arrest/apoptosis
APTO-253
Ongoing Phase 1b Dose Escalating Clinical Trial

R/R AML
And
High Risk MDS

- Planned up to 20 Patients
- Safety, PK, MTD, DLT, RP2D
- Responses and Transfusions
- MYC and p21 Biomarkers

- Dosing Day 1 of Each Week on 28-day Cycle
- Dosing Levels Planned
  - 20 (1pt), 40 (1pt), 66 (3x3pts), 100, 140, 180, 220mg/m²
- Patients Dosed
  - 20mg/m² dose: Completed with 1 AML patient
  - 40mg/m² dose: Completed with 1 MDS patient
  - 66mg/m² dose: Screening for 3 patients

- Observed inhibition of MYC expression in PBMC from AML patient
  - Cycle one at 20mg/m² for 28 days
  - Sampled pre-dose and 24 hr post-dose day 1, 8, 15, 22
  - MYC and p21 gene expression analyzed in-house by qPCR analysis

- MYC Suppression & Well Tolerated
2019 Anticipated Catalysts

**CG-806**
- 2Q: First B-cell cancer patient dosed with CG-806
- 2H: FDA approval for AML trials
- 2H: First AML patient dosed with CG-806
- 2H: Formal presentation of clinical data at ASH 2019

**APTO-253**
- 2Q: Successful completion of second dose level
- 2H: Initiation of AML/MDS patients with third dose level
- 2H: Formal presentation of clinical data at ASH 2019

**Management**
- 2H: Further expansion of management team
Aptose Executive Summary

Developing Highly Differentiated / Targeted Drugs for Blood Cancers

**CG-806 1st-in-Class Pan-FLT3 / Pan-BTK Inhibitor**

- Potently Inhibits all forms of FLT3, BTK and inhibits “oncogenic rescue” pathways
- Potential to treat FLT3i-resistant, IDH1-mutant, and elderly segments of AML population
- Potential to treat B cell cancer patients resistant to / discontinuing other BTKi
- Phase 1 with CLL/SLL/NHL trial underway and subsequent AML trial planned in 2019

**APTO-253 1st-in-Class MYC Inhibitor in Phase Ib for AML/MDS**

- Dosing of R/R-AML / hr-MDS patients ongoing and throughout 2019
- Demonstrated MYC inhibition : Watch for safety, tolerance, and patient responses
- Potential to expand into B cell malignancy patients (role of MYC)

**Strong Leadership and KOL Support**

**Strong Financial Foundation**

- > 12 Months operating capital on hand and additional availability
Thank You!