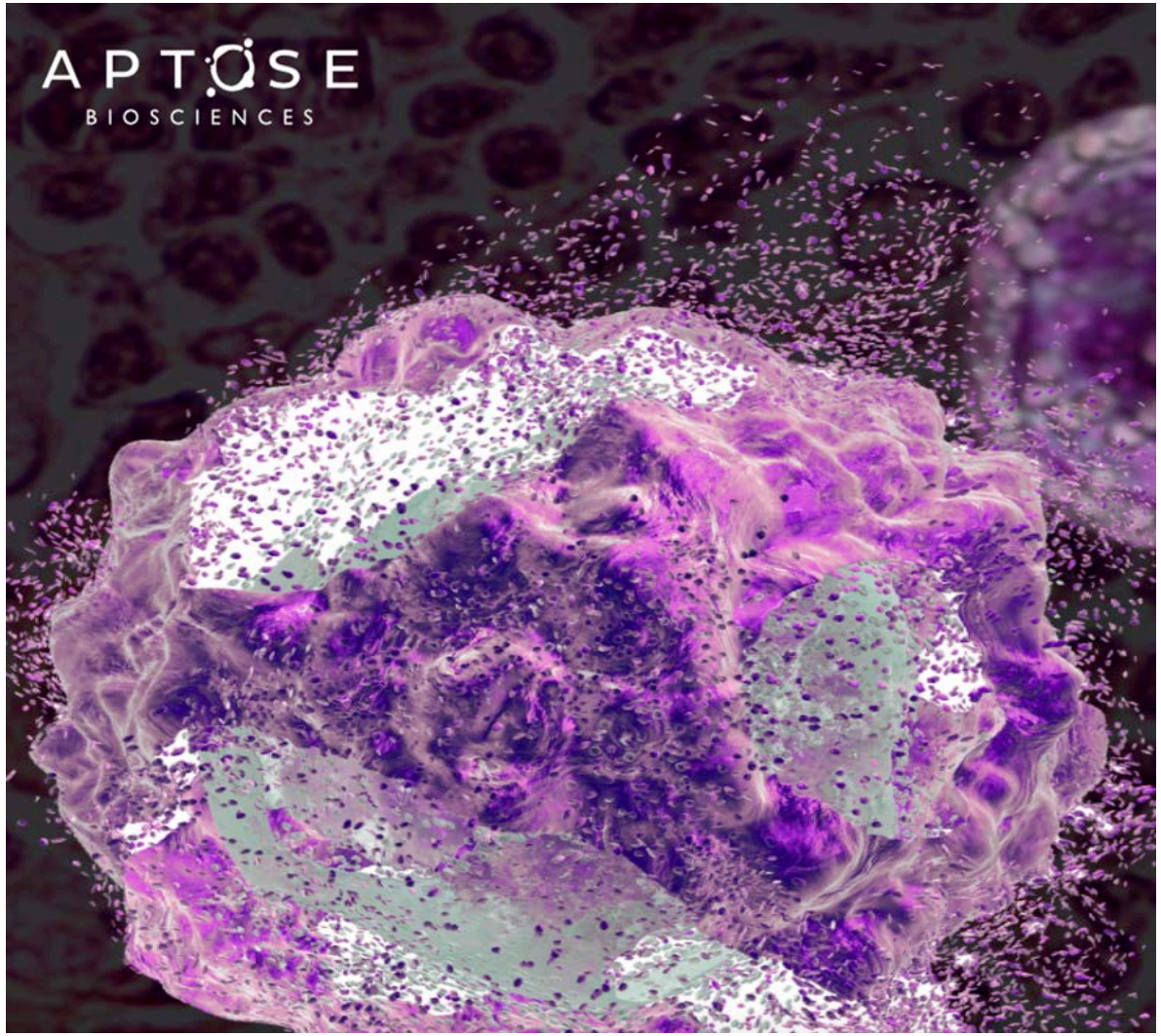
Early clinical findings from a phase 1a/b dose escalation trial to evaluate the safety and tolerability of CG-806 in patients with relapsed or refractory CLL/SLL or non-Hodgkin's lymphomas



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AACR 2020
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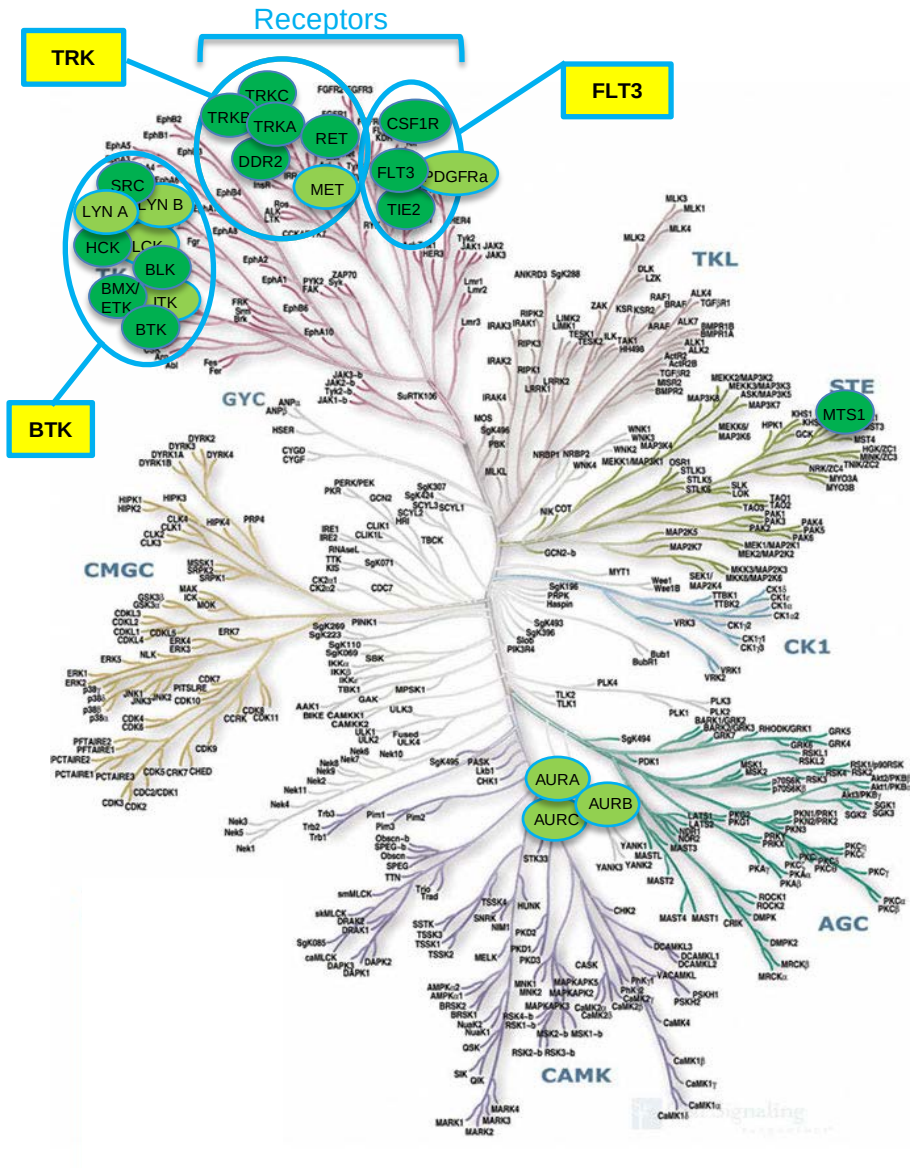
Cluster-Selective Kinase Inhibitor:
CG-806 Potently and Selectively Inhibits Clusters of Related Kinases



- **Orally Available, Non-Covalent Kinase Inhibitor**
  - Targets clusters of related kinases
  - Potently inhibits WT and all mutant forms of **FLT3** and **BTK**
  - Targets multiple related oncogenic signaling pathways
- **Inhibits Clinically Validated Kinase Targets that Drive Lymphoid and Myeloid Hematologic Malignancies**
- **Robust Safety Profile to Date**
  - Avoids off-target kinases that impact safety and tolerability (e.g., TEC, EGFR, ERBB2)
  - No pre-clinical toxicity encountered *in vitro* or *in vivo*
  - No drug-related AEs seen to date in patients

CG-806 Phase 1a/b Clinical Trial Underway: First in Patients with R/R CLL & NHL Lymphoid Malignancies

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

Dose Escalation Phase

- Patients administered **oral capsules**
- **Twice daily** on a **28-day cycle**
- Plan to perform 6 dose levels
- **Accelerated titration** design
- Planned expansion cohorts

Development Plan for Severe Unmet Needs in B Cell Tumors

CLL Patients Resistant or Intolerant to:

- Covalent BTK inhibitors (ibrutinib)
- BCL2 inhibitors (venetoclax)
- Anti-CD20 therapy (rituximab)
- PI3K inhibitors (idelalisib)
- Cytotoxic agents
- Non-covalent BTK inhibitors

NHL Patients with Unmet Needs

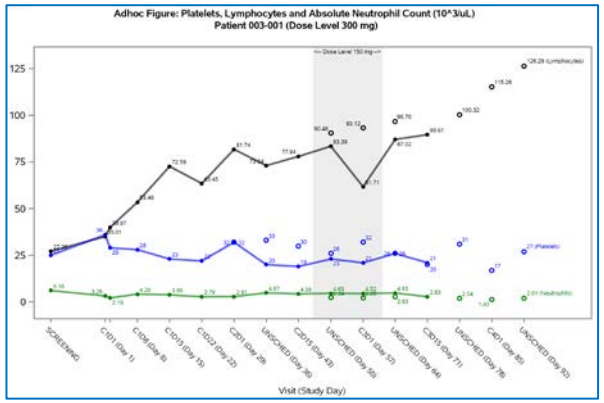
- Richter's Transformation
- Tx-refractory DLBCL
- Tx-refractory FL

Patient Enrollment: 1, 1, 3x3

- ***Fewer patients early in the study, but…..***
- ***Dose escalate quickly to effective dose***

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

CG-806 Now in Dose Level 4 of Phase 1a/b Clinical Trial in CLL/NHL



Dose Level 1 (150mg BID for 28d) Completed

Only One Patient Required in Dose Level 1

- **R/R-CLL/SLL** with TP53 mutation ; Heavily pretreated
- **Challenging Case with TP53 mutation – No DLTs and in Cycle 10 (now dose escalated)**

Dose Level 2 (300mg BID for 28d) Completed

Only One Patient Required in Dose Level 2

- **R/R-CLL** with unmutated IGHV ; Marrow involvement, neutropenia and thrombocytopenia
- **Highly complicated disease to manage – No DLTs and completed Cycle 4**

Dose Level 3 (450mg BID for 28d) Completed

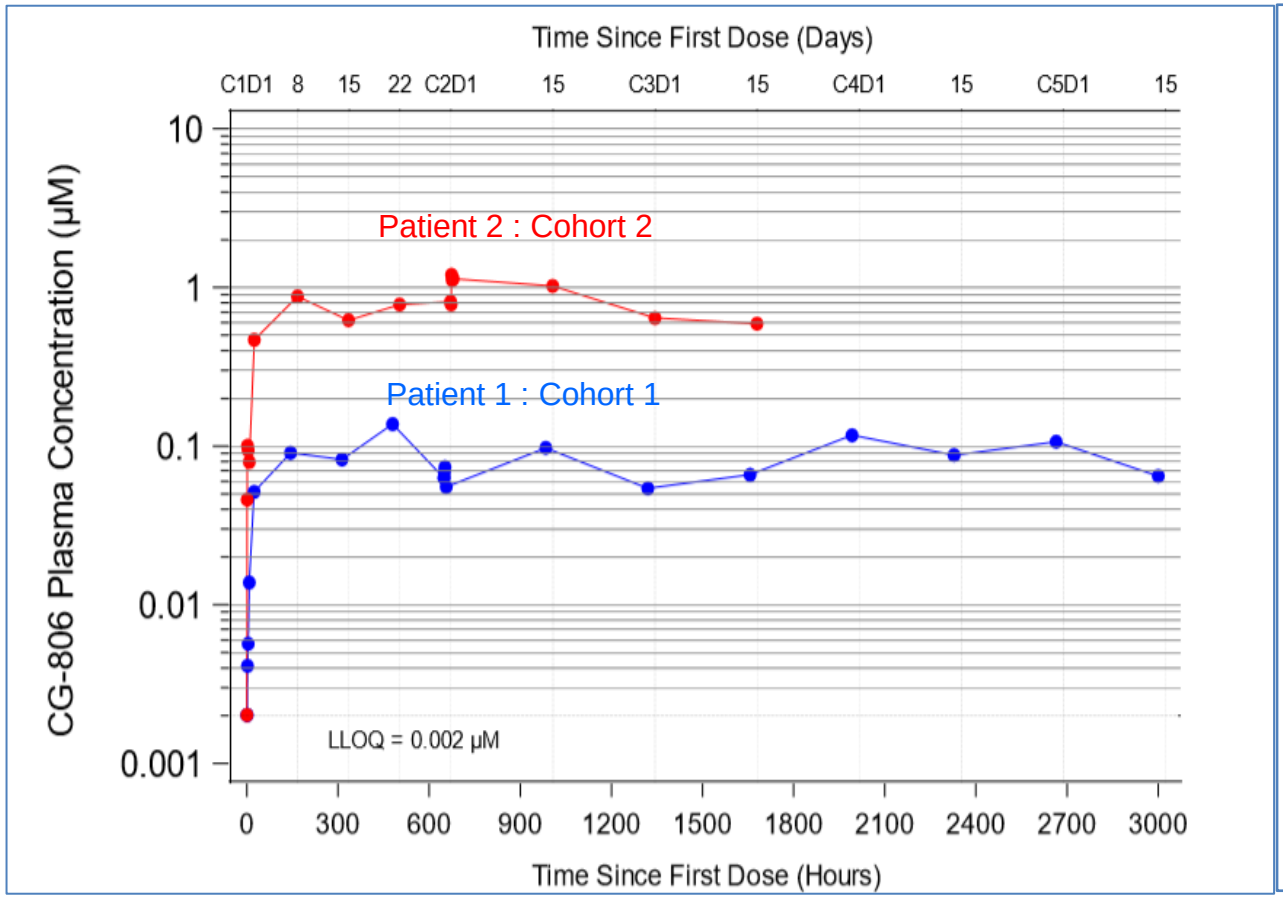
Three Patients Required in Dose Level 3 – 3 Patients completed Cycle 1

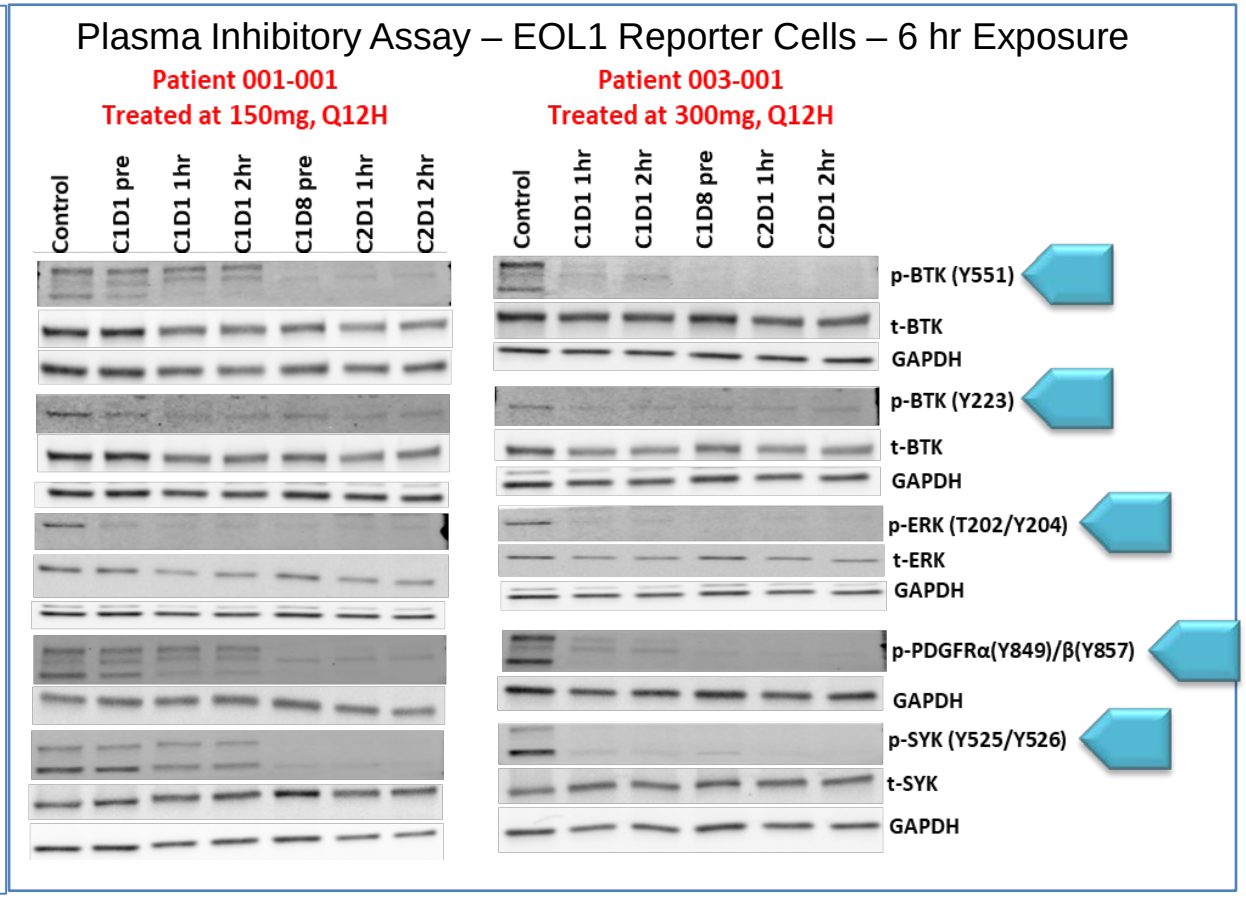
- **No drug-related adverse events or DLTs in Cycle 1**

Dose Level 4 (600mg BID for 28d) Dosing Ongoing

Three Patients Required in Dose Level 3

CG-806 Favorable Steady-State Pharmacokinetics (C_{MIN}) and Pharmacologic Activity

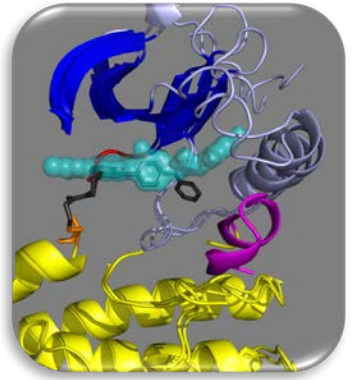




- **Oral steady-state (C_{min}) PK 0.6-1µM at Dose Level 2 : No observed drug-related toxicities**
- **Pharmacologically active at Dose Level 2 :** Inhibits P-BTK, P-ERK, P-PDGFRα, and P-SYK
- **Lymphocytosis at Dose Level 2:** BTK inhibition in CLL promotes exfiltration

CG-806 Clinical Summary and Acknowledgements

- **Uniquely and Selectively Inhibits Clusters of Kinases**
  - Potently targets kinase driver of lymphoid AND myeloid malignancies (BTK and FLT3)
- **Phase 1 Ongoing in R/R CLL & NHL Lymphoid Cancer Patients**
  - Targeting BTK and multiple survival pathways to treat patients failing other agents
  - Observed safety, pharmacologic activity and predictable PK characteristics
- **Phase 1 Planned in R/R Acute Myeloid Leukemia Patients**
  - FLT3 mutant and WT and multiple survival pathways to treat patients failing other agents



Acknowledgements:

- **We thank our study PIs, clinical site staff, and most importantly, our patients!**

- **To learn more, please go to:** http://aptose.com/news-media/presentations

Thank You!

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