

June 10, 2023

# APTOSE INTERIM CLINICAL UPDATE

IN CONJUNCTION WITH EHA 2023

INTERNATIONAL CONGRESS OF THE  
EUROPEAN HEMATOLOGY ASSOCIATION  
FRANKFURT, GERMANY



PRECISION ONCOLOGY FOR THERAPIES OF TOMORROW

NASDAQ: **APTO**  
TSX: **APS**

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# Aptose

**Precision oncology  
company developing  
oral targeted agents  
to treat hematologic  
malignancies**

## Aptose Investment Highlights

### **Tuspetinib (TUS) lead agent : Once daily, oral agent to treat AML**

- **Orphan Drug** and **Fast Track** Status
- **CRs across 4 dose levels** with no DLTs
- **Broad activity** across diverse AML populations
- **Highly favorable safety** and tolerability profiles
- **Ideal agent for combination** therapy in 1L/2L/3L AML
- **Accelerated approval paths** projected in 2L AML and R/R AML
- **Merits > \$Billion AML market potential** – Plus, potential for **MDS**

### **Luxeptinib oral agent : Clinically active on AML, FL, DLBCL**

- Generation 3 formulation promising and expect dose escalation soon

### **Value-driving near-term clinical milestones during 2023**

- Multiple opportunities to report additional responses | ESH | ASH

# Tuspetinib Headlines

## Finalized \$25 Million Financing with Keystone Capital

- Common stock | no warrants | proceeds support tuspetinib development program

## Completed Dose Escalation/Dose Exploration Trial in 77 R/R AML Patients

- Monotherapy Responses (CRc) | Four Dose Levels with No DLT | Favorable Safety
- Mutationally Diverse Populations of R/R AML (incl. FLT3<sup>MUT</sup> and FLT3<sup>WT</sup>)
- TP53<sup>MUT</sup> CR/CRh = 20% (CRc = 40%) | RAS<sup>MUT</sup> CR/CRh = 22% (CRc = 22%)

## Held a Successful End of Phase 1 (EOP1) Meeting with US FDA

- RP2D = 80mg once daily | Single arm accelerated approval path remains open
- No extraordinary CYP450 metabolite or QTc monitoring requirements

## Initiated APTIVATE Expansion Trial in R/R AML Patients

- Tuspetinib | Tuspetinib + Venetoclax (TUS/VEN) Doublet | Brisk Enrollment 25+ Dosed
- TUS/VEN doublet well tolerated | All patients remain on study | Preliminary CR activity

# Tuspetinib:

Safe, effective, once daily,  
oral kinase inhibitor

Being developed for the  
treatment of AML and MDS



## Kinase Inhibition Profile Supports Broad Commercial Applications

### Review Timelines & Catalysts

### Review Clinical Journey

Dose Esc/Exp Trial

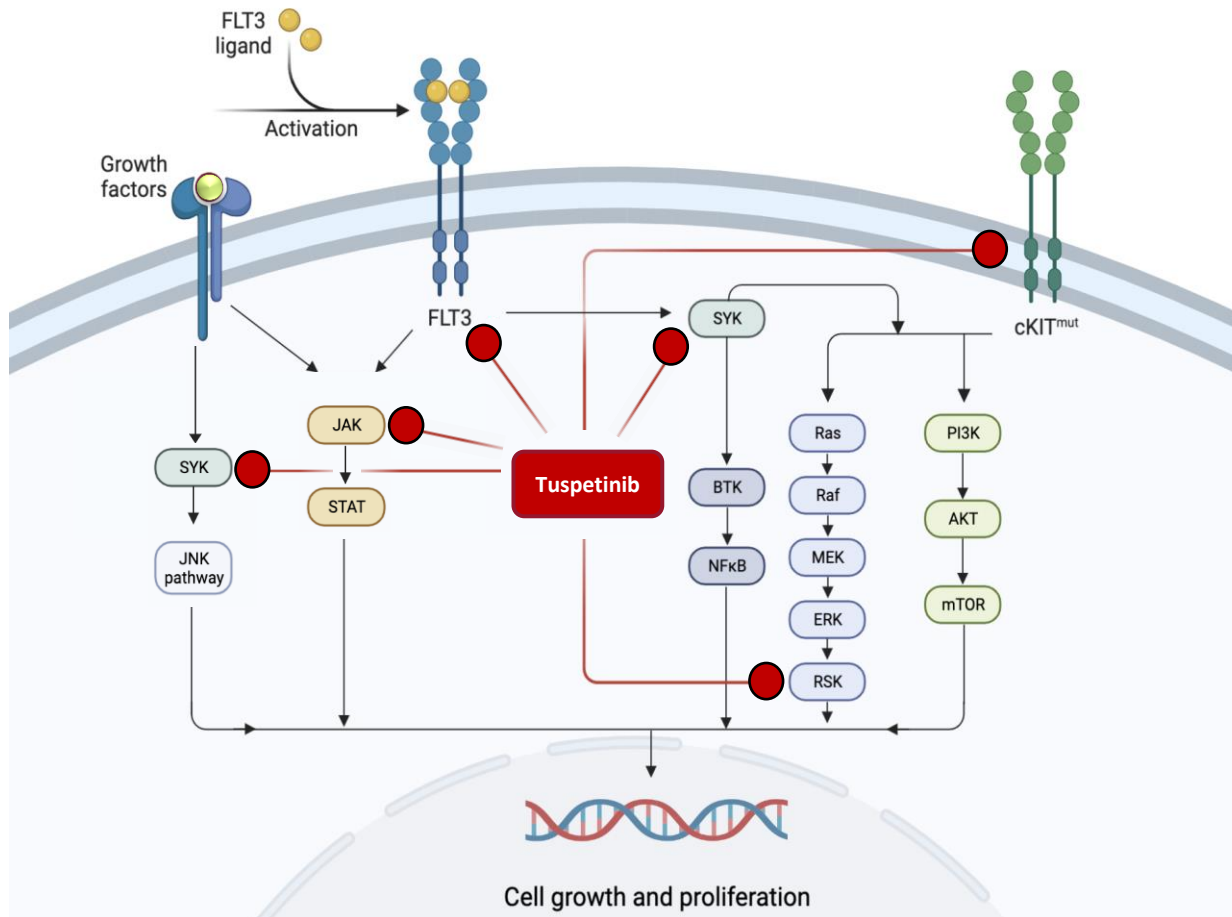
APTIVATE Tus and TUS/VEN Trial

Drug Resistance Study



# Tuspetinib simultaneously suppresses a select handful of clinically validated kinases that drive oncogenic signaling pathways in AML

## *Safety is differentiating feature*



## Multi-drug therapy in single tablet

- Potently targets **FLT3**, **SYK**, **JAK1/2**, **cKIT<sup>MUT</sup>**, and **RSK1/2** ( $IC_{50} = 0.5-6nM$ )
- Suppresses multiple oncogenic signal transduction pathways that drive AML proliferation and resistance
- Lower exposure levels achieve CRs and avoid common toxicities of other agents
- Ideal for **monotherapy**, **combination therapy**, and **maintenance therapy**

# Building a long-term strategy for tuspentinib blockbuster potential

Addresses multiple AML patient populations and commercial opportunities

## Potential for Accelerated Approval in R/R AML

Potential for Single Arm Accelerated Approval

## Doublet Combination in 2L AML

Potential for Accelerated Approval with Interim Data Analysis

## Triplet Combination for 1L AML

## Maintenance Therapy Post-CR

Near Term

Long Term

## Tuspentinib Clinical Headlines

- Delivers potent single agent CRs among refractory AML regardless of adverse mutation status
- CRs among wildtype FLT3 patients, representing 70% of AML population
- Avoids typical toxicities of other kinase inhibitors, including myelosuppression
- Paths identified for accelerated approval
- Ideal for oral maintenance & combination therapy representing significant markets

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**Review Timelines & Catalysts**

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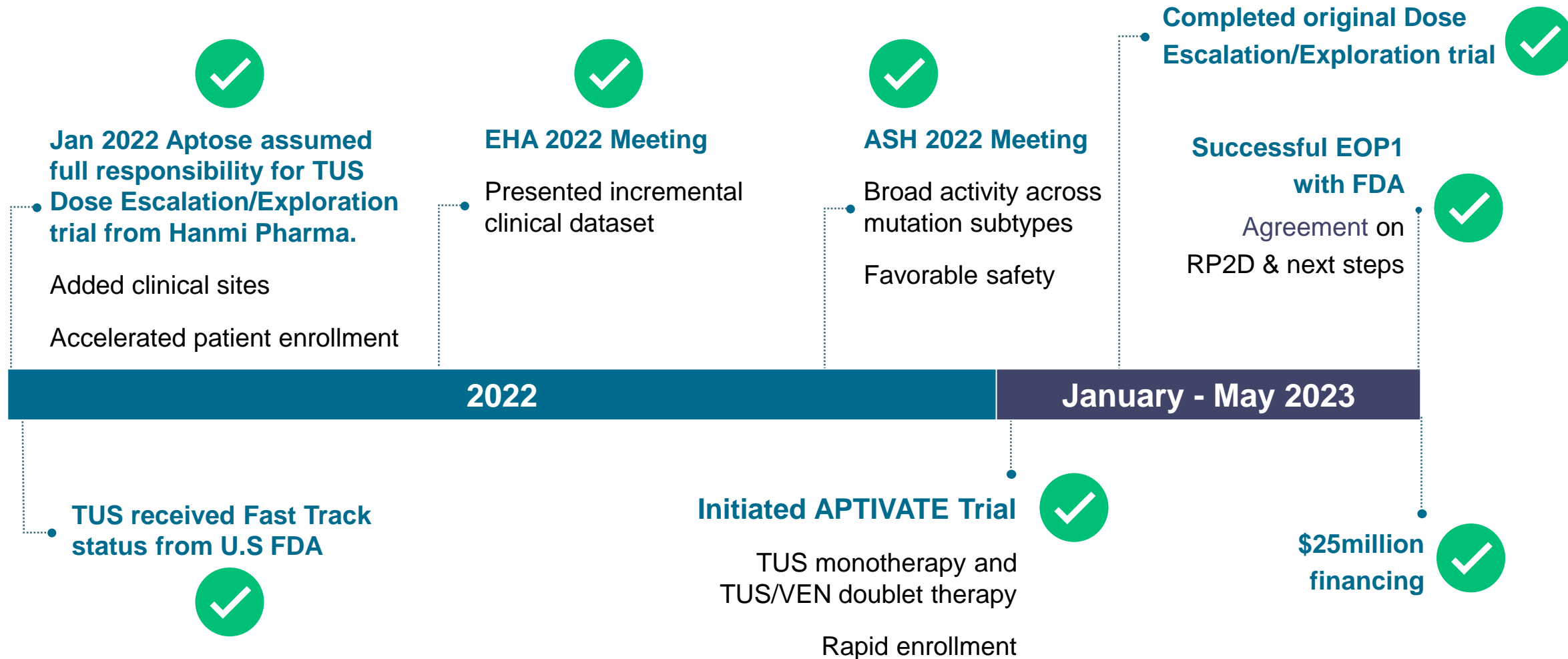
APTIVATE Tus and TUS/VEN Trial

Drug Resistance Study



# Tuspetinib exciting agent with “best new agent” profile for treating R/R AML

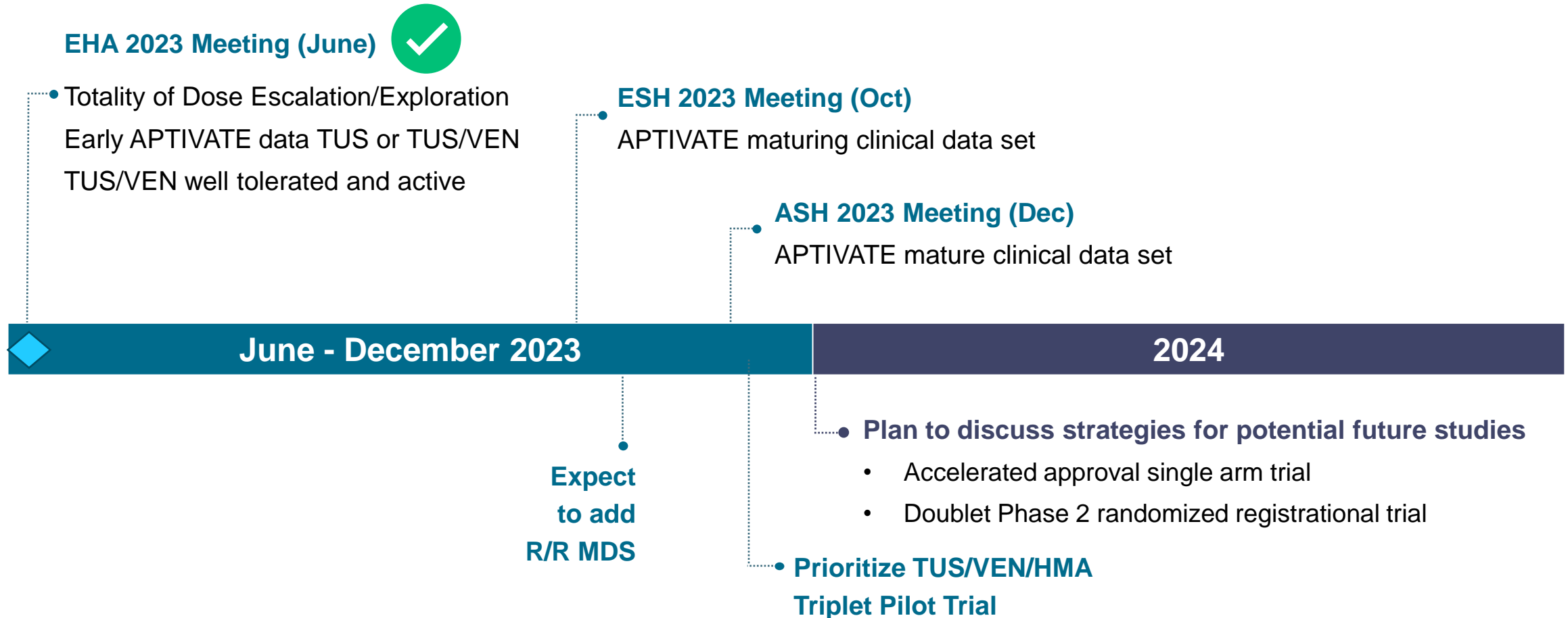
## Highlight of Achievements During 2022 and 1H 2023



# Tuspetinib exciting agent with “best new agent” profile for treating R/R AML

## Anticipated Milestones / Catalysts Over the Next Year

### Anticipated Release of New Data and Reporting New Responses



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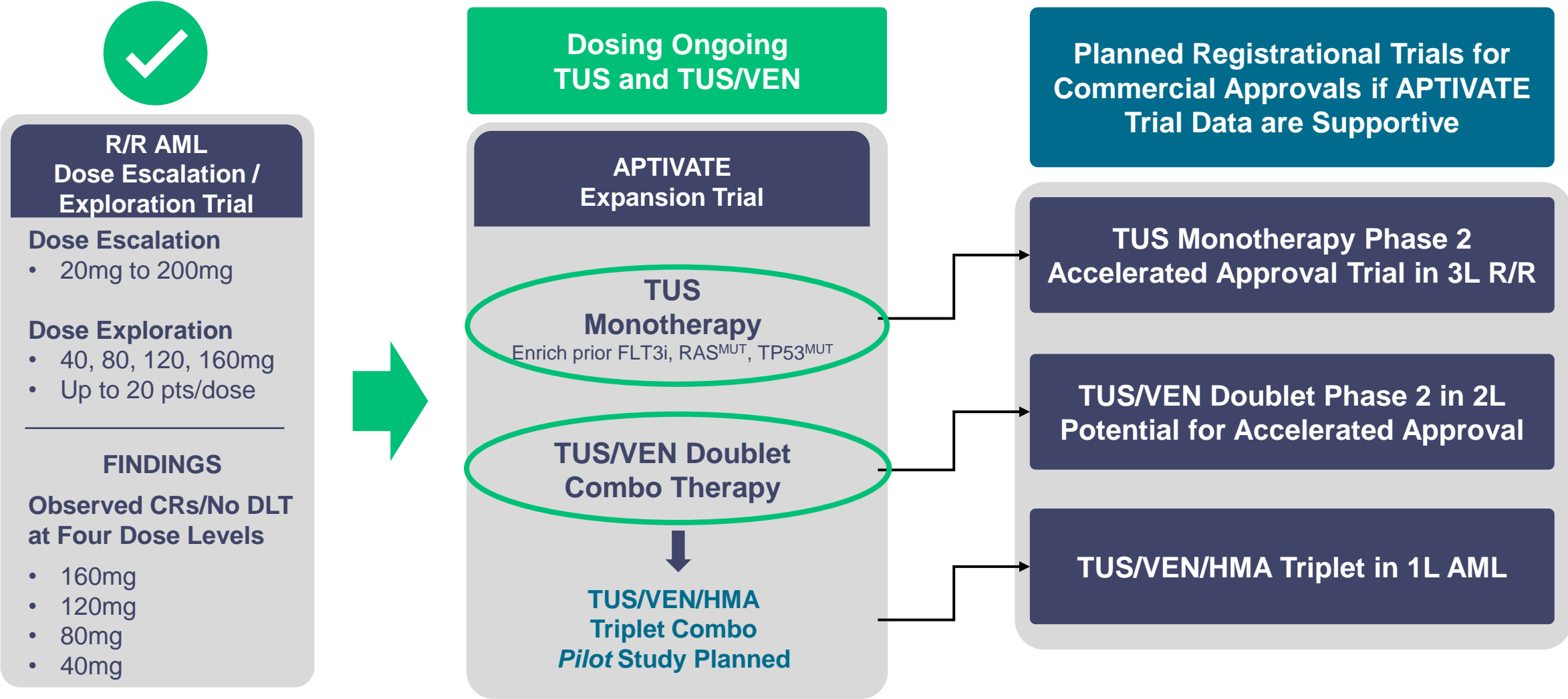
**Dose Esc/Exp Trial**

**APTIVATE Tus and TUS/VEN Trial**

**Drug Resistance Study**

**Rafael Bejar, MD, PhD: SVP and Chief Medical Officer**

# Journey to commercialization: APTIVATE dose expansion trial ongoing globally to support registrational studies for commercial approvals



Single agent Expansion studies designed to collect data on a small number of patients in "high need" groups and segue into Ph 2 Registrational Trial(s)

Combination Expansion studies designed to illustrate safety and efficacy of Tuspentinib with venetoclax and segue into Phase 2-3 randomized trials and demonstrate Tuspentinib can be the preferred agent for combination therapy

# Tuspetinib Phase 1/2 study in r/r AML:

## Dose escalation & dose exploration completed

Dose Escalation 18 patients dosed		Dose Exploration 42 patients dosed			Dose	n
Cohort 1: 20 mg QD	✓ Completed				20mg	2
Cohort 2: 40 mg QD	✓ Completed	40 mg QD	CRs	No DLT	40mg	17
Cohort 3: 80 mg QD	✓ Completed	80 mg QD	CRs	No DLT	80mg	20
Cohort 4: 120 mg QD	✓ Completed	120 mg QD	CRs	No DLT	120mg	18
Cohort 5: 160 mg QD	✓ Completed	160 mg QD	CRs	No DLT	160mg	16
Cohort 6: 200 mg QD	✓ Completed				200mg	4

**Total n = 77**

As of 4/26/2023

**Favorable safety profile across six dose levels showing no overt myelosuppression with prolonged dosing:**

- No drug-related SAE, deaths, differentiation syndrome
- No drug-related QTc prolongation or rhabdomyolysis
- Initial plasma  $t_{1/2}$  estimated at 40+ hours
- No DLT through 160 mg dose level

# Tuspetinib updated safety data demonstrate favorable safety profile and broad therapeutic window – Efficacy without limiting toxicities

Treatment-emergent AEs (TEAEs), Safety Analysis Set, Parts A and B (N=77)	
<b>Patients Experiencing TEAEs</b>	
Any	73 (94.8%)
Most Frequent TEAEs (≥ 15% of patients)	
Pneumonia	24 (31.2%)
Nausea	16 (20.8%)
Pyrexia	16 (20.8%)
Diarrhea	12 (15.6%)
≥ Grade 3	52 (67.5%)
SAEs	41 (53.2%)
Leading treatment discontinuations	7 (9.1%)
Leading to death	14 (18.2%)
<b>Patients Experiencing TEAEs Related to HM43239</b>	
Any	25 (32.5%)
Most Frequent Related TEAEs (≥ 5% of patients)	
Diarrhea	8 (10.4%)
Nausea	8 (10.4%)
≥ Grade 3	7 (9.1%)
Muscle weakness	2 (2.6%)
Neutrophil count decreased	2 (2.6%)
Epistaxis	1 (1.3%)
Leukopenia	1 (1.3%)
Nausea	1 (1.3%)
White blood cell count decreased	1 (1.3%)
SAEs	0
Leading to death	0
Dose Limiting Toxicity (DLT)	1 (1.3%)

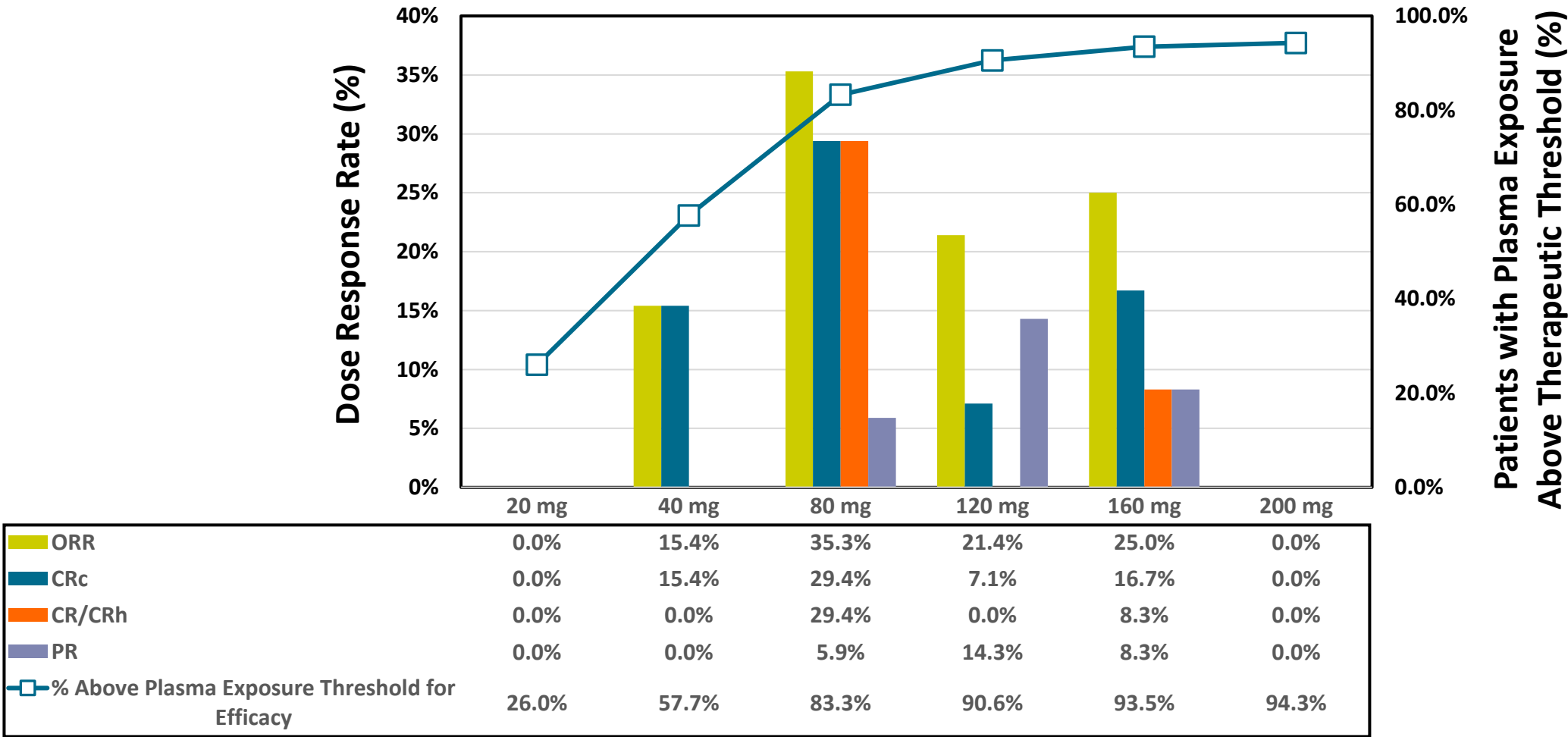
## Favorable Safety Profile

- No drug-related myelosuppression in remission
- No drug related AE of QTc prolongation
- No observed differentiation syndrome
- No drug related SAE, deaths, or discontinuations
- No DLT from 20 mg level through 160 mg level
- One DLT of muscle weakness at 200 mg
  - Reversibility in patient with high exposure
  - Not rhabdomyolysis | No muscle destruction
  - No AE of elevated creatine phosphokinase (CPK)
- Avoids many of the typical toxicities observed with other TKI and menin inhibitors



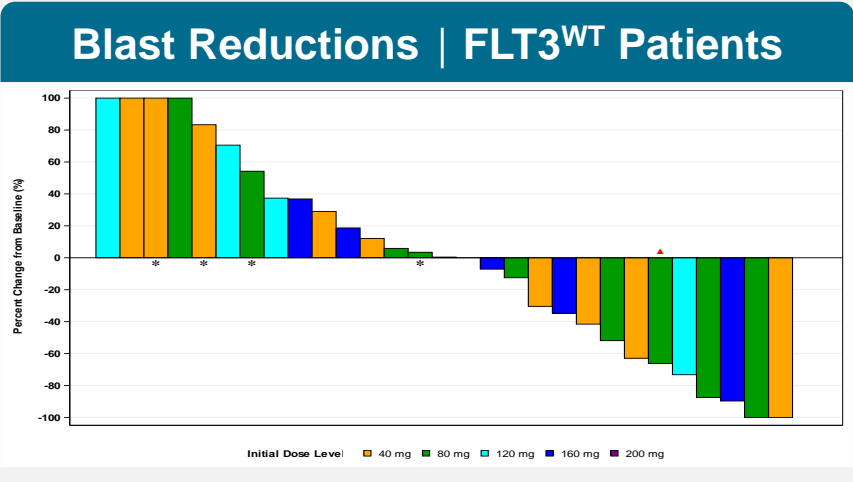
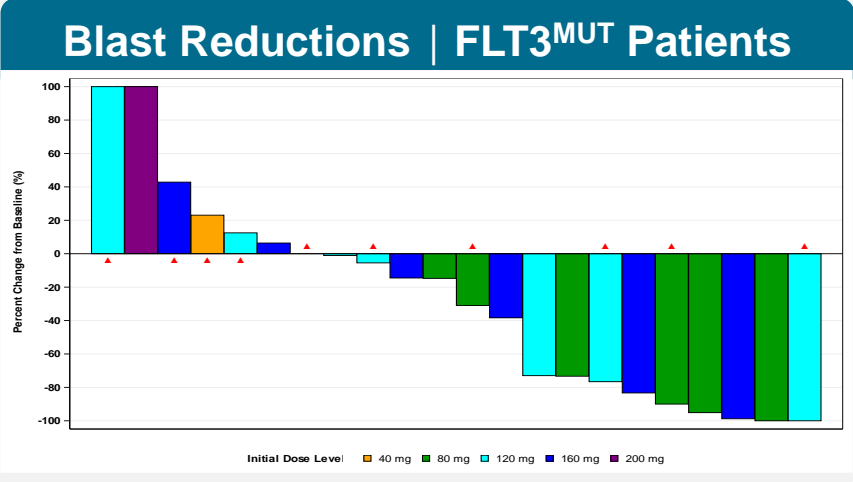
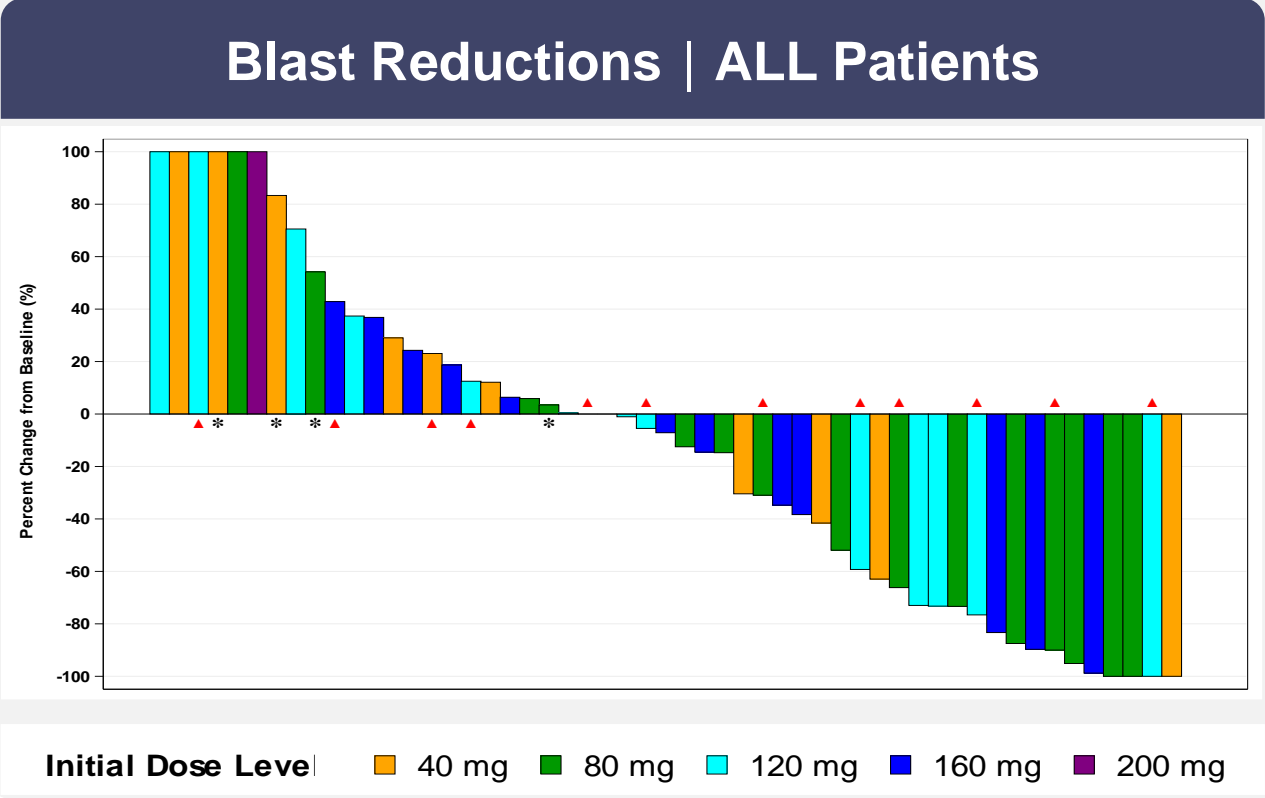
# Tuspetinib Dose Escalation/Dose Exploration Phase Trial

## Response Rates and Percent of Patients with Exposure Levels Above Efficacy Threshold at Each Dose Level



# Updated Waterfall plot : bone marrow blast percent change from baseline

(TUS Monotherapy - Data Extracted June 01, 2023)



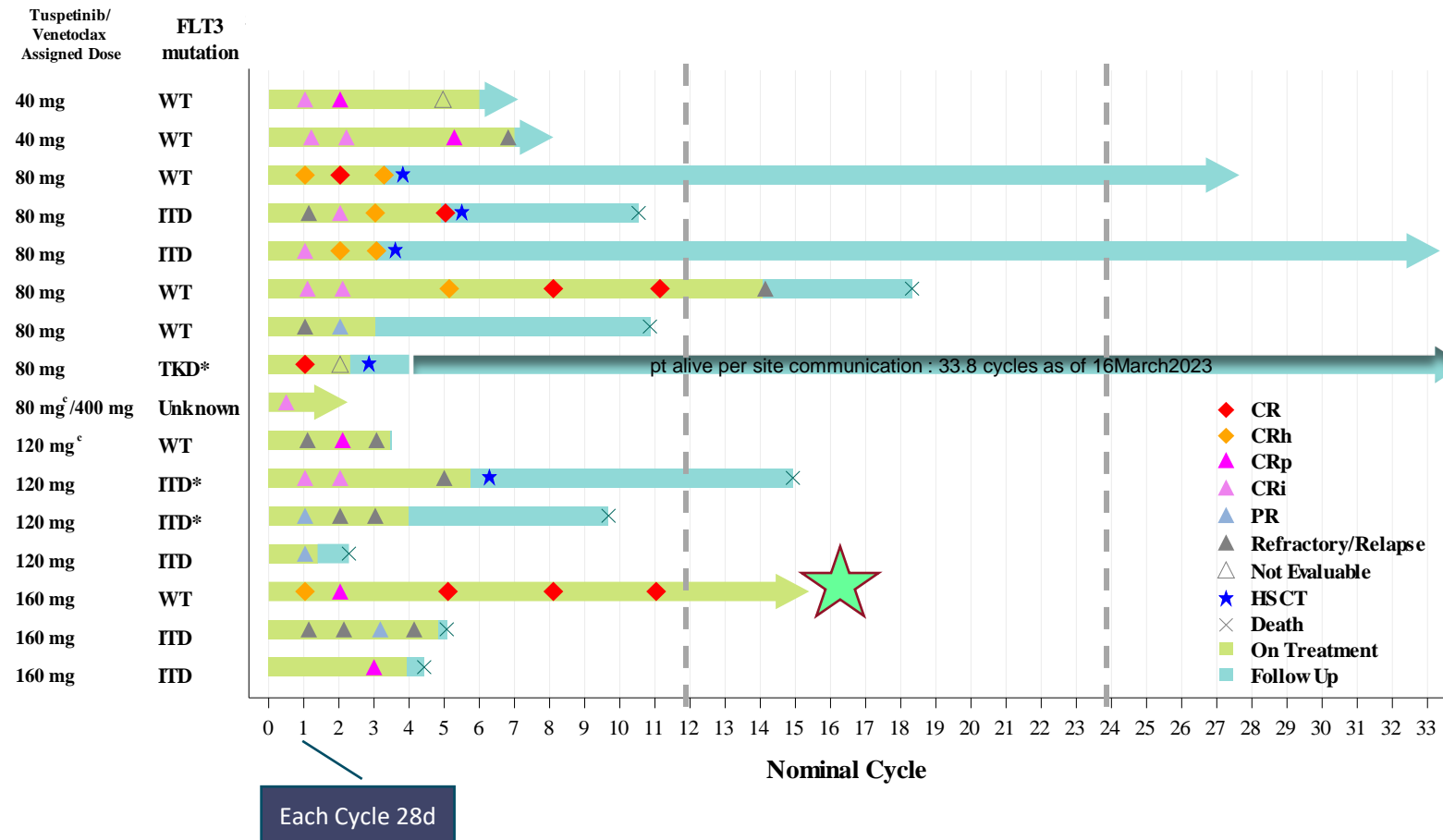
Significant blast reductions with 40mg, 80mg, 120mg & 160mg

Blast reductions in patients with unmutated and mutated FLT3

Note: Blast percent change was calculated as 100 X (the lowest post-baseline bone marrow blast - baseline bone marrow blast)/baseline bone marrow blast. Patients with blast percent change >=100% are shown as 100%. Only patients who reported both baseline and any post-baseline bone marrow blast results are included in the figure. Black asterisk indicates patients who administered hydroxyurea within 7 days prior to the lowest marrow blast value. Red triangle indicates patients who received prior FLT3 inhibitors before starting HM43239, including gilteritinib, midostaurin, and/or sorafenib.

# Patients who achieved clinical responses with tuspetinib monotherapy

(Data Extracted June 01, 2023)



## Responder Analysis

Responses achieved across four dose levels

Responses mature over time with ongoing continuous dosing

Many bridged to potentially life-saving transplant (HSCT★)

Durability observed when HSCT unavailable

Abbreviation: CR, complete response; CRh, complete response with partial hematologic recovery; CRi, complete response with incomplete hematologic recovery; CRp, complete response with incomplete platelet recovery; HSCT, hematopoietic stem cell transplantation; PR, partial remission.

Note: The bone marrow aspiration/biopsy date was used as response date. Actual time relative to the first dose date was used to plot events. The right arrow at the end of horizontal bar indicates patients are still ongoing, whereas without the right arrow indicates patients discontinued from study. The nominal cycle is calculated in 28 days increment in study days.

\*Indicates patients who received prior FLT3 inhibitors, including gilteritinib and/or midostaurin.

<sup>c</sup> Indicates patients in Part C.

# Case Study: CR | FLT3-WT | RAS<sup>MUT</sup> | 160mg | 16 Cycles | No Myelosuppression

R/R AML	<b>FLT3-unmutated</b> (FLT3 wildtype) <b>NRAS-mutated</b> BCOR-mutated, U2AF1-mutated, SETBP1-mutated Cytogenetics: Normal
Demographics	55-year-old male
Diagnosis at Study Entry	<b>Refractory AML with MDS-related changes</b> 42.1% bone marrow blasts at diagnosis
Prior Therapies	<ul style="list-style-type: none"><li>Failed by induction chemotherapy (cytarabine / daunorubicin)</li><li>Failed by salvage therapy (cytarabine / fludarabine)</li></ul>
Dose	<b>160 mg</b> daily oral tablet tuspetinib
Response	<ul style="list-style-type: none"><li><b>CRh</b> at Cycle 1</li><li><b>CR</b> at Cycle 5 and ongoing</li><li>Patient became transfusion independent</li><li>Continuous dosing with no DLT / no SAE / no myelosuppression to date</li></ul>

*Patient continues on study in cycle 16 with CR and no myelosuppression*

# Case Study: CR | FLT3-WT | RAS<sup>MUT</sup> | 160mg | 16 Cycles | No Myelosuppression

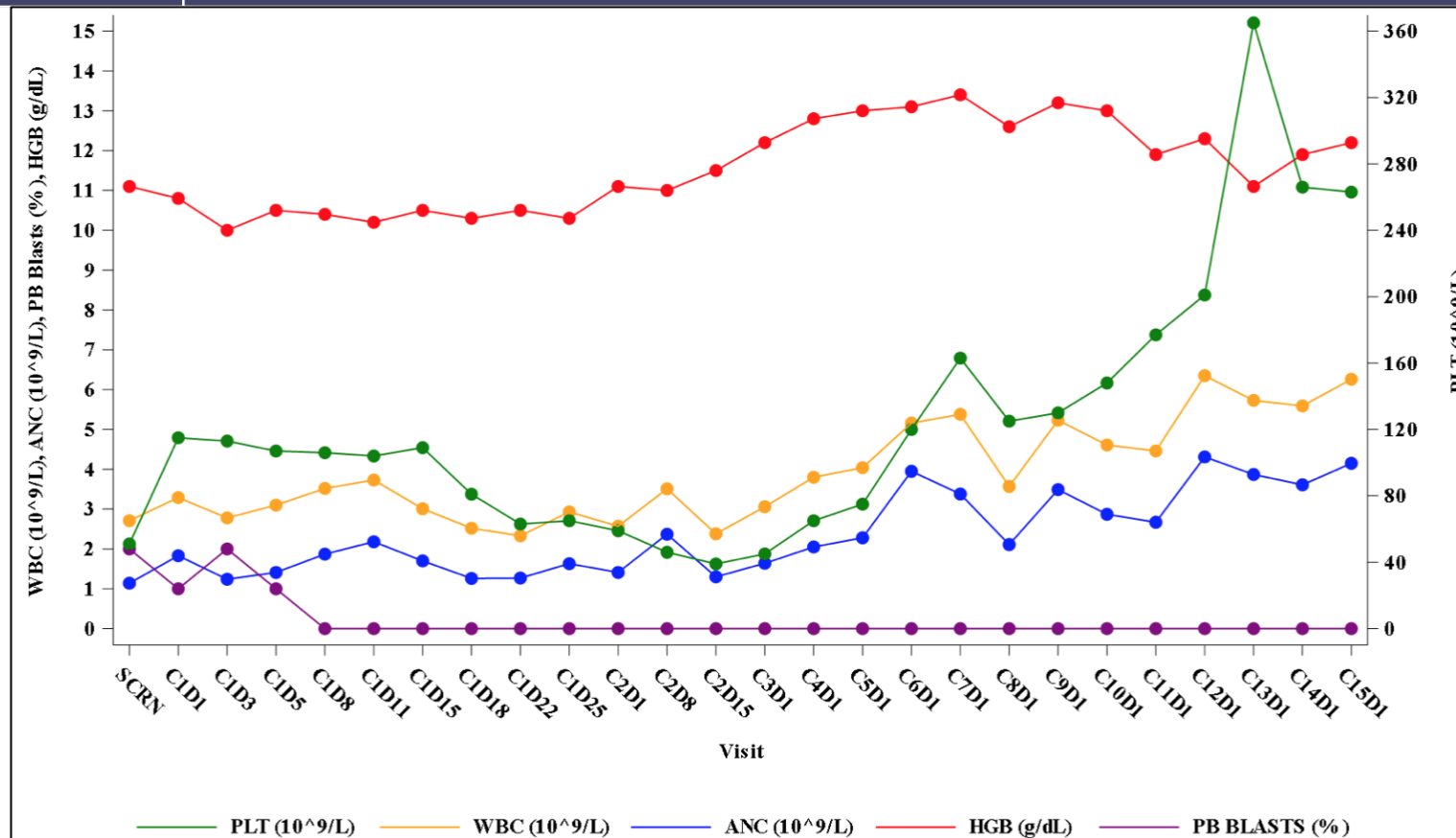
R/R AML

FLT3-unmutated (FLT3 wildtype)

NRAS-mutated

BCOR-mutated, U2AF1-mutated, SETBP1-mutated

Cytogenetics: Normal



# Tuspetinib safely delivers monotherapy responses across diverse AML populations

FLT3 Mutation status + Mutations present at diagnosis per Site reports									
Pt.	FLT3 <sup>MUT</sup>	RAS	NPM1	DNMT3A	RUNX1	IDH	Other Mutations	Dose Level	Best Response
1							TP53	80mg	CR
2							TP53, TET2	40 mg	CRp
3	•	•			•			80mg	CRh
4		•					U2AF1, BCOR, SETBP1	160mg	CR
5	•	•	•	•			PTPN11	120mg	PR
6	•		•	•				80mg	CR
7	•		•					160mg	CRp
8	•		•	•		•		160mg	PR
9						•	SRSF2	80mg	CR
10	•				•		SF3B1, RB1	80mg	CR
11	•				•		MLL-PTD	120mg	CRi
12				Not yet reported				40mg	CRp
13	•			Not yet reported				120mg	PR
14							ASXL1, CBL	80mg	PR

• Indicates mutation has been reported in patients

## Mutation Response Analysis

Responses across populations with highly adverse mutations: TP53, RAS, NPM1, FLT3, IDH, DNMT3A, RUNX1, MLL genes

5 of the 10 (50%) of the CRc Responders are FLT3<sup>WT</sup>

TP53<sup>MUT</sup> / complex karyotype responders

## Monotherapy Responses in Key Mutational Subpopulations

	CR/CRh Rate
TP53 <sup>MUT</sup>	20%
RAS <sup>MUT</sup>	22%



# Summary of Completed Tuspetinib Monotherapy Phase 1 Dose Escalation and Dose Exploration Trial

- **Dosed 77 difficult to treat R/R AML patients across six dose levels**
- **Dose related PK exposures observed for single dose and at steady state**
- **Monotherapy achieved responses across 4 dose levels with no DLT**
  - CR/CRh (n=6), CRc (n=10), PR (n=4) in mutationally diverse patients
  - TP53-mutated CR/CRh = 20% (CRc = 40%) | RAS-mutated CR/CRh = 22% (CRc = 22%)
- **Completed Successful EOP1 Meeting with FDA**
  - RP2D = 80mg | Single arm accelerated path open | No special metabolite or QTc monitoring
- **Favorable safety profile**
  - No drug-related SAE, deaths, differentiation syndrome, QTc prolongation
  - No overt myelosuppression with prolonged dosing, rhabdomyolysis, or transaminitis

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**Kinase Inhibition Profile Supports  
Broad Commercial Applications**

**Review Timelines & Catalysts**

**Review Clinical Journey**

**Dose Esc/Exp Trial**

**APTIVATE Tus and TUS/VEN Trial**

**Drug Resistance Study**

✓ Dosing  
Completed

### Phase 1/2 trial tuspetinib single agent

#### Part A: **Dose Escalation:**

- 6 cohorts: 20mg to 200mg
- N=18 dosed



#### Part B: **Dose Exploration:**

- 4 cohorts: 40, 80, 120, 160mg
- N=42+ dosed
- No dose-limiting toxicities
- Mutation agnostic responses



Dosing Ongoing

### Phase 1/2 APTIVATE Expansion Trial

#### Tuspetinib Monotherapy ➡ 14 Patients Dosed

- FLT3-mutated cohort:
  - Enrich Prior FLT3i
- FLT3-unmutated cohort
  - Enrich TP53<sup>MUT</sup> / complex karyotype

#### Doublet Combination of Tuspetinib + Venetoclax ➡ 12 Patients Dosed



#### Plan to add R/R MDS

- Planned 2H2023

#### Triplet Combo Pilot Study

- Planned 2H2023
- Tus | Ven | HMA

# TUS/VEN Doublet in R/R AML Patients : Preliminary observations

## Rapid Enrollment

Investigator enthusiasm  
12 patients enrolled as of today  
10 FLT3-unmutated  
2 FLT3-mutated

## Doublet Well Tolerated

Critically ill and aged population  
All remain on study as of now

## Preliminary Efficacy

Early response data includes CRs.  
Awaiting confirmatory assessments.

- Example:
  - 65 year-old with mutations in *RUNX1*, *ASXL1*, *ETNK1*, *SETBP1*, and *SRSF2*
  - No response to Chemo or HMA/VEN
  - CRi achieved C1D15 - awaiting count recovery and repeat marrow evaluation
  - Marrow blasts 18% → 0% on C1D15

Encouraging preliminary findings | Potential to treat AML patients who previously failed VEN and other agents.



## Phase 1/2 Dose Escalation & Dose Exploration Trial R/R AML

### Dose Escalation

- 20mg to 200mg

### Dose Exploration

- 40, 80, 120, 160mg
- Up to 20 pts/dose

### CRs/No DLT at Four Dose Levels

- 40, 80, 120, 160mg
- 12 CRc, 6 CR/CRh, 4 PR



FDA  
EOP1

## APTIVATE Phase 1/2 Expansion Trial R/R AML

**TUS Monotherapy : R/R AML**  
14 dosed: ongoing



**TUS/VEN Doublet : R/R AML**  
12 dosed: early data emerging



**Plan TUS/VEN/HMA Triplet**  
Pilot in 1L AML

**Plan to add 2L MDS**

# Tuspetinib:

## Project:

In vitro selection of acquired resistance to tuspetinib

## Findings:

Resistance to tuspetinib drives hypersensitivity to venetoclax

Kinase Inhibition Profile Supports Broad Commercial Applications

Review Timelines & Catalysts

## Review Clinical Journey

Dose Esc/Exp Trial

APTIVATE Tus and TUS/VEN Trial

Drug Resistance Study



# Concurrent administration of TUS and VEN may discourage the emergence of drug resistance

**Project: In vitro sensitivity testing of TUS-Resistant (TUS/R) AML cells to various drugs**

**MOLM-14 FLT3-IDT AML cells grown in increasing concentrations of tuspentinib (TUS) over 4 months**

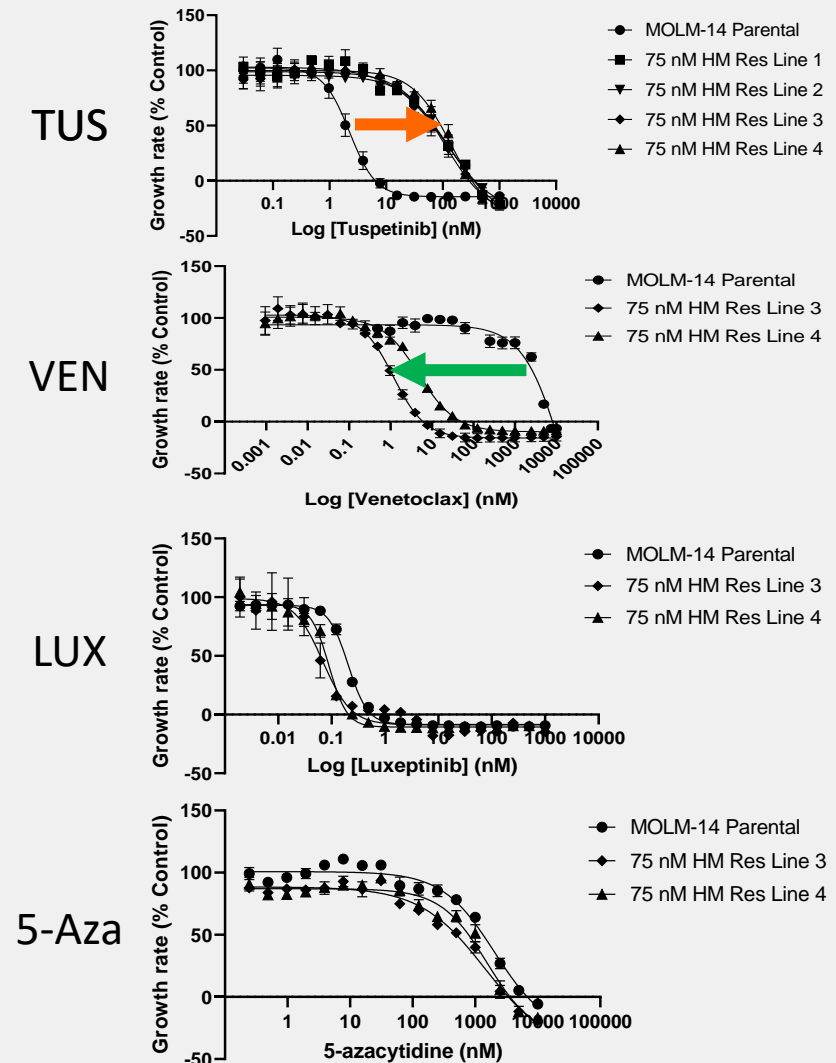
- TUS-resistant (TUS/R) sublines grow in 75 nM TUS

**TUS/R cells tested for sensitivity to TUS, venetoclax (VEN), luxepatinib (LUX), 5-azacytidine (5-Aza):**

- Resistance to tuspentinib
- Synthetic lethal vulnerability to venetoclax (VEN) of unusually high magnitude (~2000-fold)
- No change in sensitivity to luxepatinib
- No change in sensitivity to 5-azacytidine

**Findings reinforce combination of TUS and Ven in the clinical setting**

## TUS/R Cells



# Luxeptinib

**Secondary Program**  
**Oral Lymphoid and**  
**Myeloid Kinase**  
**Inhibitor**

**Being developed in Phase 1 for**  
**R/R AML and MDS**

and

**Being developed in Phase 1 for**  
**B-Cell Cancers**

# Luxeptinib: B-Cell Cancer Ph1 Trial

## 1 CR : DLBCL

- Complete metabolic response by EOY1
- CR with biopsy negative after 22 cycles

## 1 PR : Follicular Lymphoma

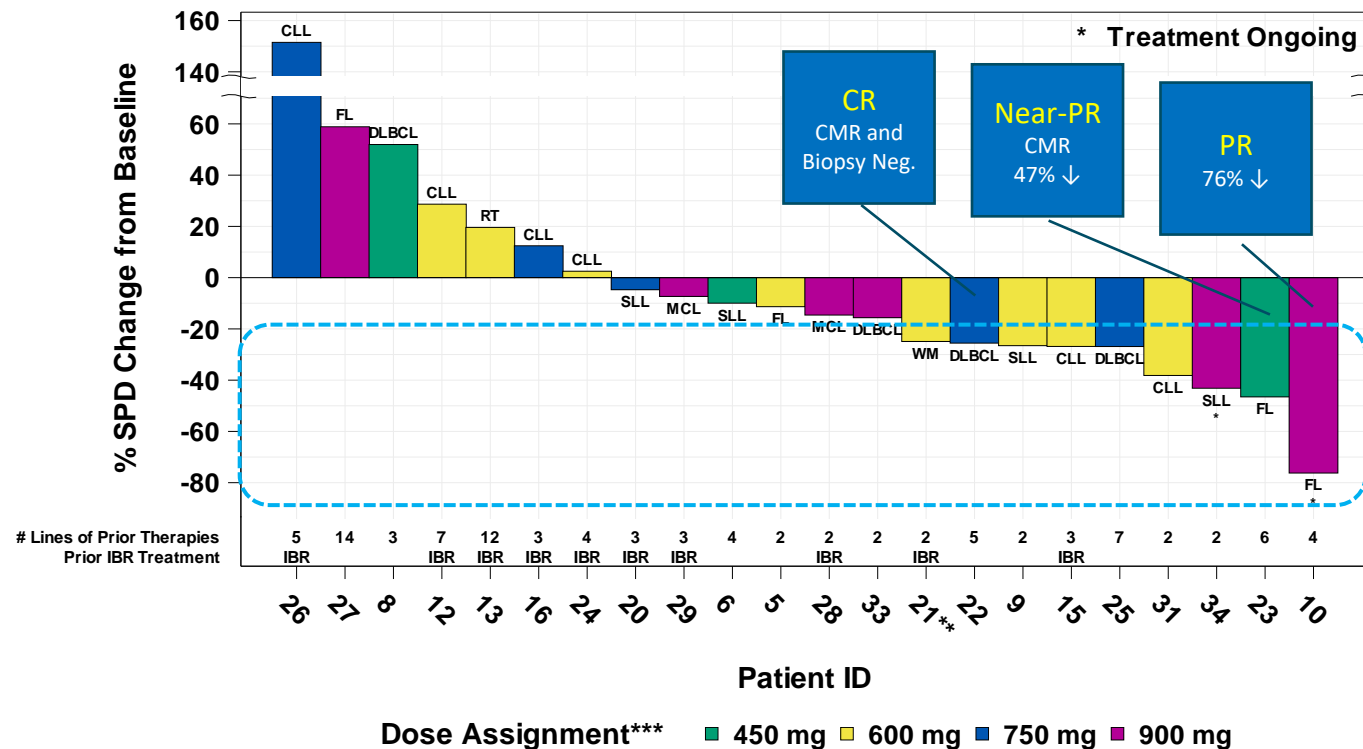
- The % SPD change was -76%

## 1 Near-PR : Follicular Lymphoma

- The % SPD change was -47%
- Complete metabolic response

## % SPD Change from Baseline

Tumor shrinkage in Diverse B-cell Cancers



Note: IBR = ibrutinib

Note: Only patients with post-screening assessments are shown on plot

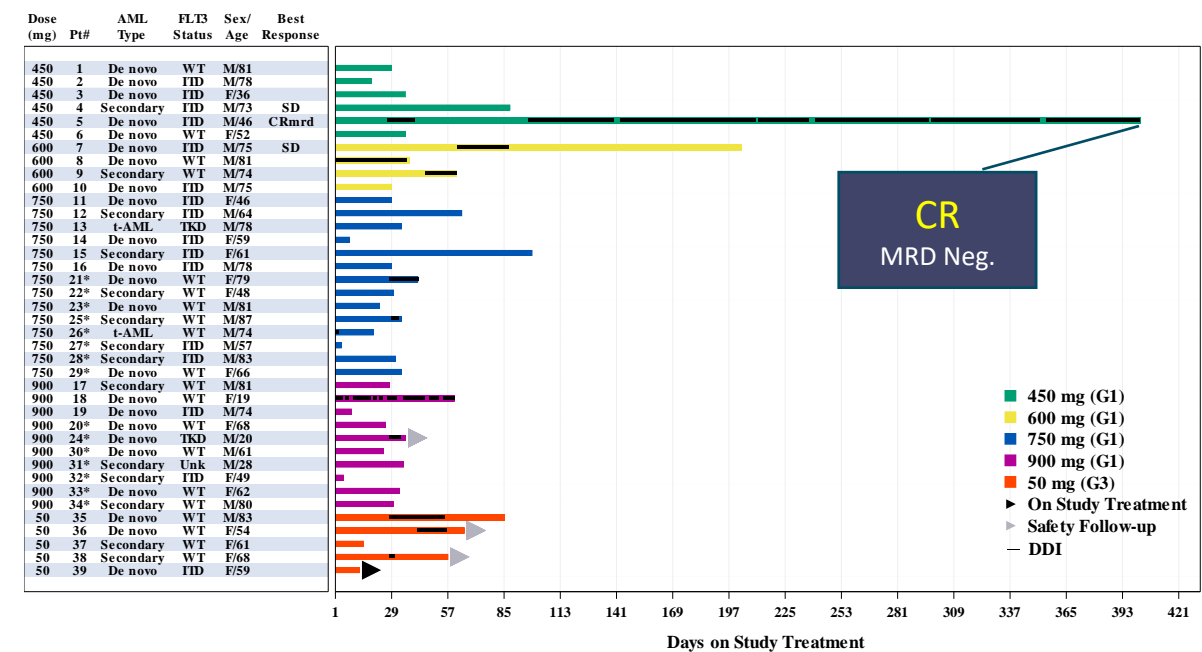
\*\*WM patient(s) measuring % IgM

\*\*\*Dose level shown from time of disease assessment, if at least 1 cycle of doses received at this level

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# Luxepatinib: AML Ph1 Trial

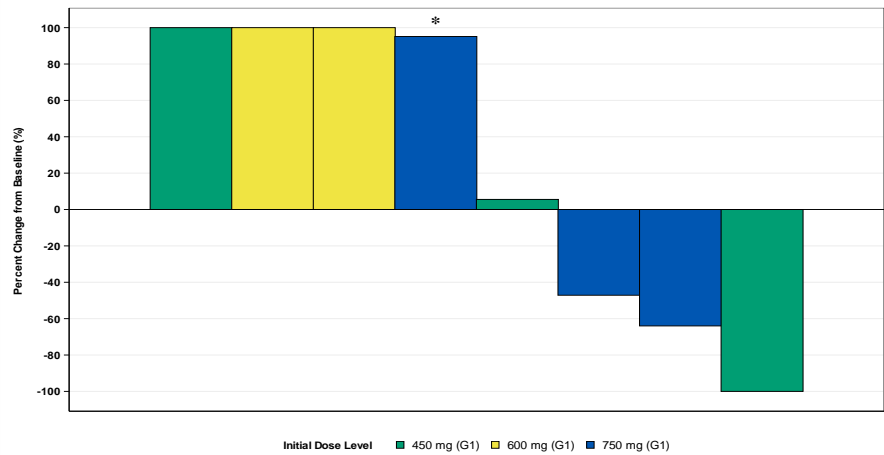
Standard Waterfall Plot illustrating reductions in bone marrow blast counts for AML Patients (FLT3<sup>MUT</sup> and FLT3<sup>WT</sup>)



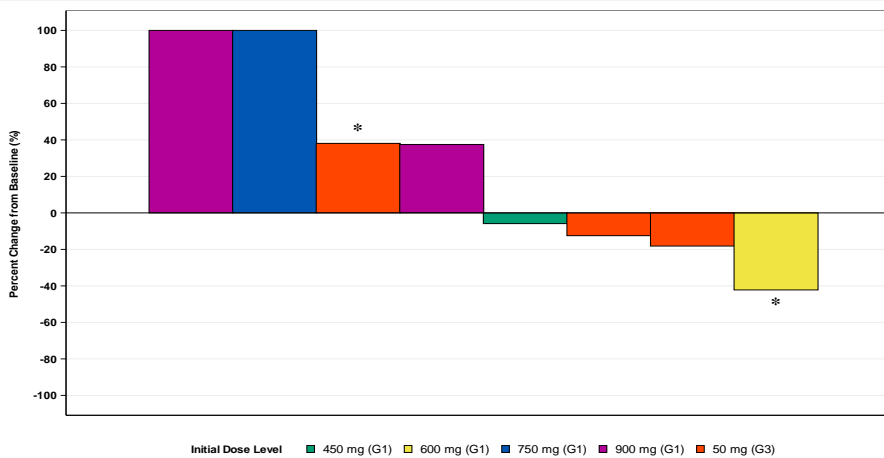
Note: Patient Status captured in EDC up to datacut. \* = Patients enrolled for RBA G3 Sub-study.  
Best Response is defined as the best AML response to study drug for all visits (in the order of CRmrd, CR, SD, PD) through end of treatment visits for patients who have been on treatment for 12 weeks and beyond. CRmrd, Complete Remission without minimal residual disease; SD, Stable disease.

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## Blast Reductions | FLT3<sup>MUT</sup> Patients



## Blast Reductions | FLT3<sup>WT</sup> Patients

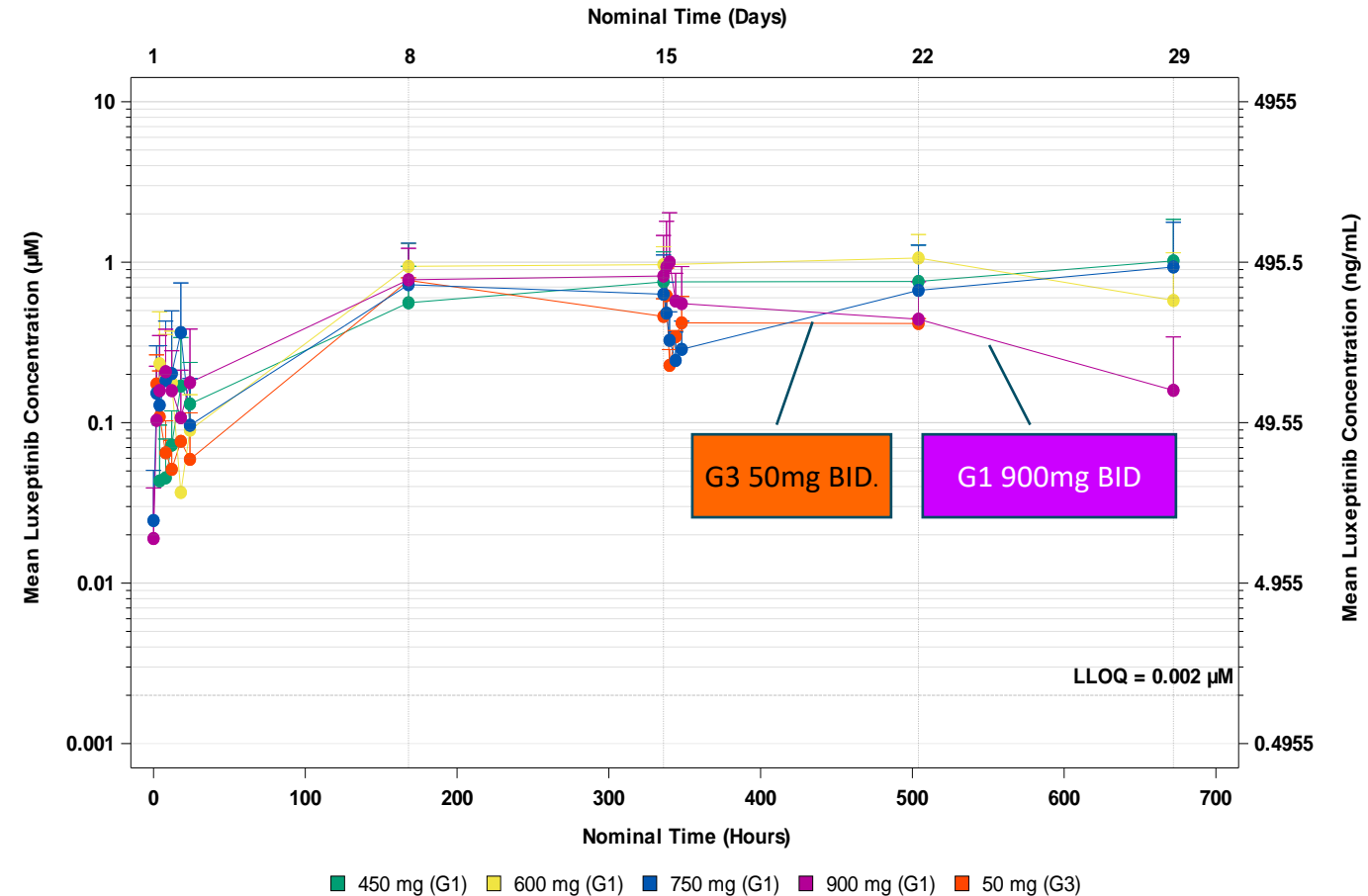


# Luxepitinib G3 formulation (50mg BID) PK properties

## Mean Plasma PK Conc's (+SD) of G1 and G3 formulations by Dose Cohorts for Cycle 1

### PK Profile of 50mg BID G3

- Roughly equivalent to PK profile of the original G1 formulation administered at 900mg BID
- Plan to dose escalate G3



Note: Concentrations below LLOQ are graphed at LLOQ value. Grey dot denotes record excluded per PK Exclusion Working Instructions. C/D = G3 Continuous Dose. The horizontal lines represented in royal blue, pink and green colors indicate the use of proton pump inhibitors/H2 receptor antagonists, sucralfate and anti-fungal medications, respectively. Left arrow indicates medication started prior to first dose of study drug and right arrow indicates medication ongoing. Otherwise the start and end of line indicates the start and end of the medication.

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# Luxepitinib: G3 Formulation is Promising and Expect to Dose Escalate Soon



## Targets Kinases Important in Lymphoid & Myeloid Cancers

- Inhibits **BTK**, **LCK**, **LYN**, **FLT3**, **CSF1R**, **PDGFR $\alpha$** , **TRK**, **AURK**, **MAPKs**, others
- **G1 formulation generally well-tolerated** through 900mg BID
- Delivered clinical responses in diverse B-cell cancers patients | **CR in DLBCL** | **PR in FL**
- Delivered **MRD- CR** in **relapsed AML patient** with high exposure

## Luxepitinib G3 Development in 2022 Led to Continuous Dosing 2023

- No exploring **G3 formulation (18X improved absorption)** to lower pill burden and boost exposure
- Ongoing G3 dose escalation as **monotherapy**
- **Continuous dosing of 50mg BID G3** in AML patients delivered plasma exposures equivalent to 900mg BID G1
- **Seek exposure levels above 1uM**
- **Expect soon to increase dose level of G3 with continuous dosing**

## Recent Findings Identify Paths for Future Development

- **Improved exposure levels with G3** could position Lux for development in combination with other drugs to treat **DLBCL, FL, MCL B-cell cancers**
- Research revealed unique suppression of **BCR** pathway, **TLR** pathway, and **NLRP3 inflammasome**
- Potential future application to **inflammation** and **autoimmunity** indications



# Wrap-up

## **Vision for the Future Applications of Tuspentinib**

# Tuspetinib Ideal for Combination & Maintenance Therapy in AML

## Convenience

- Oral tablet
- Administered once daily

## Favorable / Distinguishing Safety Profile

- No complicating QTc prolongation
- No muscle destruction (no CPK elevation)
- No transaminitis (no ALT/AST elevation)
- No myelosuppression in remission

## Broad Efficacy as Monotherapy

- Responses in patients harboring mutations in RAS, TP53, NPM1, MLL, IDH, DNMT3A, FLT3, Splicing Factor genes, as well as FLT3<sup>WT</sup>
- Combination with venetoclax suppresses drug resistance to TUS and sensitizes to VEN

**This means....**

# Tuspetinib has Sizable Commercial Potential for AML ... plus MDS

## > \$ 1Billion Market Potential in AML

- 3L AML with TUS
- 2L AML with TUS/VEN
- 1L AML with TUS/VEN/HMA
- **Post-CR maintenance** with TUS
- **Plus, planned expansion to MDS** with large market planned

## Tuspetinib Development Goals

- Become ideal agent for combination and maintenance therapy in AML
- Plans to move into MDS patient population
- Not merely single agent for AML subpopulation

## Large Biotech/Pharma Type Agent with Sizable Commercial Potential

- Safety, breadth of activity, convenience, combinability
- Substantial markets for AML
- Ability to expand market into MDS
- Ability to expand sales of current franchise agents
- > \$1Billion commercial market

## Tuspetinib Clinical and Commercial Properties Fit Large Pharma Profile

## Focusing Activities to Position Accordingly

# Aptose

Precision oncology  
company developing  
oral targeted agents  
to treat hematologic  
malignancies

## Aptose Investment Highlights

### **\$25 Million Financing with Keystone Capital**

- Common stock, no warrants

### **Tuspetinib (TUS) lead agent : Once daily, oral agent to treat AML**

- Orphan Drug and Fast Track Status
- CRs across 4 dose levels with no DLTs
- Broad activity across diverse AML populations
- Highly favorable safety and tolerability profiles
- Ideal for combination therapy in 1L/2L/3L AML
- Accelerated approval potential in 2L AML and R/R AML
- > \$Billion AML market potential – Plus, potential to add MDS

### **Luxeptinib oral agent : Clinically active on AML, FL, DLBCL**

- Generation 3 formulation promising and expect dose escalation soon

### **Value-driving near-term clinical milestones during 2023**

- Multiple opportunities to report additional responses | ESH | ASH





THANK YOU

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APT:OSE  
BIOSCIENCES

PRECISION ONCOLOGY FOR THERAPIES OF TOMORROW