Aptose Corporate Presentation January 2023

Incorporating clinical data from 2022 ASH Annual Meeting

APTOSE BIOSCIENCES

PRECISION ONCOLOGY FOR THERAPIES OF TOMORROW

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

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APTOSE Precision Oncology Company Developing Oral Kinase Inhibitors to Treat Life-threatening Hematologic Malignancies

Tuspetinib | *Safely* Treats AML Disease Heterogeneity | Orphan Drug Status | Fast Track Status

Disease heterogeneity is the greatest obstacle to the effective treatment of AML

- Caused by malleable and adaptable patchwork of adverse mutations and altered gene expression
- Renders patients unresponsive to current therapies, leading to diverse populations of R/R AML
- Suppressing a single target insufficient to disrupt redundant and adaptable signaling pathways

Tuspetinib is a Safe and Effective, Once Daily, Oral Drug to Treat AML Disease Heterogeneity

Best-in-Class TKI simultaneously targets clinically-validated oncogenic signaling kinases: SYK | JAK1/2 | $FLT3^{WT/MUT}$ | $cKIT^{MUT}$

Non-myelosuppressive, favorable safety profile
No drug-related SAE, QT_C prolongation, differentiation syndrome

Drug of choice for combination therapy
Safety and breadth of efficacy position for doublet & triplet therapy

Broad application across diverse AML populations
NPM1-mutant | MLL-mutant | RAS-mutant | TP53-mutant | FLT3-mutant

Accelerated paths to market as monotherapy
Potential to treat R/R AML of high unmet need | Prior FLT3i Failure

Single agent CRs across 4 dose levels with no DLT
Once daily oral tablet | 40 mg | 80 mg | 120 mg | 160 mg

$1B market potential & broad IP coverage
Potential to become preferred agent for multiple applications

Expect near term value creation as monotherapy in deep R/R AML populations of high unmet need

Expect long term value creation as ideal TKI for doublet/triplet combination therapy in 1L/2L AML

Tuspetinib Treats AML Disease Heterogeneity

Why We Believe Tuspetinib Can Address the Greatest Needs of AML Patients and Achieve ≥ $1B Commercial Success

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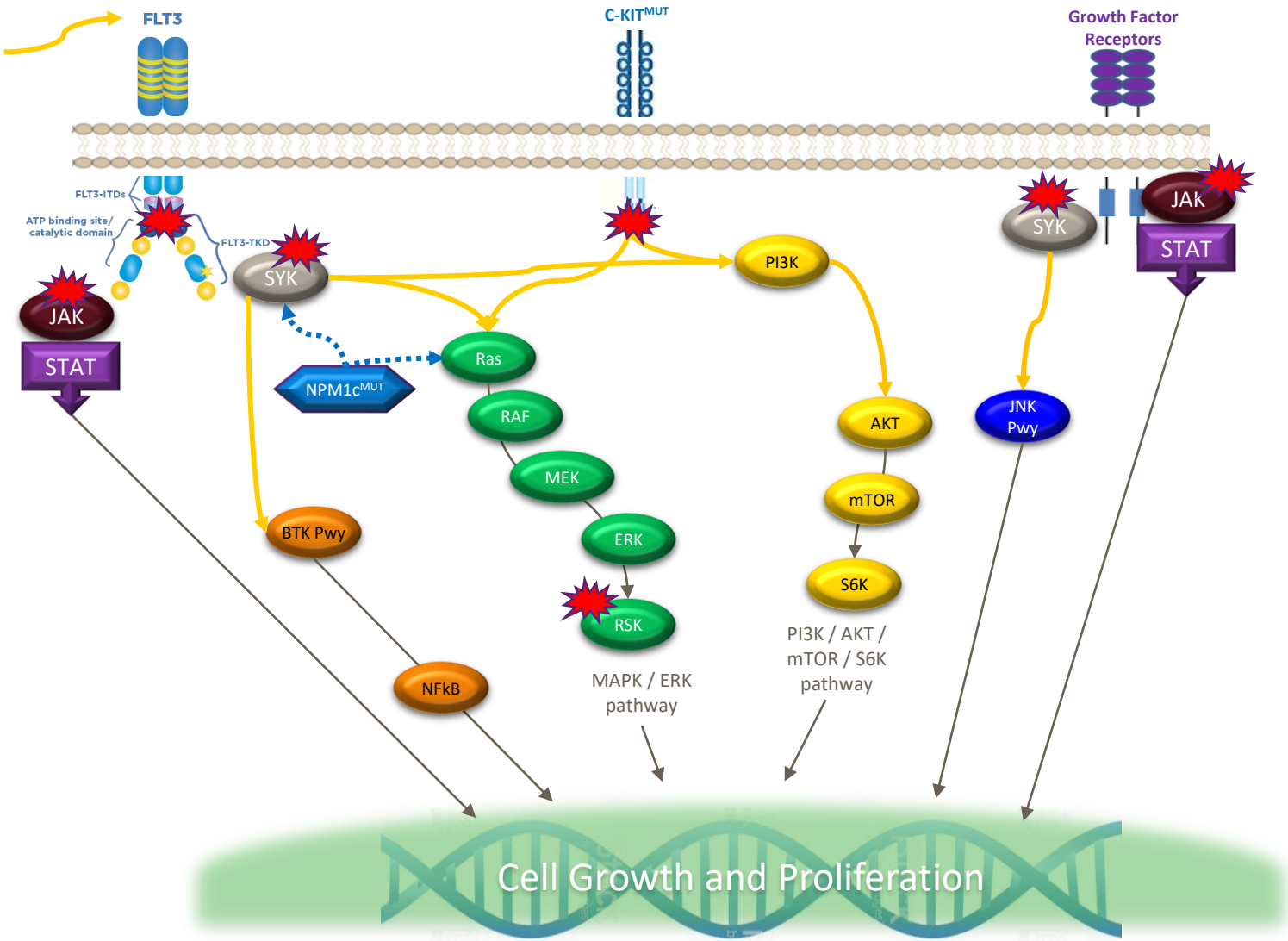
Tuspetinib Targets Clinically Validated Kinases in Oncogenic Signaling Pathways

Excessive levels of **FLT3 ligand** bind to FLT3 Receptor (WT & Mutated)

Direct Inhibition



Potent suppression of multiple kinases operative in AML

- **All forms of FLT3**
- **SYK** signal transduction kinase
- **JAK 1/2** signal transduction kinases
- **cKIT^MUT** alternative receptor kinases
- **RSK** in RAS pathway

→ **Multi-drug therapy in a single tablet**

→ **Simultaneously suppresses multiple dysregulated signal transduction pathways that drive AML proliferation and resistance mechanisms**

→ **Ideal for MONOTHERAPY and COMBINATION therapy**

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Tuspetinib Creating Near Term Value

Ideal TKI Monotherapy for Accelerated Approval in R/R AML Who Failed Prior FLT3i

FLT3^{MUT} AML Treated with FLT3 Inhibitors

- Midostaurin
- Quizartinib
- Gilteritinib
- Sorafenib

FLT3i Failure

Tuspetinib Monotherapy

- Active against all forms FLT3 and other targets
- Responses in patients who failed prior FLT3i
- Potential to address an unmet medical need

Planning a Phase 2 Accelerated Approval Path

Tuspetinib

Accelerated Development May Offer

- ✓ Value creation in 2023 and beyond
- ✓ First approval in AML indication
- ✓ Well tolerated therapy
- ✓ Bridge to stem cell transplant
- ✓ Longer survival and give hope!

R/R FLT3^{MUT} AML / Prior FLT3i Failures

3L+ R/R population with no approved options

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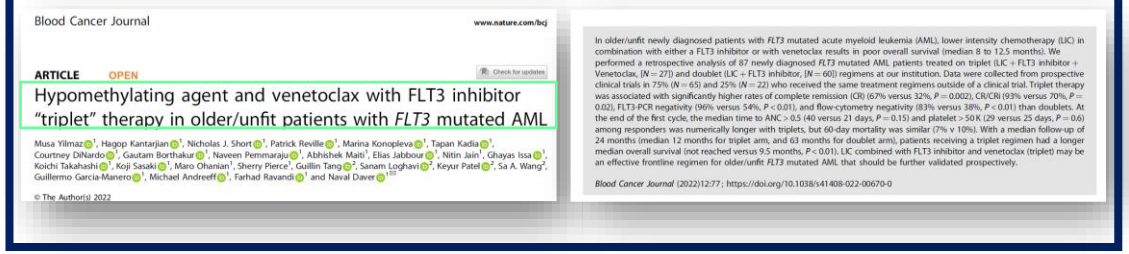
Tuspetinib Creating Near Term and Long Term Value

Tuspetinib Ideal Safe and Broadly Active TKI for Triplet Therapy in 1L AML

Triplet Therapy is Highly Effective, but….

Need Better Triplet : Broader Activity and Safer



Blood Cancer Journal www.nature.com/bcj

ARTICLE OPEN

Hypomethylating agent and venetoclax with FLT3 inhibitor "triplet" therapy in older/unfit patients with *FLT3* mutated AML

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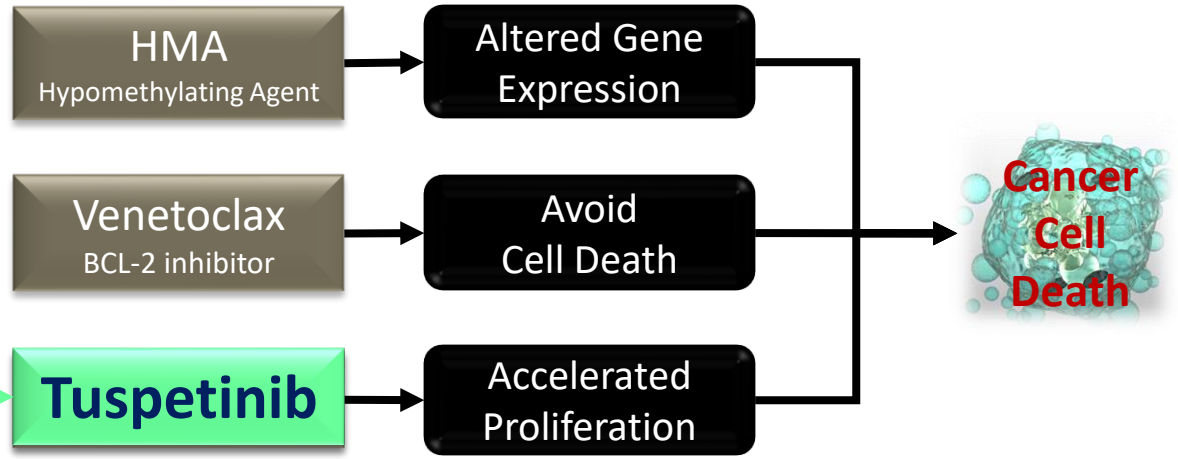
In older/unfit newly diagnosed patients with *FLT3* mutated acute myeloid leukemia (AML), lower intensity chemotherapy (LIC) in combination with either a FLT3 inhibitor or with venetoclax results in poor overall survival (median 8 to 12.5 months). We performed a retrospective analysis of 87 newly diagnosed *FLT3* mutated AML patients treated on triplet (LIC + FLT3 inhibitor + Venetoclax, [N = 27]) and doublet (LIC + FLT3 inhibitor, [N = 60]) regimens at our institution. Data were collected from prospective clinical trials in 75% (N = 65) and 25% (N = 22) who received the same treatment regimens outside of a clinical trial. Triplet therapy was associated with significantly higher rates of complete remission (CR) (67% versus 32%, P = 0.002), CR/CRi (93% versus 70%, P = 0.02), FLT3-PCR negativity (96% versus 54%, P < 0.01), and flow-cytometry negativity (83% versus 38%, P < 0.01) than doublets. At the end of the first cycle, the median time to ANC > 0.5 (40 versus 21 days, P = 0.15) and platelet > 50 K (29 versus 25 days, P = 0.6) among responders was numerically longer with triplets, but 60-day mortality was similar (7% v 10%). With a median follow-up of 24 months (median 12 months for triplet arm, and 63 months for doublet arm), patients receiving a triplet regimen had a longer median overall survival (not reached versus 9.5 months, P < 0.01). LIC combined with FLT3 inhibitor and venetoclax (triplet) may be an effective frontline regimen for older/unfit *FLT3* mutated AML that should be further validated prospectively.

Blood Cancer Journal (2022)12:77 ; https://doi.org/10.1038/s41408-022-00670-0



Current Triplet : HMA + Venetoclax + FLT3i-TKI

- Improves CR/CRh/CRi to >90%
- Improves MRD-negative status
- Improves OS (survival) and gives hope
- Problem with QT_c prolongation by TKI
- Problem with myelosuppression by TKI
- Limited breadth of antileukemic activity

Ideal Triplet : HMA + Venetoclax + Tuspetinib

Tuspetinib ideal TKI for triplet combination due to its safety profile and ability to block key proliferation pathways….

Position for 1L, R/R disease, Unfit and Fit, $FLT3^{MUT/WT}$

- No signal of cardiotoxicity or differentiation syndrome observed
- Not myelosuppressive with continuous dosing in remission
- Active on $FLT3^{MUT}$ and $FLT3^{WT}$ and other adverse mutations

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Tuspetinib US Sales Potential in AML Could Reach ≥ $ 1B

PRIOR FLT3 INHIBITOR FAILURES
Superior Monotherapy for Accelerated Approval

MAINTENANCE THERAPY
Maintain Patients Long Term MRD-negative CR

DOUBLET/TRIPLET COMBINATION
Place R/R Patients into MRD-NEGATIVE CR

TRIPLET COMBINATION
Place 1L Patients into MRD-NEGATIVE CR

Potential Annual Sales ≥ $1 B

Kinase inhibitors represent the most successful and proven class of targeted leukemia drugs in history….

Tuspetinib blockbuster potential….

- Delivers potent single agent CRs among refractory AML with a diversity of adverse mutations
- Avoids typical toxicities of other kinase inhibitors
- Path identified for accelerated approval
- Ideal for maintenance & combination therapy

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Tuspetinib Phase 1/2 Clinical Trial

Emerging Clinical PK & Safety Data

APTIVATE Phase 1b/2 Expansion Trial Ongoing with Once Daily Oral Tuspetinib in R/R AML Patients with Adverse Mutations

Phase 1a
Dose Escalation
20 mg to 200 mg

Phase 1b
Dose Exploration
40 mg, 80 mg, 120 mg, 160mg

Phase 1b/2
APTIVATE Expansion Trial
120 mg Monotherapy and
80 mg Combination with Venetoclax

✓ **Completed**

Phase 1a Dose Escalation

- Doses from **20 mg to 200 mg**
- **Once daily oral dosing** of a tablet
- Demonstrated **safety / tolerability**
- Dose-related **pharmacokinetics**
- Antileukemic **activity** (CR & PR)

✓ **Completed**

Phase 1b Dose Exploration

- Increased number of patients at doses demonstrating efficacy
- **4 dose levels** with CRs and no DLTs
- **Safety profile** remarkable
- **120 mg** selected for monotherapy
- **80 mg** selected for combination with venetoclax

Enrolling

APTIVATE Phase 1b/2 Expansion

- **Monotherapy**
  - *Position for accelerated approvals* in $FLT3^{MUT}$/Prior FLT3i
- **Combination Tuspetinib with Venetoclax**
  - *Position for Tus|Ven|HMA in 1L AML*
  - *Position for Tus|Ven in R/R AML*

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Tuspetinib Phase 1/2 Study in R/R AML
Dose Escalation & Dose Exploration Completed

PART A DOSE ESCALATION (18 Pts Dosed)			PART B DOSE EXPLORATION (42 Pts Dosed)		
Cohort 6	200 mg QD	Completed			
Cohort 5	160 mg QD	Completed	160 mg QD	Completed	CRc DLT
Cohort 4	120 mg QD	Completed	120 mg QD	Completed	CRc DLT
Cohort 3	80 mg QD	Completed	80 mg QD	Completed	CRc DLT
Cohort 2	40 mg QD	Completed	40 mg QD	Enrolling	CRc DLT
Cohort 1	20 mg QD	Completed			

Favorable , non-myelosuppressive safety profile:

- No drug related SAE or deaths
- No drug-related QT_c prolongation
- No DLT through 160 mg dose level
- Plasma $t_{1/2}$ estimated at 40hrs
- Patients fasted in this trial

Dose Escalation and Dose Exploration completed across six dose cohorts

- Total patients dosed in Part A + Part B = 60
- Total evaluable for efficacy in Part A + Part B = 48
- Total evaluable for efficacy at 80/120/160mg = 42
- Additional patients being placed on 40mg dose level

Executed: 31OCT2022 Data filtered through: 06OCT2022

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Data from 2022 ASH Annual Meeting

Tuspetinib Phase 1/2 Study in R/R AML: Patient Profiles

- As of **October 6, 2022, 60 patients** have been treated across 6 dose levels (20, 40, 80, 120, 160, and 200 mg) in Dose Escalation (Part A) and Dose Exploration (Part B) at **8 sites in the US and Korea**, Republic of (South).
- Patients treated include male (58.3%), Asian (53.3%), or White (36.7%).
- **Median age = 61** years of age (range 18-84).
- **Patients heavily pre-treated**, with prior **cytotoxic chemotherapy (72%)**, **HMAs** (60%), **venetoclax** (50%), **prior HSCT** (28.3%).
- More than half (14/26) of FLT3-mutated patients had been **failed by prior FLT3 inhibitor**.

Patient Disease Characteristics	
FLT3 Mutation Status	**N (%)**
$FLT3^{MUT}$	26 (43.3%)
$FLT3^{WT}$	33 (55.0%)
Unknown	1 (1.7%)
Prior Lines of AML Therapy - Mean (range)	2.7 (1 to 8)
Type of Prior Therapy	**N (%)**
Prior Drug Therapy (Chemotherapy/Not Radiation)	60 (100%)
Cytotoxic Chemotherapy	43 (71.7%)
HSCT	17 (28.3%)
FLT3 Inhibitor	14 (23.3%)

Prior Therapy	Number of Patients Receiving HMA or Venetoclax Among 60 Total Patients Dosed in Trial
HMA (Azacitidine and/or Decitabine)	36 (60%)
Venetoclax	30 (50%)

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Tuspetinib Delivers Safety and Broad Therapeutic Window
Broad Therapeutic Window as a Single Agent in R/R AML Patients

- **Safety Profile Favorable to Date**
  - No drug-related myelosuppression
  - No drug related AE of QT_c 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 (not rhabdomyolysis) – high exposure
  - No observed muscle destruction and no AE of elevated creatine phosphokinase (CPK)
  - **Avoids many of the typical toxicities observed with other TKI and menin inhibitors**

- **Broad Therapeutic Window**
  - **Achieved efficacy (CRs) across four separate dose levels** (40mg, 80 mg, 120 mg, 160 mg)
  - **Achieved safety across all four dose levels that delivered efficacy**
  - Demonstrated **broad therapeutic range** across safe dose levels
  - Safety profile supports **combination therapy with other agents**

- **Our Patients are Heavily Pretreated with Chemotherapy, FLT3i, HMAs, Venetoclax and Other Targeted Agents**
  - Most $FLT3^{MUT}$ patients had failed midostaurin &/or gilteritinib, chemo, Ven, Aza, others

Treatment-emergent AEs (TEAEs), Safety Analysis Set, Parts A and B (N=60)	
Patients Experiencing TEAEs	**N (%)**
Any	56 (93.3%)
Most Frequent TEAEs (>15% of patients)	
Pneumonia	18 (30.0%)
Pyrexia	12 (20.0%)
Nausea	11 (18.3%)
Diarrhea	9 (15.0%)
≥ Grade 3	41 (68.3%)
SAEs	31 (51.7%)
Leading to treatment discontinuation	6 (10.0%)
Leading to death	11 (18.3%)
Patients Experiencing TEAEs Related to HM43239	**N (%)**
Any	17 (28.3%)
Most Frequent Related TEAEs (>5% of patients)	
Diarrhea	7 (11.7%)
Nausea	5 (8.3%)
≥ Grade 3	6 (10.0%)
Decreased neutrophil count	2 (3.3%)
Muscle weakness	2 (3.3%)
Decreased white blood cell count	1 (1.7%)
Nausea	1 (1.7%)
Leukopenia	1 (1.7%)
SAEs	0 (0%)
Leading to death	0 (0%)
Dose Limiting Toxicity (DLT)*	1 (1.7%)

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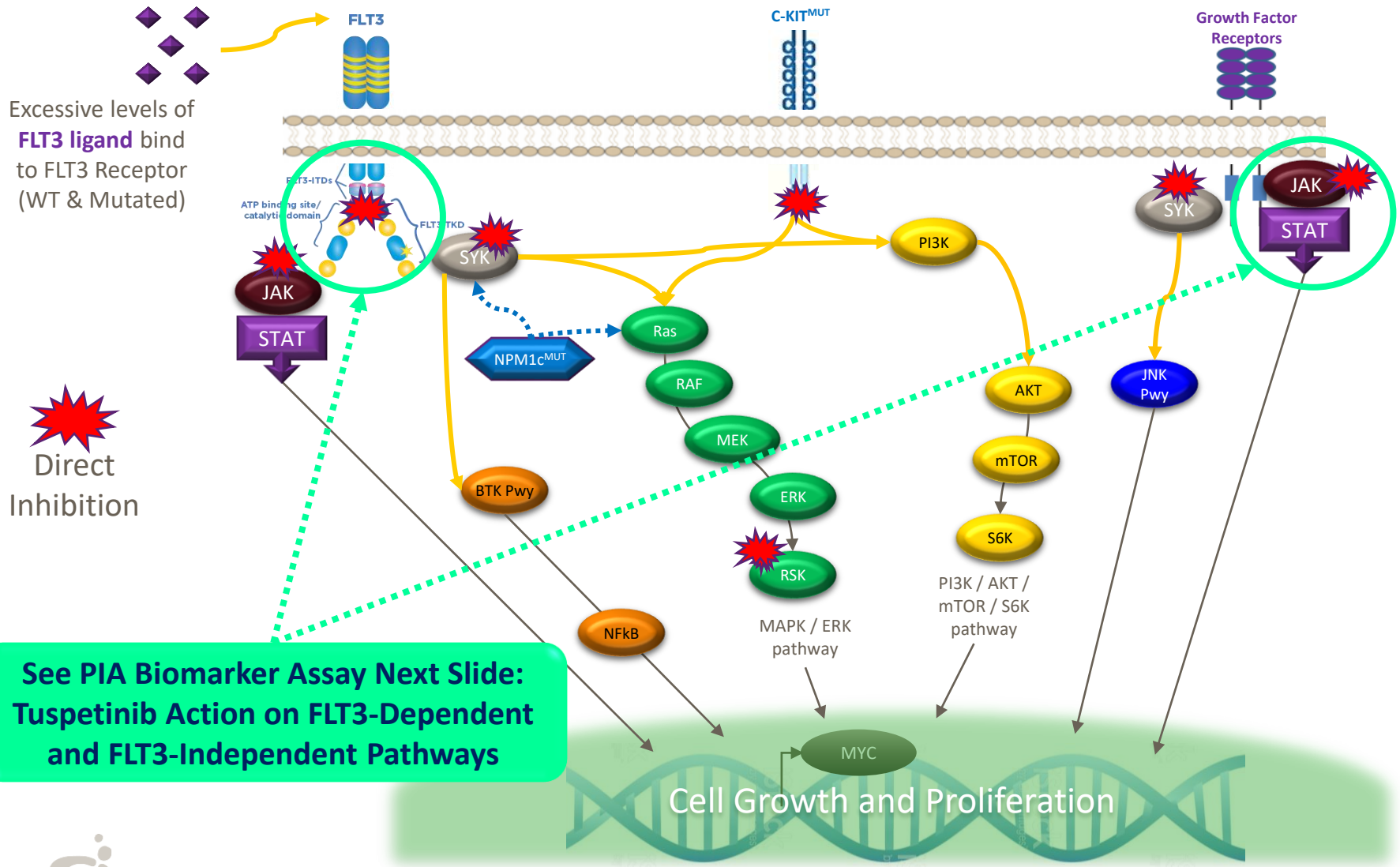
Tuspetinib Phase 1/2 Clinical Trial

Clinical Pharmacodynamic Biomarkers | “Hitting the Targets”

Tuspetinib Targets Clinically Validated Kinases in Oncogenic Signaling Pathways



See PIA Biomarker Assay Next Slide: Tuspetinib Action on FLT3-Dependent and FLT3-Independent Pathways

Potent suppression of multiple kinases operative in AML

- **All forms of FLT3**
- **SYK** signal transduction kinase
- **JAK 1/2** signal transduction kinases
- **cKIT^{MUT}** alternative receptor kinases
- **RSK** in RAS pathway

→ **Multi-drug therapy in a single tablet**

→ **Simultaneously suppresses multiple dysregulated signal transduction pathways that drive AML proliferation and resistance mechanisms**

→ **Ideal for monotherapy and combination therapy**

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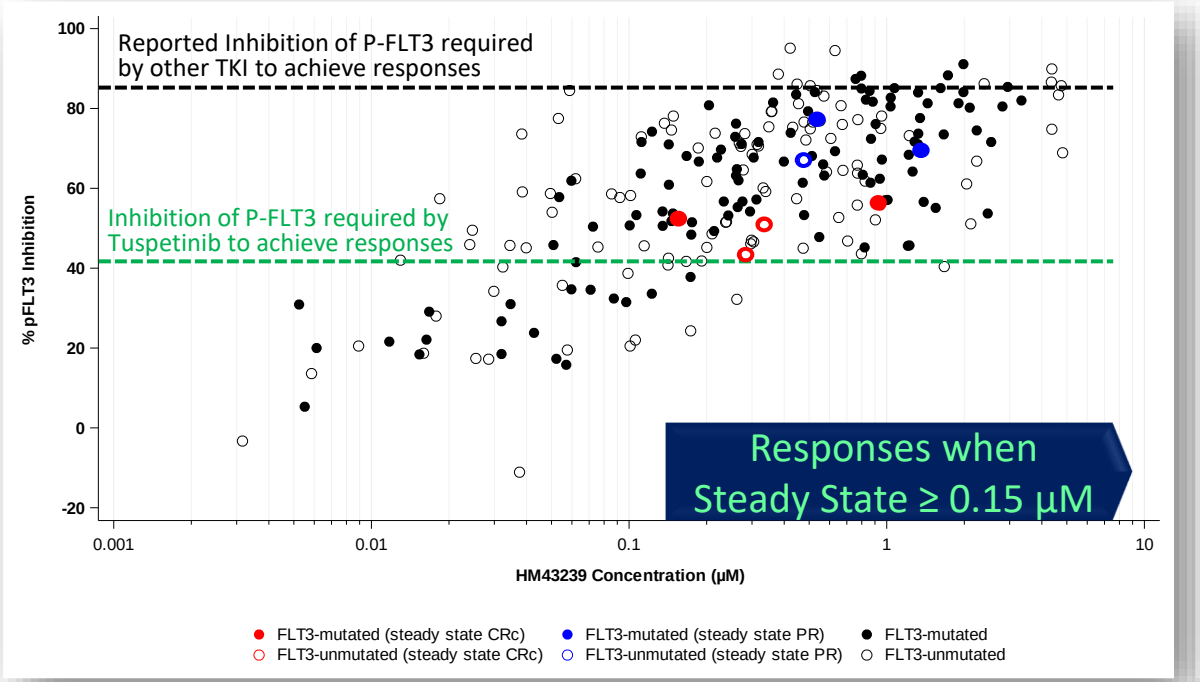
Tuspetinib Biomarkers: Inhibition of Phosho-FLT3 and JAK/Phospho-STAT5 by Patient Plasma with a PIA Reporter Assay → Hits Targets & Only Partial Inhibition Required

Inhibition of FLT3 Kinase activity by Measurement of P-FLT3 in MOLM-14 AML Cells By Patient Plasma in PIA Assay



Abbreviation: PIA, plasma inhibitory activity; PK, pharmacokinetics; PKAS, pharmacokinetics analysis set.
Note: available FLT3 PIA values with corresponding PK values at the same timepoints from patients in PKAS are plotted in this figure.
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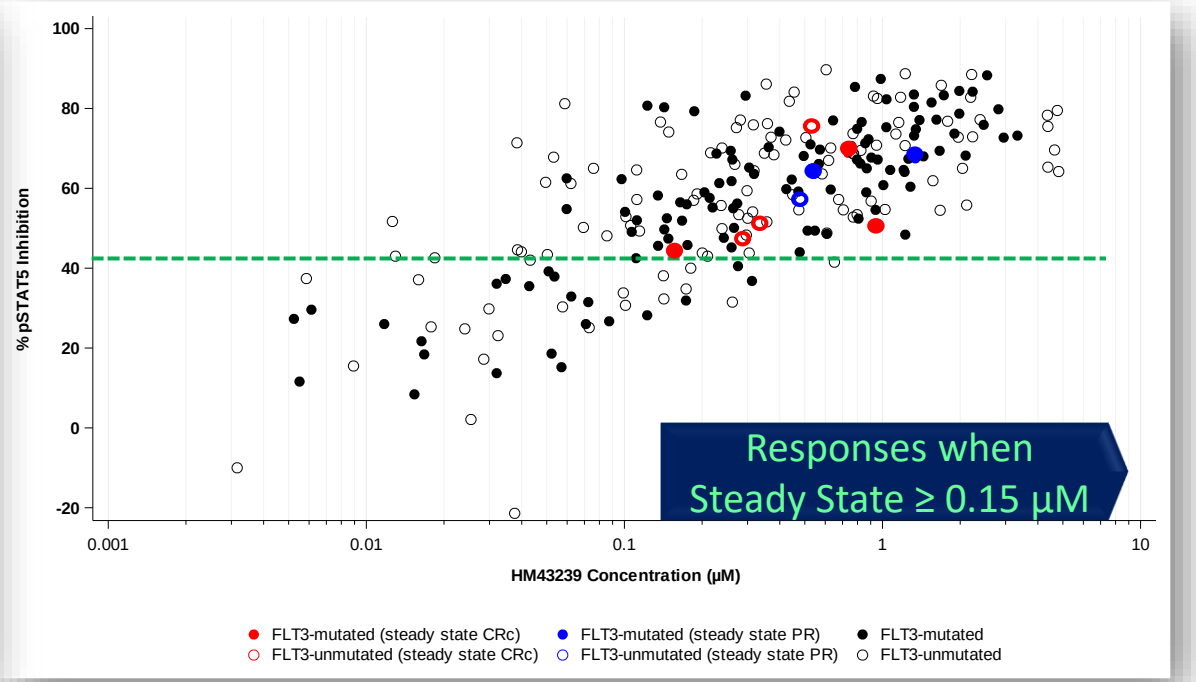
Inhibition of JAK kinase activity by Measurement of P-STAT5 in MOLM-14 AML Cells By Patient Plasma in PIA Assay



Abbreviation: PIA, plasma inhibitory activity; PK, pharmacokinetics; PKAS, pharmacokinetics analysis set.
Note: available STAT5 PIA values with corresponding PK values at the same timepoints from patients in PKAS are plotted in this figure.
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**Multiple plasma samples from individual patients ($FLT3^{MUT}$ and $FLT3^{WT}$) were measured for Tuspetinib concentration, P-FLT3 and P-STAT.
However, a red or blue circle designates the steady state concentration at which a response occurred (only one per patient).
Not all patient samples were evaluated.**

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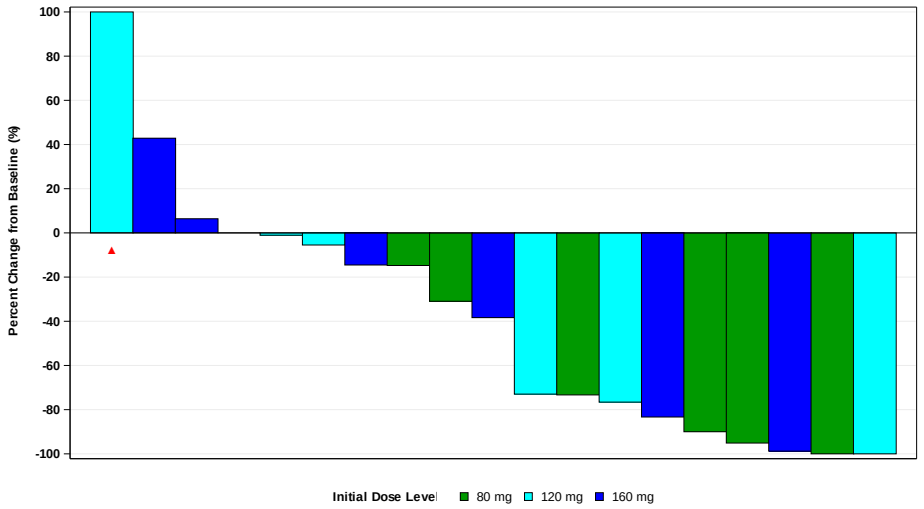
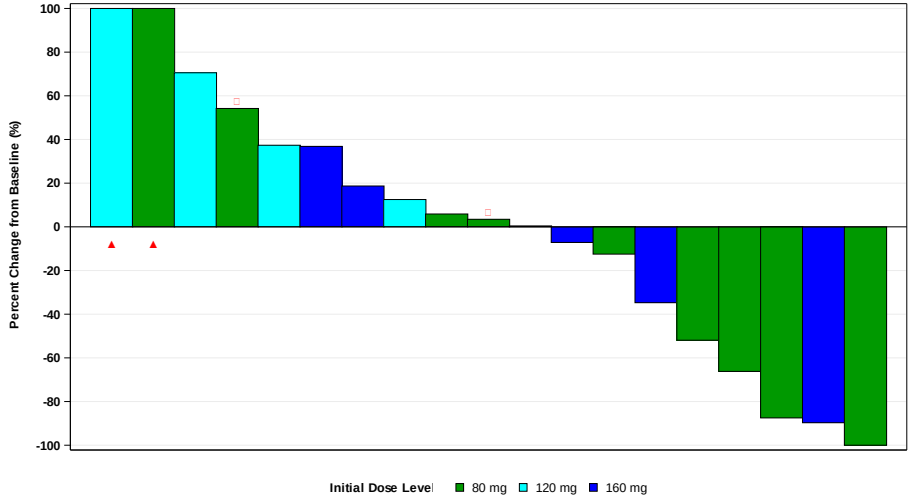
Tuspetinib Monotherapy Delivers Blast Reductions in AML Patients

Tuspetinib: Waterfall Plot of Bone Marrow Blast Reductions (Percent Change) from Baseline For Patients Assigned to 80 mg, 120 mg and 160 mg Dose Levels



FLT3^{MUT} Patients



FLT3^{WT} Patients

- **Bone Marrow Blast Reductions**
  - **CRs** achieved when blast clearance accompanied by full recovery of normal blood cells
  - **Observed broadly** across heavily pretreated r/r AML patients across multiple doses levels
- **Meaningful:** Bone marrow blast reductions without full recovery of normal blood cells
  - **Highlights the potential of tuspetinib to reach a CR when combined** with hypomethylating agents, venetoclax, or other therapies
  - **Patients with CRi as best response may proceed to transplant**

Tuspetinib Note: Blast percent change was calculated as 100 X (the lowest post-baseline bone marrow blast - baseline bone marrow blast)/baseline bone marrow blast. Only patients who reported both baseline and any post-baseline bone marrow blast results are included in the figure.
*indicates patients who administered hydroxyurea within 7 days prior to the lowest marrow blast value. Patients with percent change from baseline > 100% are shown as 100% and indicated with a triangle.
Data Extracted 03Oct2022 and Data Executed 13Oct2022

Gilteritinib Note: [1] Perl AE, et al, Selective Inhibition of FLT3 by Gilteritinib in Relapsed/Refractory Acute Myeloid Leukemia: a Multicenter, First-in-human, Open-label, Phase 1/2 Study, *Lancet Oncol*. 2017 August; 18(8): 1061-0175. Plots are from Supplemental Figure 2a.
Note: Maximum change from baseline across all visits for each subjects was plotted. The percent myeloblast change from baseline = [(post baseline myeloblast – baseline myeloblast)/baseline myeloblast] X 100%.

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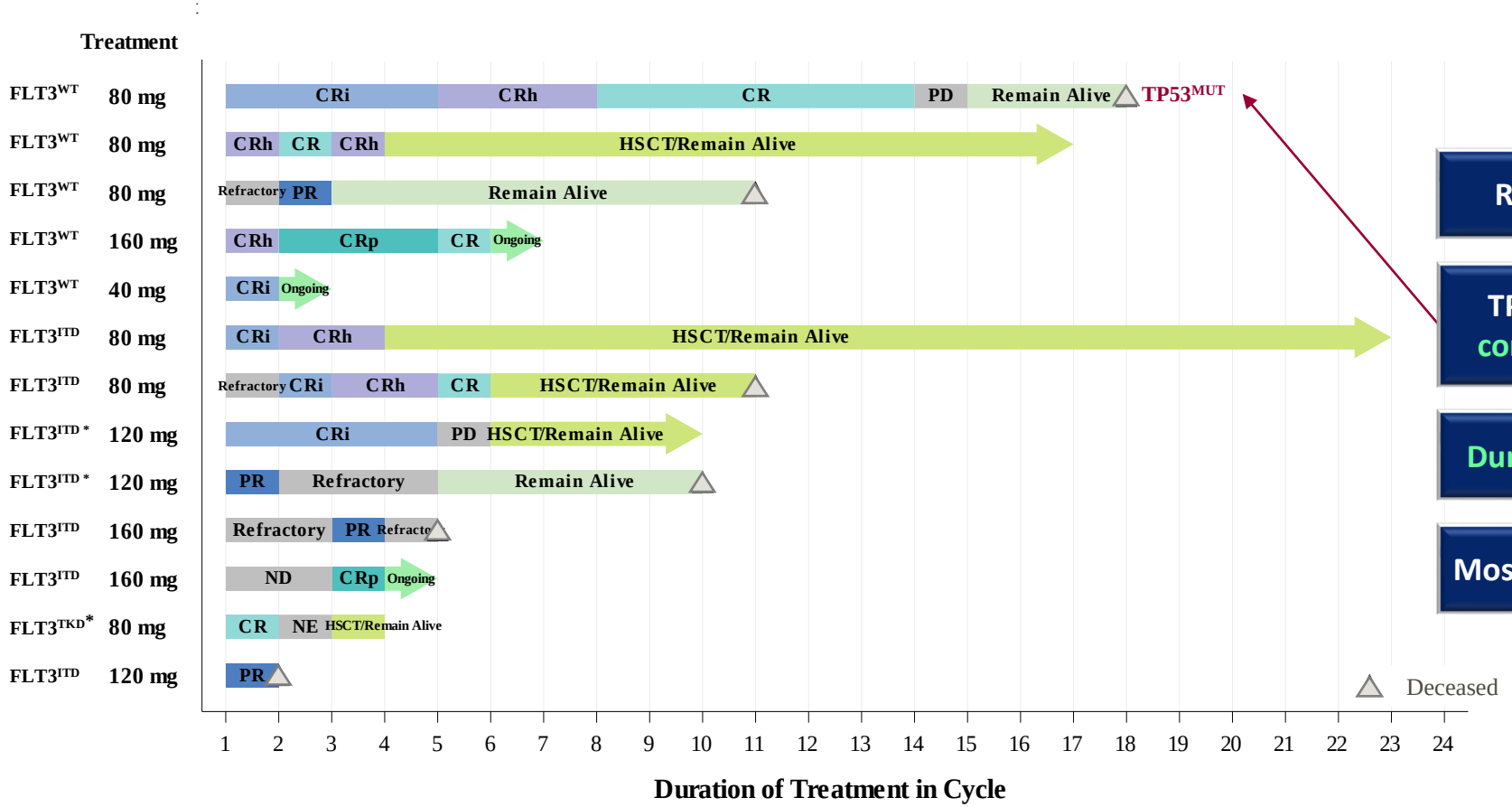
Tuspetinib Emerging Clinical Response Data

Potential Superior AML Therapy

R/R AML Patients Achieving Clinical Responses with Tuspetinib Monotherapy

Swimmer Plot of Responses Reported to Date



RESPONDERS

- Responses achieved across four dose levels
- TP53MUT demonstrates breadth, durability & continuous dosing without myelosuppression
- Durability observed when -/+ HSCT unavailable
- Most bridged to potentially life-saving transplant

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; ND, not done; NE, not evaluable; PD, progressive disease; PR, partial remission.
Note: 'Ongoing' means treatment is still ongoing; 'Remain Alive' indicates patients' status in follow-up after treatment termination; The right arrow at the end of horizontal bar indicates patients are still on study, whereas without the right arrow indicates patients discontinued from study.
Note: The bone marrow aspiration/biopsy date was used as response date. Each response assessed at a regular visit is considered to have started 1 cycle before the assessment; however the start of the response is considered the integer part of (study day/28) if the response occurred at the End of Treatment visit.
*Indicates patients who received prior FLT3 inhibitors, including gilteritinib and/or midostaurin.
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Tuspetinib Monotherapy Clinical Responses Across R/R AML Patients with a Diversity of Adverse Mutations (Disease Heterogeneity)

Patient	Important Mutations	FLT3 Status	Dose Level	Best Response	Bridged to HSCT
1	TP53	WT	80mg	CR	No
2	NRAS RUNX1	ITD	80mg	CRh	Yes
3	NRAS BCOR U2AF1 SETBP1	WT	160mg	CR	Tx Ongoing
4	KRAS NPM1 DNMT3A PTPN11	ITD – *Prior FLT3i*	120mg	PR	No
5	NPM1 DNMT3A	ITD	80mg	CR	Yes
6	NPM1	ITD	160mg	CRp	Tx Ongoing
7	NPM1 IDH1 DNMT3A	ITD	160mg	PR	No
8	IDH2 SRSF2	WT	80mg	CR	Yes
9	RUNX1 SF3B1 RB1	TKD – *Prior FLT3i*	80mg	CR	Yes
10	MLL-PTD RUNX1	ITD – *Prior FLT3i*	120mg	CRi	Yes
11	Not Yet Reported	WT	40mg	CRi	Tx Ongoing
12	Not Yet Reported	ITD	120mg	PR	No
13	ASXL1 CBL	WT	80mg	PR	No
14	Not Yet Reported	ITD	160mg	SD	Tx Ongoing

Most Responders Bridged to Potentially Life-Saving Transplant

Responses Across Populations With Highly Adverse Mutations TP53, RAS, NPM1, FLT3, DNMT3A, IDH, RUNX1, MLL

Responses in FLT3-MUT & WT 37.5% of CRc Responders are FLT3-WT (3 of 8)

$FLT3^{MUT}$ (ITD, TKD) Responders Who Failed Prior FLT3i
Potential for Accelerated Approval

$TP53^{MUT}$ Responder
Potential for Accelerated Approval

DR, CRh, CRp, CRi, CRc and PR : Data Derived from Ongoing Phase 1/2 Clinical Trial
Abbreviation: CRc, composite complete remission; PR, partial remission

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Case Study Vignettes
of r/r AML Patients Responding to Tuspetinib

Tuspetinib Case Study
CR in FLT3-WT / NRAS-Mutant R/R AML Patient

R/R AML S2601	FLT3-WT NRAS-mutated BCOR-mutated, U2AF1-mutated, SETBP1-mutated Cytogenetics: Normal
Demographics	55-year-old male
Diagnosis at Study Entry	**Refractory AML with MDS-related changes** 42.1% bone marrow blasts at diagnosis
Prior Therapies	• Failed by induction chemotherapy (cytarabine / daunorubicin) • Failed by salvage therapy (cytarabine / fludarabine)
Dose	160 mg daily oral tablet HM43239
Response	• **CRh** at Cycle 1 • **CR** at Cycle 5 and ongoing • No DLT and no SAE to date • Patient became *transfusion independent* post-dose

Patient continues on study

Data from 2022 ASH Annual Meeting

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Tuspetinib Case Study
CR in FLT3-WT / TP53-Mutant R/R AML Patient

R/R AML S2203	FLT3-WT TP53-Mutated Cytogenetics: Complex Karyotype
Demographics	60-year-old Male
Diagnosis at Study Entry	**Refractory AML with MDS-related changes** 70.8% bone marrow blasts at diagnosis
Prior Therapies	• Induction chemotherapy (cytarabine / daunorubicin) • Salvage therapy (cytarabine / idarubicin/ fludarabine) • Conditioning (busulfan /fludarabine / antithymocyte immunoglobulin) • Prior HSCT
Dose	80 mg daily oral tablet HM43239
Response	• **CRi** at Cycle 1 • **CRh** at Cycle 5 • **CR** at Cycle 8 • Patient became *transfusion independent* post-dose

Patient continued on study more than 13 cycles – Later failed by venetoclax and decitabine

Data from 2022 ASH Annual Meeting

Tuspetinib Case Study
CR in FLT3-ITD / Prior-FLT3i Failure R/R AML Patient

R/R AML S2220	FLT3-ITD Prior FLT3i Failure MLL-PTD, RUNX1-mutated Cytogenetics: Normal
Demographics	49-year-old Female
Diagnosis at Study Entry	**Relapsed AML** 66% bone marrow blasts at diagnosis
Prior Therapies	• Induction therapy (cytarabine / daunorubicin / **midostaurin**) • Consolidation therapy (cytarabine / **midostaurin**) • Conditioning (busulfan /fludarabine / antithymocyte immunoglobulin) • Prior HSCT
Dose	120 mg daily oral tablet HM43239
Response	• **CRi** at Cycle 1

Patient bridged to HSCT

Data from 2022 ASH Annual Meeting

Tuspetinib Case Study
CR in FLT3-TKD / Prior FLT3i Failure R/R AML Patient

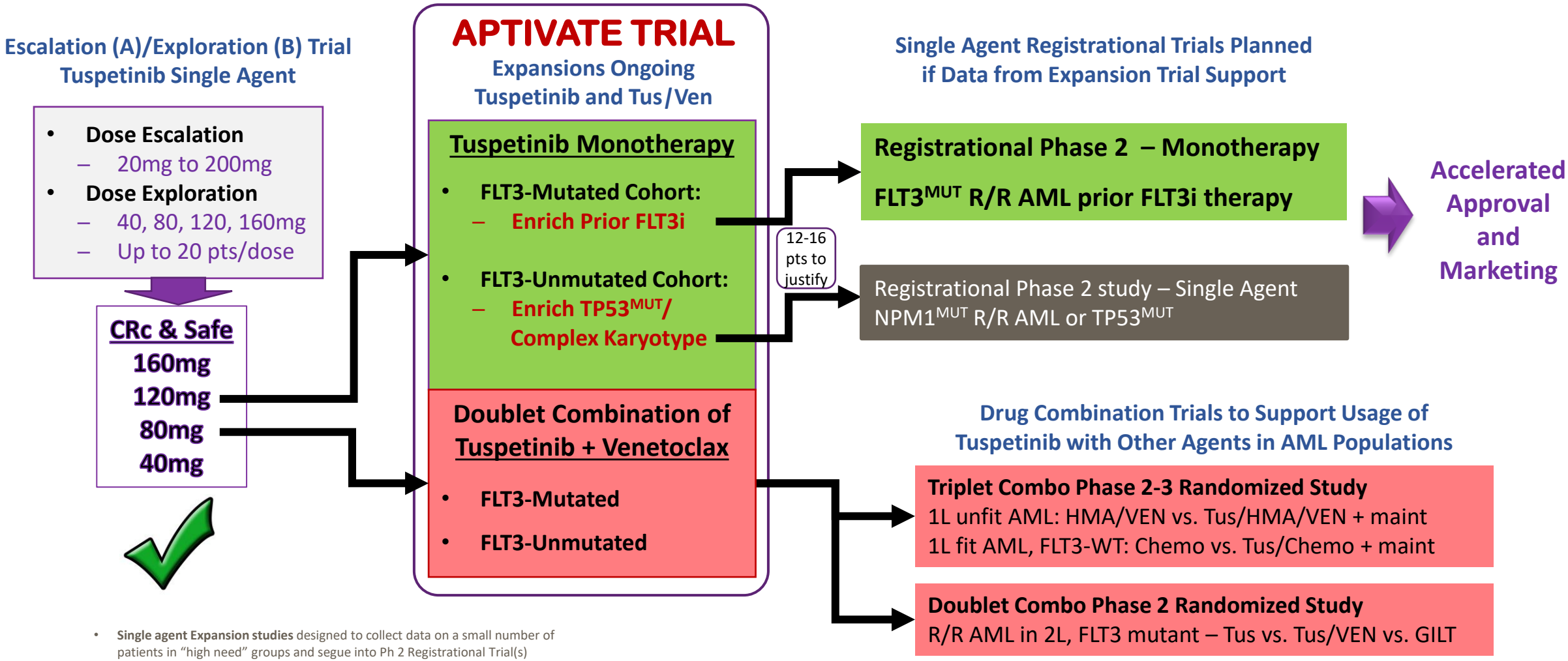
R/R AML S1301	FLT3-TKD Prior FLT3i Failure RUNX1-mutated, SF3B1-mutated, RB1-mutated Cytogenetics: Normal
Demographics	67-year-old Female
Diagnosis at Study Entry	**Refractory AML** 40% bone marrow blasts at diagnosis
Prior Therapies	• Induction therapy (cytarabine / daunorubicin / **midostaurin**) • Consolidation therapy (azacitidine / **gilteritinib**)
Dose	80 mg daily oral tablet HM43239
Response	• **CR** at Cycle 1

Patient bridged to HSCT

Data from 2022 ASH Annual Meeting

Tuspetinib Going Forward

Tuspetinib Global Dose Expansion Trial Planned to Support Registrational Trials for Accelerated Approval and Drug Combination Trials for Broad Commercialization



- **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 Tuspetinib with venetoclax and segue into Phase 2-3 randomized trials and demonstrate Tuspetinib can be the preferred agent for combination therapy

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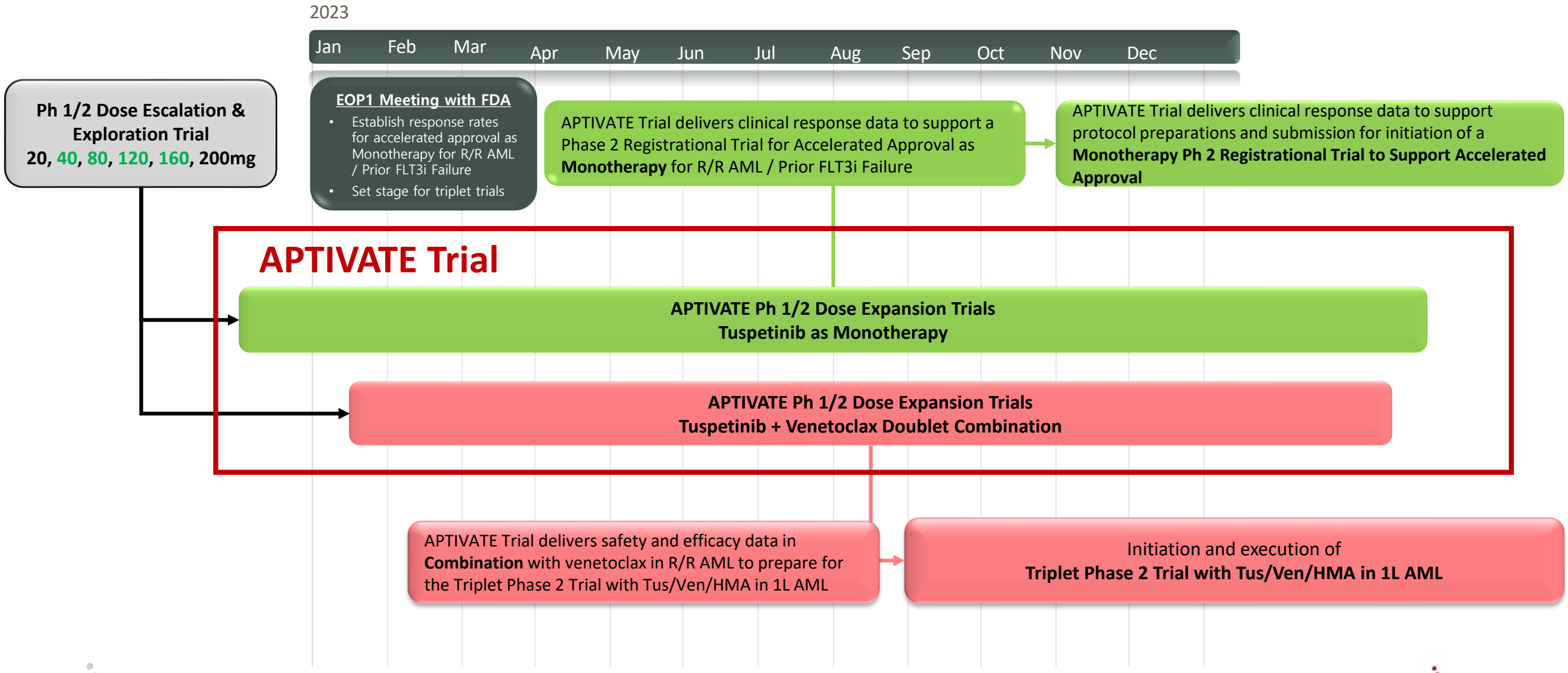
Tuspetinib APTIVATE Trial Delivering Value Creating Milestones in 2023



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Tuspetinib APTIVATE Trial Delivering Value Creating Milestones in 2023

Tuspetinib as Monotherapy

1Q 2023 : **EOP1 Meeting with FDA** to establish response rates required for accelerated approval:
Monotherapy for R/R AML / Prior FLT3i Failure

2H 2023 : **APTIVATE Trial deliver early response data** to support development concept:
Phase 2 Registrational Trial for an Accelerated Approval as Monotherapy for R/R AML / Prior FLT3i Failure

2H 2023 : **APTIVATE Trial deliver response rates** to support a protocol submission:
Phase 2 Registrational Trial for an Accelerated Approval as Monotherapy for R/R AML / Prior FLT3i Failure

Tuspetinib in Combination

1H 2023 : **APTIVATE Trial** demonstrate **safety and efficacy in combination with venetoclax in R/R AML**

2H 2023 : **Triplet Phase 2 Trial** initiation with “all oral” Tus/Ven/HMA **in 1L AML**

2H 2023 : **Potential Accelerated Approval** path identified for **Doublet Phase 2 Trial** with Tus/Ven **in R/R AML**

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Tuspetinib Monotherapy for Treatment of R/R FLT3^{MUT} AML Patients | Prior FLT3i Failures

Likely Bar for Tuspetinib Accelerated Approval in R/R FLT3^{MUT} AML | Prior FLT3i Failures

- **Gilteritinib FLT3i Approved with CR/CRh = 21% in 2L FLT3^{MUT} AML Patients**
  - **FDA Review: *Interim* CR/CRh = 21% based on data from the First Interim Analysis of the ADMIRAL trial**
    - **Gilteritinib approved** **CR/CRh = 21%** (29/138) |CR = 11.6% | DOCR = 9 months | OS = 9.3 months
    - USPI Package Insert CR/CRh = 22.6% (55/243) final analysis of response rate
  - **NEJM Article:** *Implied CR/CRh* = 34% (84/**247**), but this *included the CR/CRh that occurred after HSCT in Admiral trial*
  - **NEJM Article:** *Actual CR/CRh* = 26.3% (65/**247**) only included the CR/CRh prior to on-study HSCT (NEJM supplemental table)
- **Tuspetinib Monotherapy will be Assessed in More Tx-experience AML Patients that Already Failed FLT3i**
  - Gilteritinib patients were 2L, mostly FLT3i-naïve (few had seen midostaurin), Venetoclax-naïve
  - Tuspetinib patients are **3L** (or later), **failed prior FLT3i**, likely **failed venetoclax & other agents (chemo and/or HMA)**
- **Tuspetinib Proposed Bar for Approval : CR/CRh = 13%**
  - The **proposed CR/CRh = 13% for Tus in 3L/FLT3-failure/Ven-failure/older/less fit population** will include any patient that achieved a CR or CRh as best response after receiving Tus (95% CI that excludes 6% as the lower bound of the CRc)
  - Propose Duration of CR/CRh = 6 months and approximately 100 patients to power trial sufficiently

Tuspetinib Safely Delivers Monotherapy Responses Across Diverse AML Populations

Best-in-Class TKI to Treat AML Disease Heterogeneity

- Safety and High Response Rates: ORR (up to 75%) and CR/CRh/CRi (up to 50%)
- Among Efficacy Evaluable R/R AML Patients From 40, 80, 120, 160mg Dose Levels and with No DLT
- Impressive Response Rates for Any Single Mutant Group → More Impressive to See Responses in Multiple Mutant Groups

Example AML Populations with Adverse Mutations — % of AML Patients

• TP53-mutant	8-10%
• RAS-mutant	15-40%
• NPM1-mutant -/+ FLT3-mutant	30% / 15%
• FLT3-mutant	25-30%
• FLT3-mutant failed prior FLT3i therapy	15-20%

Immediate Development Plans for **R/R AML**

- Monotherapy for R/R FLT3-mutant AML who failed Prior FLT3 inhibitors ($FLT3^{MUT}$/Prior FLT3i)
- Combination Therapy with venetoclax for AML patients who failed standard therapies

Immediate Development for **1L AML**

- Triple combination in fit and unfit patients, FLT3-mutant and FLT3-unmutated

Mutation-Enriched Groups of AML Patients	ORR	CR/CRh/CRi
$TP53^{MUT}$ | Complex Karyotype	1/3 (33%)	1/3 (33%)
$N/K\text{-}RAS^{MUT}$	3/8 (38%)	2/8 (25%)
$NPM1^{MUT}$ | $FLT3^{MUT}$	4/6 (67%)	2/6 (33%)
$FLT3^{MUT}$	8/21 (38%)	5/21 (24%)
$FLT3^{MUT}$ / Prior FLT3i Failure	3/11 (27%)	2/11 (18%)

Data from 2022 ASH Annual Meeting

TUSPETINIB Best in Class TKI for AML : Targets FLT3 + SYK + JAK-1/2 + C-KIT
Comparison to Other Approved or Investigational Agents

	Tuspetinib	Gilteritinib	Quizartinib	Emavusertib	Revumenib	Ziftomenib	Lanraplenib
MOA / Targets	SYK, JAK1/2 FLT3$^{ITD/TKD/WT}$ c-KIT^{MUT}	FLT3 $^{ITD/TKD}$	FLT3 ^{ITD}	IRAK4/FLT3	Menin-MLL	Menin-MLL	SYK
Safety Supports Broad Tx Window	✓	–	✗	✗ Rhabdomyolysis	–	–	–
Avoids QTc Prolongation	✓	✗	✗	✓	✗	✓	✓
Avoids Differentiation Syndrome	✓	✗	–	✓	✓	✗	✓
Single Agent Efficacy In AML	MLL^{MUT}, NPM1^{MUT} RAS^{MUT}, TP53^{MUT} FLT3$^{ITD/TKD/WT}$ DNMT3A^{MUT} ✓	FLT3$^{ITD/TKD}$ ✓	FLT3^{ITD} Only –	SF3B1^{MUT} U2AF1^{MUT} FLT3^{ITD} ✓	MLL-r/ KMT2Ar ✓	NPM1^{MUT} ✓	With GILT. FLT3^{MUT} –
Potential Beyond AML	HR MDS MPNs ✓	✗	✗	HR MDS ✓	MLL-r ALL ✓	✗	✗

Gilteritinib package insert
Quizartininib 2019 ODAC filing, EMA filing
Emavusertib clinical hold, lifted; Curis Corporate presentation

Revumenib Syndax Corporate Presentation
Ziftomenib Kura Oncolocy Corporate Presentation
Lanraplenib Kronos Bio Corporate Presentation

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APTOSE Precision Oncology Company Developing Oral Kinase Inhibitors to Treat Life-threatening Hematologic Malignancies

Tuspetinib | *Safely* Treats AML Disease Heterogeneity | Orphan Drug Status | Fast Track Status

Disease heterogeneity is the greatest obstacle to the effective treatment of AML

Tuspetinib is a Safe and Effective, Once Daily, Oral Drug to Treat AML Disease Heterogeneity

– Best-in-Class TKI simultaneously targets clinically-validated oncogenic signaling kinases: SYK | JAK1/2 | $FLT3^{WT/MUT}$ | $cKIT^{MUT}$

- **Non-myelosuppressive, favorable safety profile**
- **Drug of choice for combination therapy**
- **Broad application across diverse AML populations**
- **Accelerated paths to market as monotherapy**
- **Single agent CRs across 4 dose levels with no DLT**
- **$1B market potential & broad IP coverage**

Expect near term value creation as monotherapy in deep R/R AML populations of high unmet need

Expect long term value creation as ideal TKI for doublet/triplet combination therapy in 1L/2L AML

Luxeptinib | Phase 1a/b CRs with AML & B-Cell Cancers | Dosing with New Oral G3 Formulation

Meaningful Near-term Value-driving Clinical Milestones in 2023 | Cash Runway into 2024

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THANK YOU