APTOSE Clinical Update and Data Review

Concurrent with 2022 ASH Annual Meeting

December 11, 2022

APTOSE BIOSCIENCES

PRECISION ONCOLOGY FOR THERAPIES OF TOMORROW

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

Data from 2022 ASH Annual Meeting

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Aptose Biosciences Investor Highlights (NASDAQ: APTO)
Dedicated to Targeted Precision Oncology

Developing a **Pipeline** of **Oral Kinase Inhibitors** to treat Life-threatening **Hematologic Malignancies**

Tuspetinib | **Lead Agent** | **Oral Treatment of Acute Myeloid Leukemia (AML)** | **Orphan Drug Status** | **Fast Track Status**

- Favorable safety and broad activity position tuspetinib as kinase inhibitor of choice for **1L TRIPLET COMBINATION**
- Potential to become drug of choice to achieve prolonged MRD-negative CRs for **MAINTENANCE THERAPY**
- Response rates may support accelerated approvals in **PATIENTS FAILED BY PRIOR FLT3 INHIBITORS**
- Phase 1/2 Trial 60 Patients Dosed | **Safety & Single agent CRs across diverse mutationally-defined populations**
  - Targets handful of driver kinases and oncogenic signaling pathways of AML | **SYK**, **JAK1/2**, **FLT3$^{WT/MUT}$**, **cKIT^{MUT}**
- Potential to become physician's preferred agent to address primary patient needs | **>$1B MARKET**
- **Enrolling APTIVATE Dose Expansion Trial** as Single Agent and Combination with Venetoclax in Enriched Patient Populations

Luxeptinib | **Phase 1a/b Responses with AML & B-Cell Cancers** | **Continuous Dosing Ongoing with New G3 Formulation**

Meaningful Near-term Upside | **Value-driving Clinical Milestones Through 2022 and 2023** | **Cash Runway into 2024**

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

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What We Believe are Greatest Needs of AML Patients……

Tuspetinib has Potential to Addresses Greatest Needs of AML Patients and to Achieve >$1B Annual Sales

*Note: MRD is measurable residual disease; MRD-Negative means that, using specific detection procedures, no residual disease is detected post-treatment

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What We Believe are Greatest Needs of AML Patients……

1

TRIPLET COMBINATION to Safely Place 1L Patients into MRD-Negative CR

- Need MRD-negative CR without prolonged myelosuppression or life-threatening toxicities
- Apply triplet to FLT3+, FLT3-WT, Unfit and Fit patients without other targeted therapies

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MAINTENANCE THERAPY to Keep Patients Long Term in MRD-Negative CR

- Administer following the achievement of a CR via drug therapy or HSCT to prevent relapse
- Safely apply to FLT3+ and FLT3-WT, and convert MRD-Positive into MRD-Negative

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3

SUPERIOR FLT3 INHIBITOR to Treat FLT3+ Patients who Failed Prior FLT3 Inhibitors

- FDA recognizes need for accelerated development of drugs to treat prior FLT3i failure

Tuspetinib has Potential to Addresses Greatest Needs of AML Patients and to Achieve >$1B Annual Sales

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Tuspetinib (HM43239 or “239”)

Oral, Daily, Kinase Inhibitor to Meet the Needs of AML Populations

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Tuspetinib Phase 1/2 Clinical Trial

Emerging Clinical PK & Safety Data
Potential Superior AML Therapy

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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)			Efficacy Evaluable
Cohort 6	200 mg QD	Completed				3
Cohort 5	160 mg QD	Completed	160 mg QD	Completed	CRc DLT	11
Cohort 4	120 mg QD	Completed	120 mg QD	Completed	CRc DLT	14
Cohort 3	80 mg QD	Completed	80 mg QD	Completed	CRc DLT	17
Cohort 2	40 mg QD	Completed	40 mg QD	Enrolling	CRc DLT	2
Cohort 1	20 mg QD	Completed				1

Favorable safety profile:

- No drug related SAE or death and no observed relation between exposure and delta-QTc throughout the trial
- 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

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Tuspetinib Phase 1/2 Trial (Parts A & B)
Patients Dosed and Evaluable by Safety and Efficacy Criteria

Dose Level	Total Dosed		Evaluable for Safety		Evaluable for Efficacy	
200mg	4		3		3	
160mg	14		12		11	
120mg	17	51	15	45	14	42
80mg	20		18		17	
40mg	3		1		2	
20mg	2		1		1	
TOTAL NUMBER PATIENTS	60		50		48	

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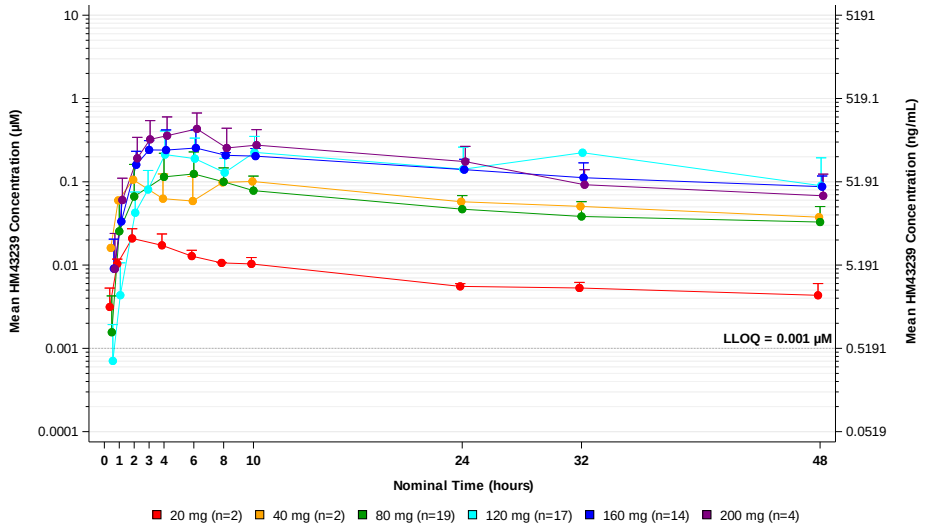
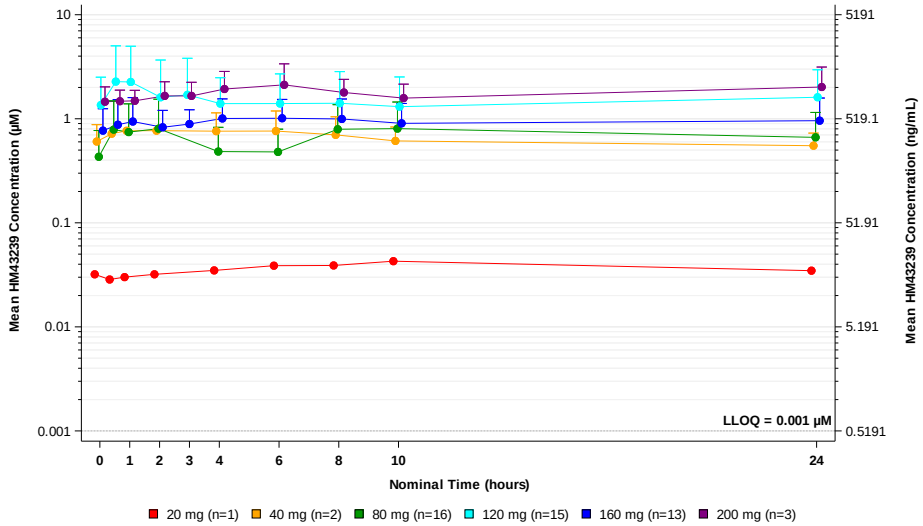
Tuspetinib Phase 1/2 Study in R/R AML: Pharmacokinetic Properties Following a Single Dose or at Steady State

Mean Plasma PK Concentrations (+SD) by Dose Cohort (Semi-log Scale) Single Dose



Mean Plasma PK Concentrations (+SD) by Dose Cohort (Semi-log Scale) Multiple Doses / Steady State



Plasma PK Findings:

- Approximately 17-28 days to approach steady state
- Generally, dose-related increase in plasma exposures after first dose and at steady state

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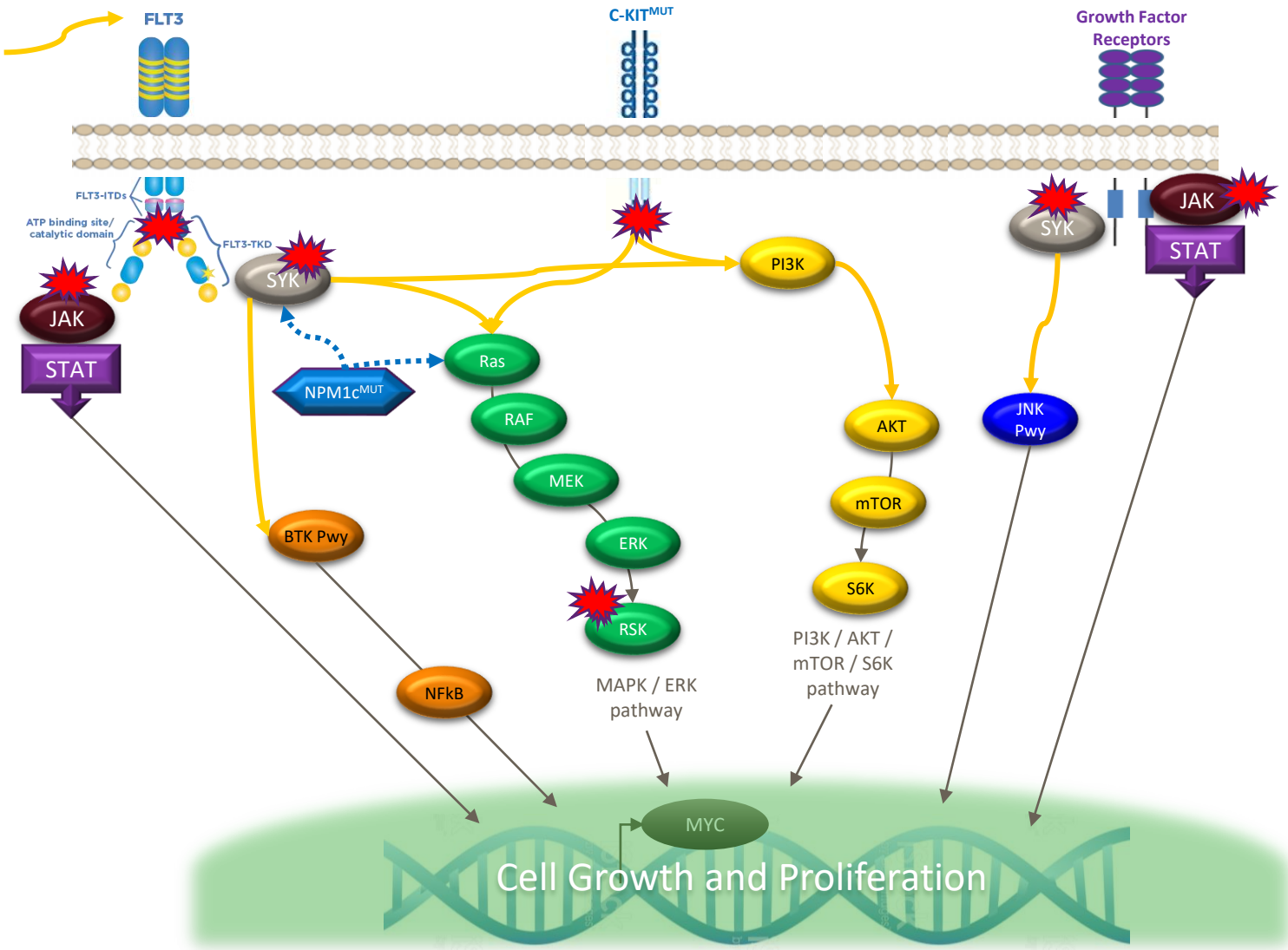
Tuspetinib Suppresses Oncogenic Myeloid Kinases / Signaling Pathways Reason for Activity on FLT3+ and FLT3-WT AML

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**: -ITD, -TKD, -GK mutations and FLT3-WT
- **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 molecule**

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

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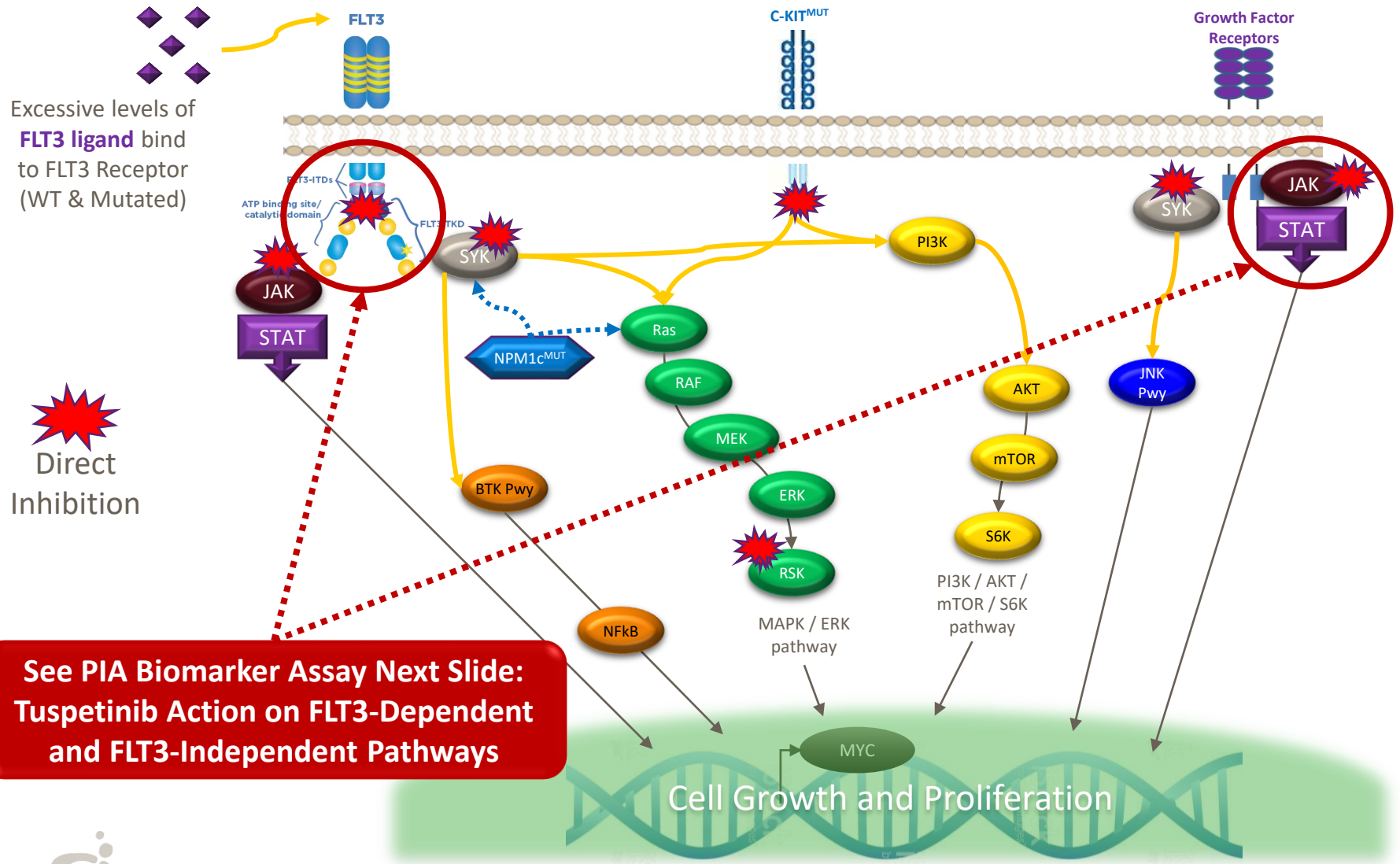
Tuspetinib Suppresses Oncogenic Myeloid Kinases / Signaling Pathways Reason for Activity on FLT3+ and FLT3-WT AML



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

Potent suppression of multiple kinases operative in AML

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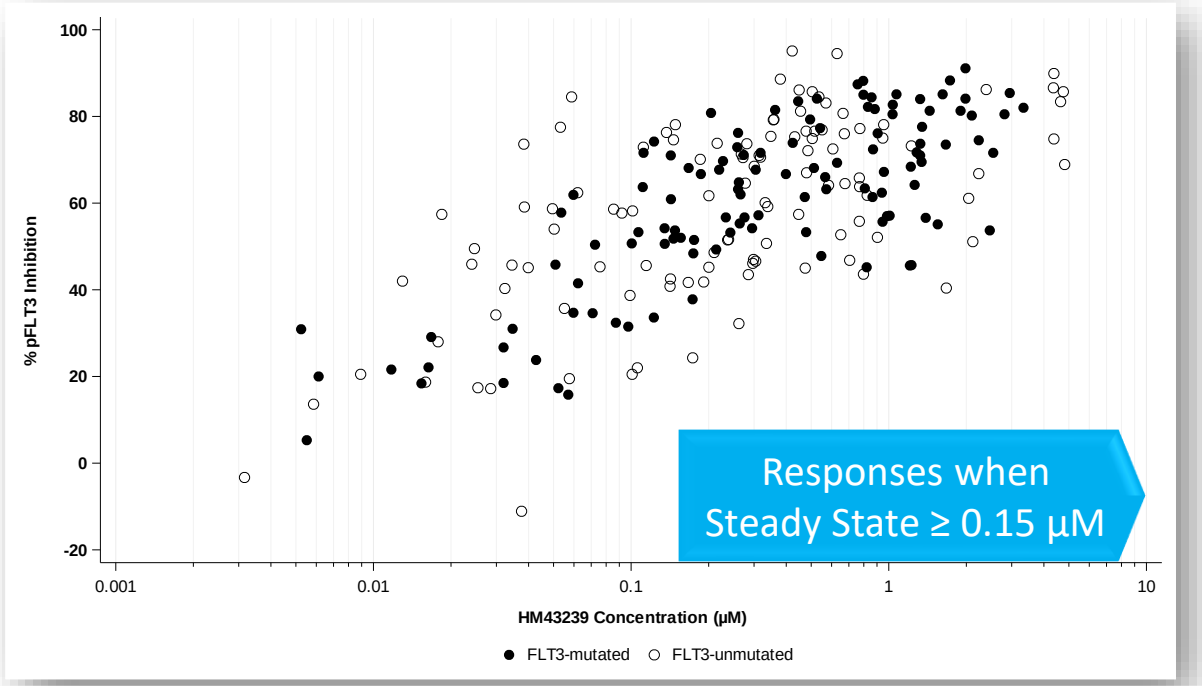
Tuspetinib Inhibition of Phospho-STAT5 and Phosho-FLT3 by Patient Plasma with a PIA Reporter Assay (Inhibition vs. Plasma Concentration)

Inhibition 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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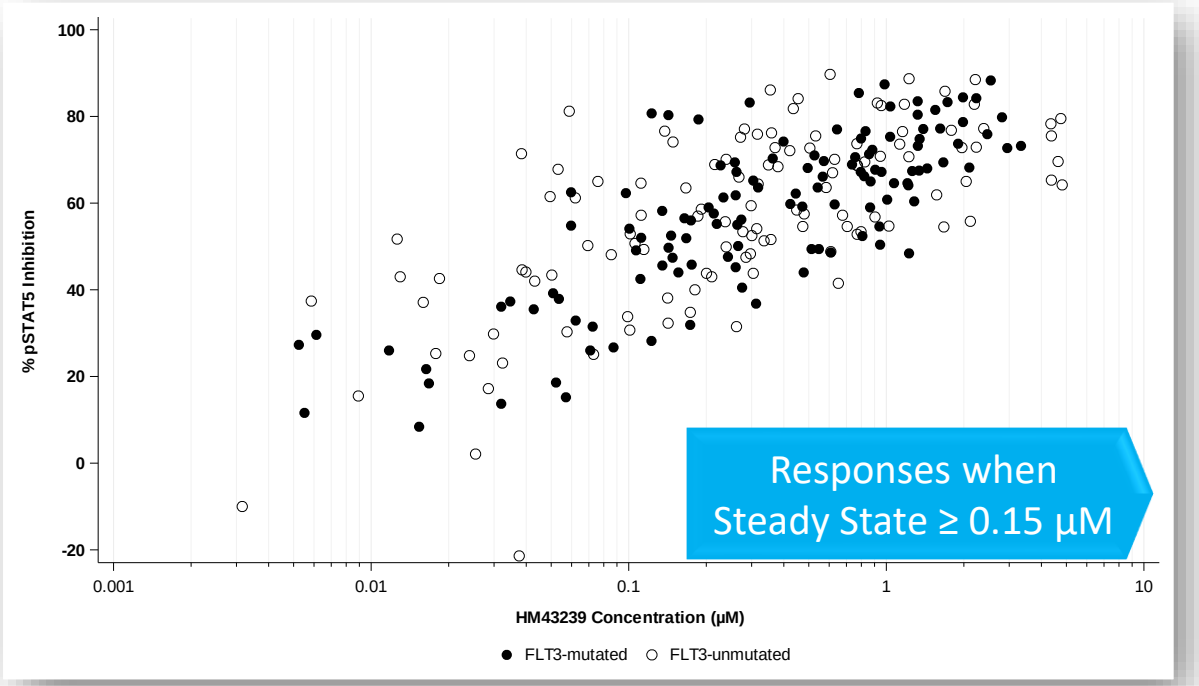
Inhibition of P-STAT5 in MOLM-14 AML Cells By Patient Plasma in PIA Assay



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

- 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%).
- The median age is 61 years of age (range 18-84).
- Patients heavily pre-treated, with 100% having received prior chemotherapy, 28.3% prior HSCT, and 23.3% prior FLT3 inhibitor.
- Approximately 40% of study patients treated have a FLT3 mutation.

Patient Disease Characteristics	
FLT3 Mutation Status	**N (%)**
FLT3+	26 (43.3%)
FLT3-	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 Phase 1/2 Study in R/R AML: Patient Safety Data

Tuspetinib Well Tolerated with No DLTs Through 160 mg QD

- Only 28.3% of patients reported related events
- The most frequent related TEAEs are diarrhea (11.7%) and nausea (8.3%) across all dose levels
- No drug-related SAEs, deaths, discontinuations, differentiation syndrome, or QT prolongation reported

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 Safety and Efficacy Data
Broad Therapeutic Window as a Single Agent in R/R AML Patients

- **Safety Profile Favorable to Date**
  - No drug related SAE, drug related deaths, differentiation syndrome, or drug related discontinuations
  - No drug related AE of QT prolongation – No observed relation between ΔQTc and dose
  - No DLT through 160 mg level – One DLT of muscle weakness at 200 mg (not rhabdomyolysis)
  - No observed muscle destruction – No AE of elevated creatine phosphokinase (CPK)
  - Avoids many of the typical toxicities observed with other tyrosine kinase inhibitors

- **Identified a 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, and Other Targeted Agents**
  - Most FLT3+ patients had failed midostaurin, gilteritinib, both mido & gilt, chemo, Ven, Aza, others

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Tuspetinib Delivers Blast Reductions in FLT3+ and FLT3-WT r/r AML Patients

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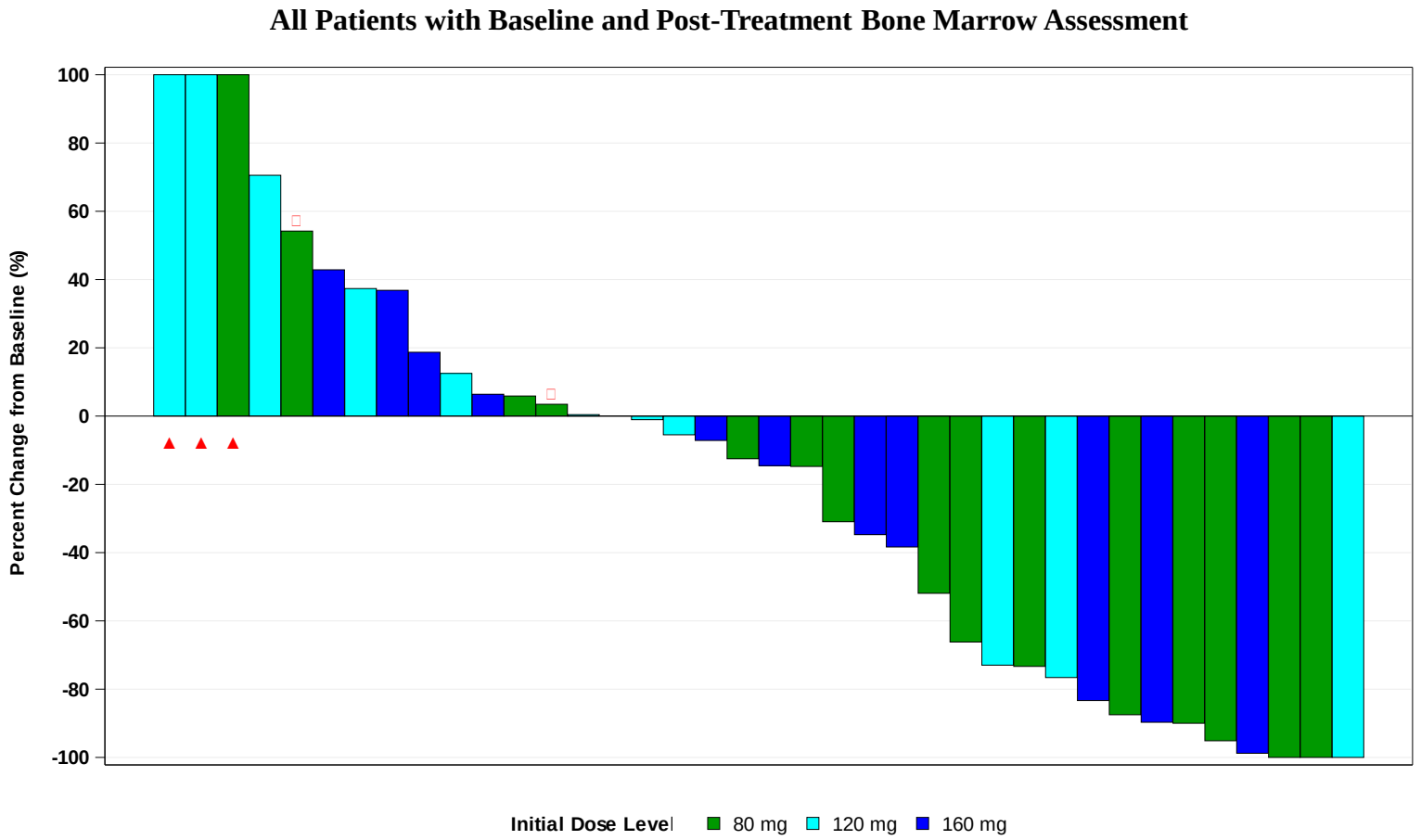
Tuspetinib: Waterfall Plot of Bone Marrow Blast - Percent Change from Baseline For Patients Assigned to 80 mg, 120 mg and 160 mg Dose Levels – Parts A and B



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

- **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
- **CRi are 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 are able to proceed with transplant**

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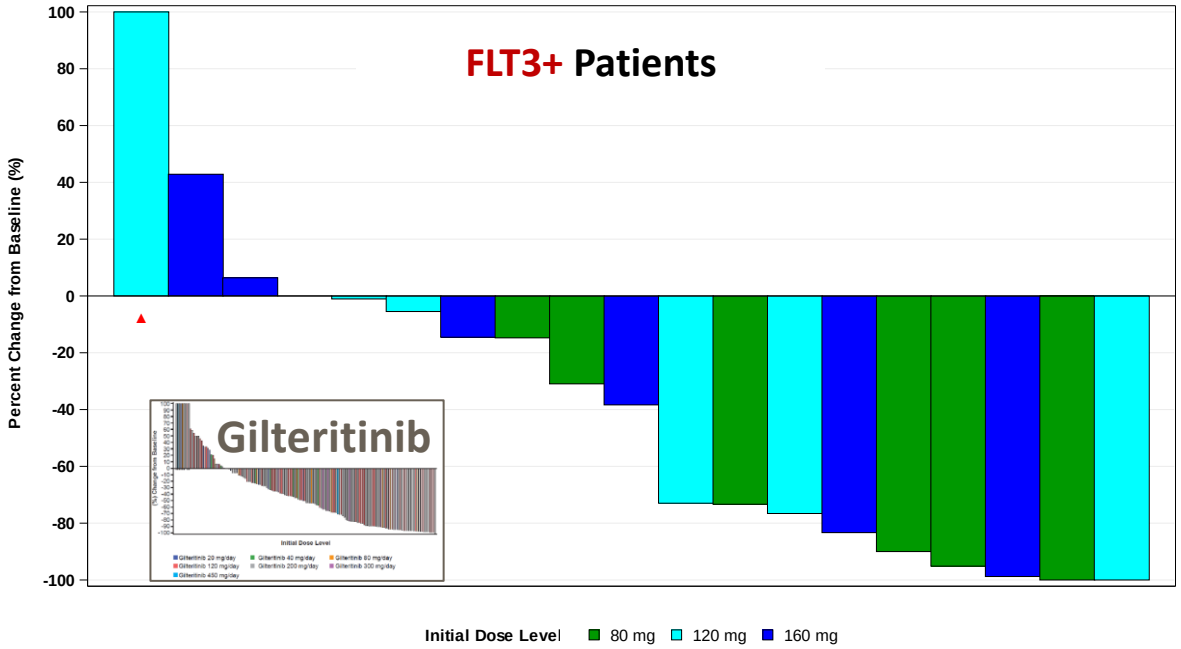

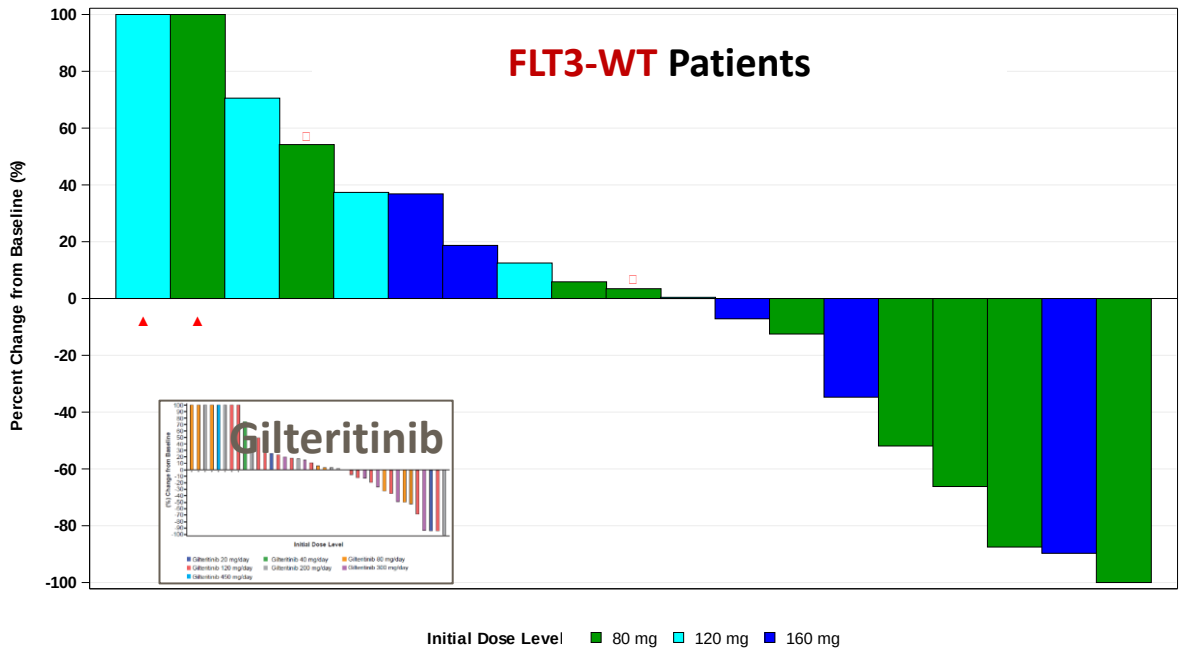

- **Tuspetinib effectively kills leukemic blasts in FLT3+ and FLT3-WT patients**
- **Tuspetinib data are as impressive as gilteritinib (shown in insert graphs), but patients treated with tuspetinib are more heavily pretreated (failed prior gilt, mido, VEN, other) r/r AML patients**

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.
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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: Waterfall Plot of Bone Marrow Blast - Absolute Change from Baseline For Patients Assigned to 80 mg, 120 mg and 160 mg Dose Levels – Parts A and B

Note: Blast change was calculated as the lowest post-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.
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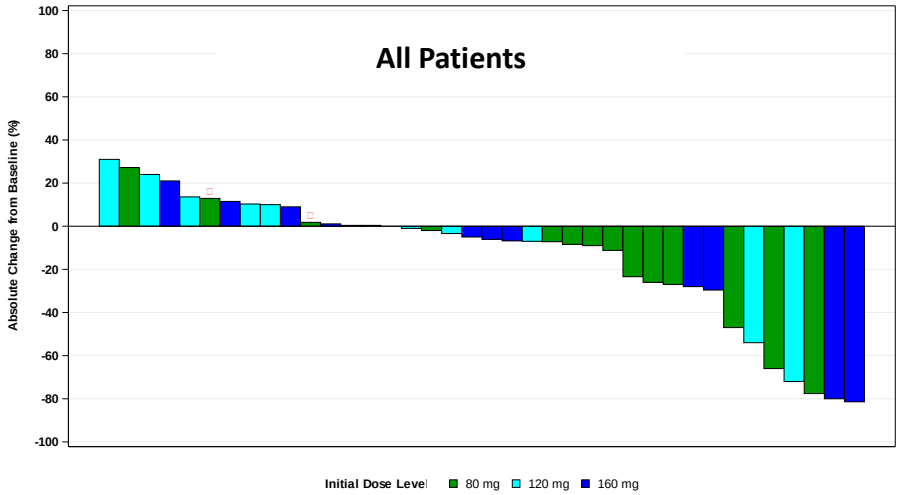

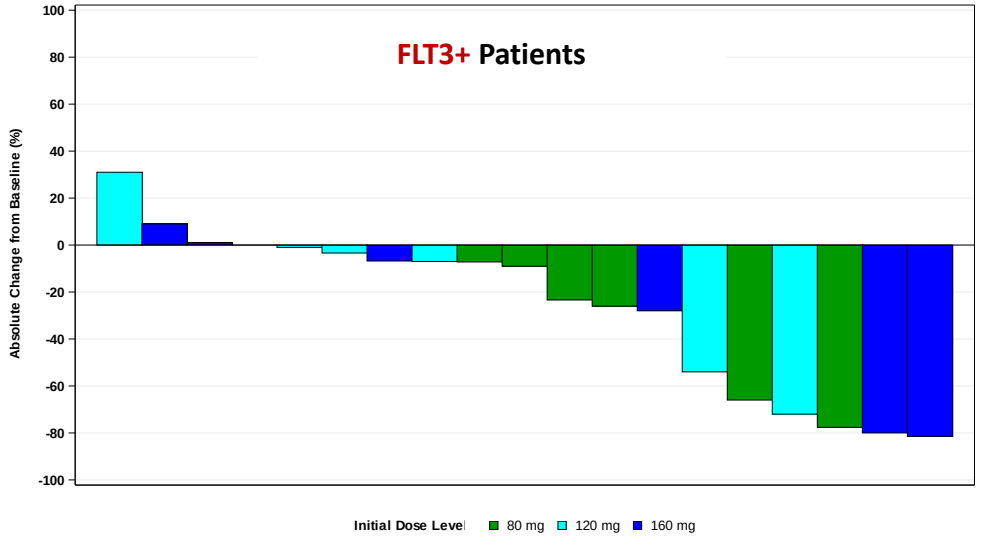

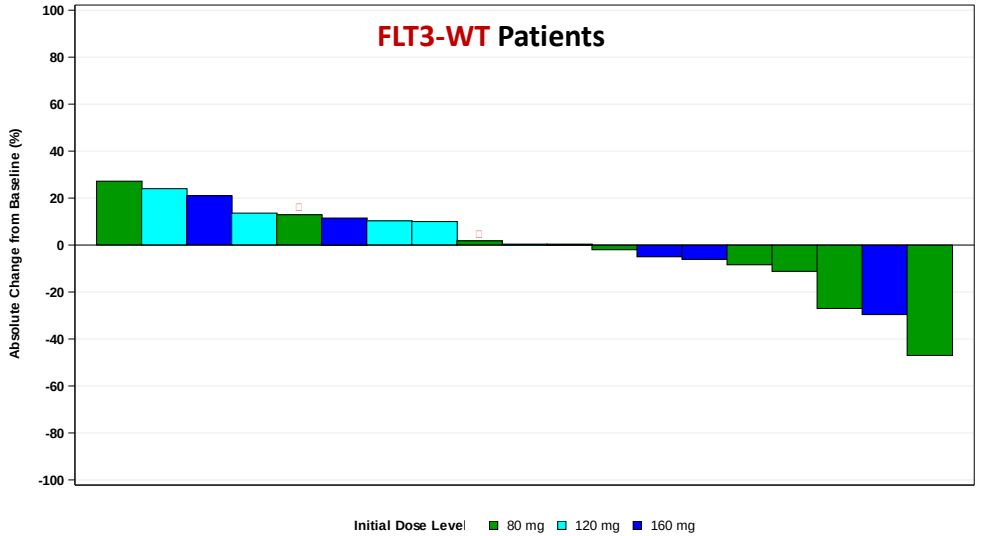

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Tuspetinib Emerging Clinical Response Data

Potential Superior AML Therapy

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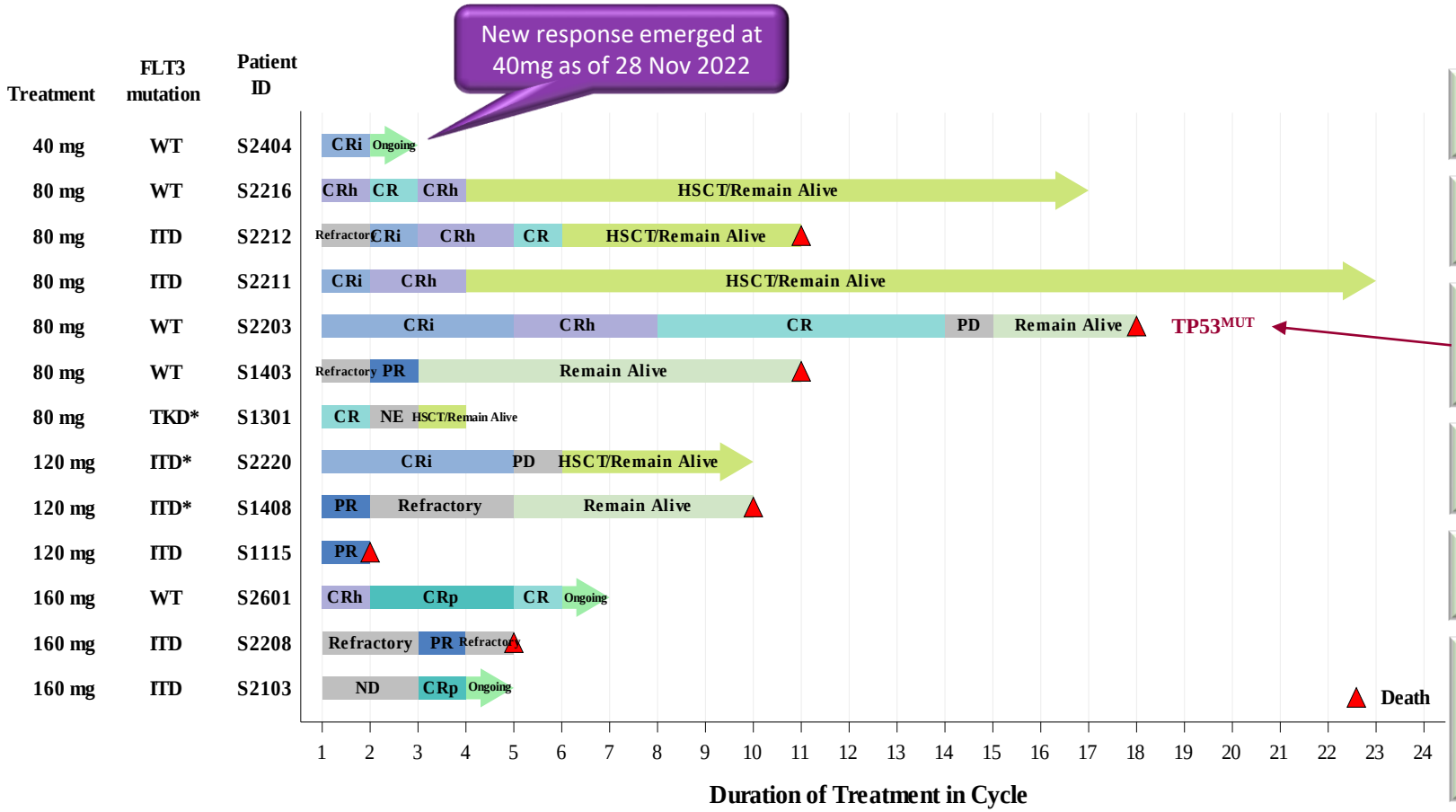
Tuspetinib Swimmer Plot of R/R AML Patients Who Achieved Clinical Responses Reported to Date in Phase 1/2 Study



RESPONDERS

- Responses achieved across four dose levels
- Most bridged to potentially life-saving transplant
- $TP53^{MUT}$ demonstrates breadth, durability & continuous dosing without myelosuppression
- Durability observed when -/+ HSCT unavailable
- $FLT3^{WT}$ and $FLT3^{MUT}$, including ITD & TKD mutations
- **3 Responses Among 11 FLT3+/Prior FLT3i failures**
  - 42 patients efficacy evaluable at 80mg/120mg/160mg
  - 21 of those patients harbored FLT3 mutations (FLT3+)
  - 11 of those FLT3+ patients had failed prior FLT3i

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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Data from 2022 ASH Annual Meeting

Tuspetinib Diversity of Adverse Mutations in R/R AML Patients Who Achieved a Clinical Response Reported to Date in Phase 1/2 Study

Patient ID	Important Mutations	FLT3 Status	Dose Level	Best Response	Bridged to HSCT
2216	IDH2 SRSF2	WT	80mg	CR	Yes
2203	TP53	WT	80mg	CR	No
2212	NPM1 DNMT3A	ITD	80mg	CR	Yes
2211	NRAS RUNX1	ITD	80mg	CRh	Yes
1301	RUNX1 SF3B1 RB1	TKD – Prior FLT3i	80mg	CR	Yes
1408	KRAS NPM1 DNMT3A PTPN11	ITD – Prior FLT3i	120mg	PR	No
Below Are New Responses Observed Since Aptose Assumed Responsibility for Clinical Trial 01 January 2022					
2220	MLL-PTD RUNX1	ITD – Prior FLT3i	120mg	CRi	Yes
1115	Not Reported	ITD	120mg	PR	No
2601	NRAS BCOR U2AF1 SETBP1	WT	160mg	CR	Tx Ongoing
2103	NPM1	ITD	160mg	CRp	Tx Ongoing
2208	NPM1 IDH1 DNMT3A	ITD	160mg	PR	No
1403	ASXL1 CBL	WT	80mg	PR	No
1118	Not Reported	ITD	160mg	SD	Tx Ongoing
2404	Not Reported	WT	40mg	CRi	Tx Ongoing

New response emerged at 40mg as of 28 Nov 2022

Most Responders Bridged to Potentially Life-Saving Transplant

Responses Across Spectrum of Genetically-defined Populations With Highly Adverse Mutations

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

$NPM1^{MUT}$ Responders Potential for Accelerated Approval

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

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

Data from 2022 ASH Annual Meeting

Tuspetinib Response Rates to Highlight for ASH

Efficacy Evaluable R/R AML Patients From Active/Safe Doses (40, 80, 120, 160mg)

Tuspetinib Best Response in Each r/r AML Population		
Population	**Dose Level(s)**	**Overall Response Rate[1]**
FLT3+	80mg	42.9% (3/7)
FLT3+	120mg	42.9% (3/7)
FLT3+	Across 80mg, 120mg, 160mg	38.1% (8/21)
FLT3+ | NPM1+	Across 80mg, 120mg, 160mg	66.7% (4/6)
FLT3+ | NPM1+ | DNMT3A+	Across 80mg, 120mg, 160mg	75% (3/4)
FLT3+ | Prior FLT3i	80mg	33.3% (1/3)
FLT3+ | Prior FLT3i	120mg	40% (2/5)
N/K-RAS+ (FLT3+/-)	Across 80mg, 120mg, 160mg	37.5% (3/8)
FLT3-WT	Across 80mg, 120mg, 160mg	19.0% (4/21)
Population	**Dose Level(s)**	**CRc Response Rate[2]**
FLT3+	Across 80mg, 120mg, 160mg	23.8% (5/21)
FLT3+ | NPM1+	160mg	50.0% (1/2)
FLT3+ | NPM1+	Across 80mg, 120mg, 160mg	33.3% (2/6)
FLT3-WT | TP53+	Across 80mg, 120mg, 160mg	33.3% (1/3)
Population	**Dose Level(s)**	**CR/CRh Response Rate**
FLT3+	80mg	42.9% (3/7)
NRAS+	Across 80mg, 120mg, 160mg	33.3% (2/6)

Plus 40mg CRi FLT3-WT reported 28 Nov 2022

Data as of the 06 Oct 2022 data cut. Numbers will change as additional data arrive.

[1]Overall Response Rate (ORR) = CR + CRh + CRi + CRp + PR
[2]CRc Response Rate = CR + CRh +CRi + CRp

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Tuspetinib Response Rates Among Efficacy Evaluable Patient in Mutation-Enriched Subgroups in the 40mg, 80mg, 120mg and 160mg Cohorts

Mutation-Enriched Group	ORR	CRc RR	CR/CRh RR
Overall (All Patients)	12/42 (28.6%)	8/42 (19.0%)	6/42 (14.3%)
FLT3+	8/21 (38.1%)	5/21 (23.8%)	3/21 (14.3%)
FLT3+ / PriorFLT3i	3/11 (27.3%)	2/11 (18.2%)	1/11 (9.1%)
FLT3+ / NPM1+	4/6 (66.7%)	2/6 (33.3%)	1/6 (16.7%)
FLT3-WT	4/21 (19.0%)	3/21 (14.3%)	3/21 (14.3%)
FLT3-WT / TP53+ / CK	1/3 (33.3%)	1/3 (33.3%)	1/3 (33.3%)

Plus 40mg CRi FLT3-WT as of 28 Nov 2022

Plus 40mg CRi FLT3-WT as of 28 Nov 2022

- Interim analysis for approval from the Gilteritinib ADMIRAL trial
  - CR rate = 11.6% (16/138)
  - CR/CRh rate = 21%
- Our patients are more heavily pretreated and failed prior FLT3i
- Expect a response rate of half that in the Gilteritinib ADMIRAL trial would be approvable in this more treatment advanced population
- Petition for CRi+HSCT to count toward approval of tuspetinib, as was done with Gilteritinib ADMIRAL trial
- Tuspetinib achieved 18.2% CR rate (2/11) if given credit for a CRi taken to HSCT before the patient had the opportunity to mature to a full CR

Abbreviations: CK, complex karyotype; CR, complete remission; CRc, composite complete remission; CRh, complete remission with partial hematological recovery; CRi, complete remission with incomplete hematologic recovery; CRp, complete remission with incomplete platelet recovery; FAS, full analysis set; FLT3i, FLT3 inhibitor; ORR, overall response rate; RR, response rate.
Note: the denominator includes patients with applicable mutation status reported in the analysis population of interest.
[1] The FAS include all patients who took at least one dose of study medication and who have at least one post-treatment data point.
[2] Efficacy evaluable patients includes those who received at least 2 cycles of treatment or discontinued due to progressive disease, unless a response has already been achieved.
[3] Overall response includes patients who reported CR, CRp, CRh, CRi or PR.
[4] CRc includes patients who reported CR, CRp, CRh, or CRi.

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

Data from 2022 ASH Annual Meeting

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

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Tuspetinib Case Study
CR in FLT3-ITD / Prior-FLT3i Failure (Midostaurin) 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 following Cycle 6

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Tuspetinib Case Study
CR in FLT3-TKD / Prior FLT3i Failure (Midostaurin & Gilteritinib) 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 following Cycle 3

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Tuspetinib Going Forward

Data from 2022 ASH Annual Meeting

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Tuspetinib Global Dose Expansion Trial Planned to Support Phase 2 Registrational Trials for Accelerated Approval and Drug Combination Trials for Broad Commercialization

Escalation (A)/Exploration (B) Trial
Tuspetinib Single Agent Ongoing

- **Dose Escalation**
  - 20mg to 200mg
- **Dose Exploration**
  - 40, 80, 120, 160mg
  - Up to 20 pts/dose

CRc & Safe
160mg
120mg
80mg
40mg

- **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 239 with venetoclax and segue into Phase 2-3 randomized sstudies and demonstrate 239 can be the preferred agent for combination therapy

Data from 2022 ASH Annual Meeting

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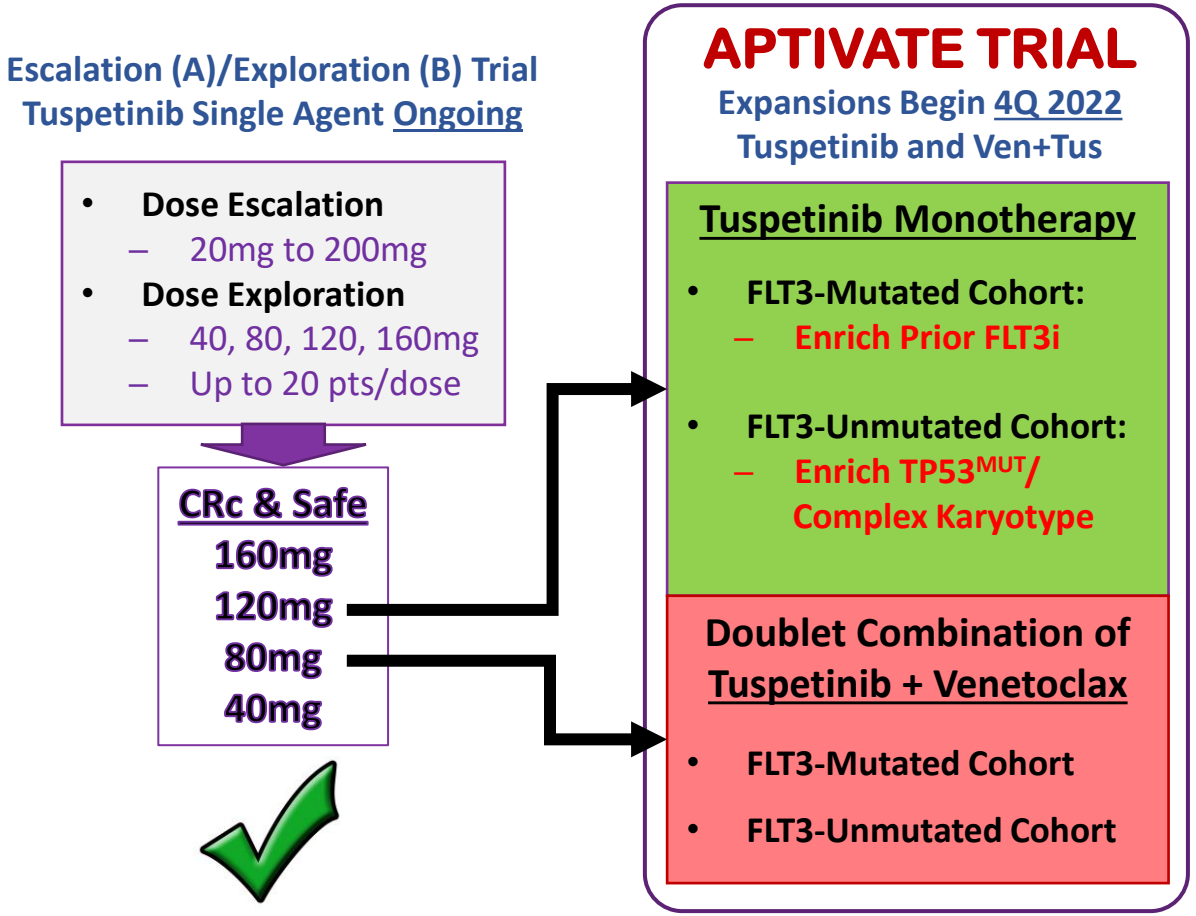
Tuspetinib Global Dose Expansion Trial Planned to Support Phase 2 Registrational Trials for Accelerated Approval and Drug Combination Trials for Broad Commercialization



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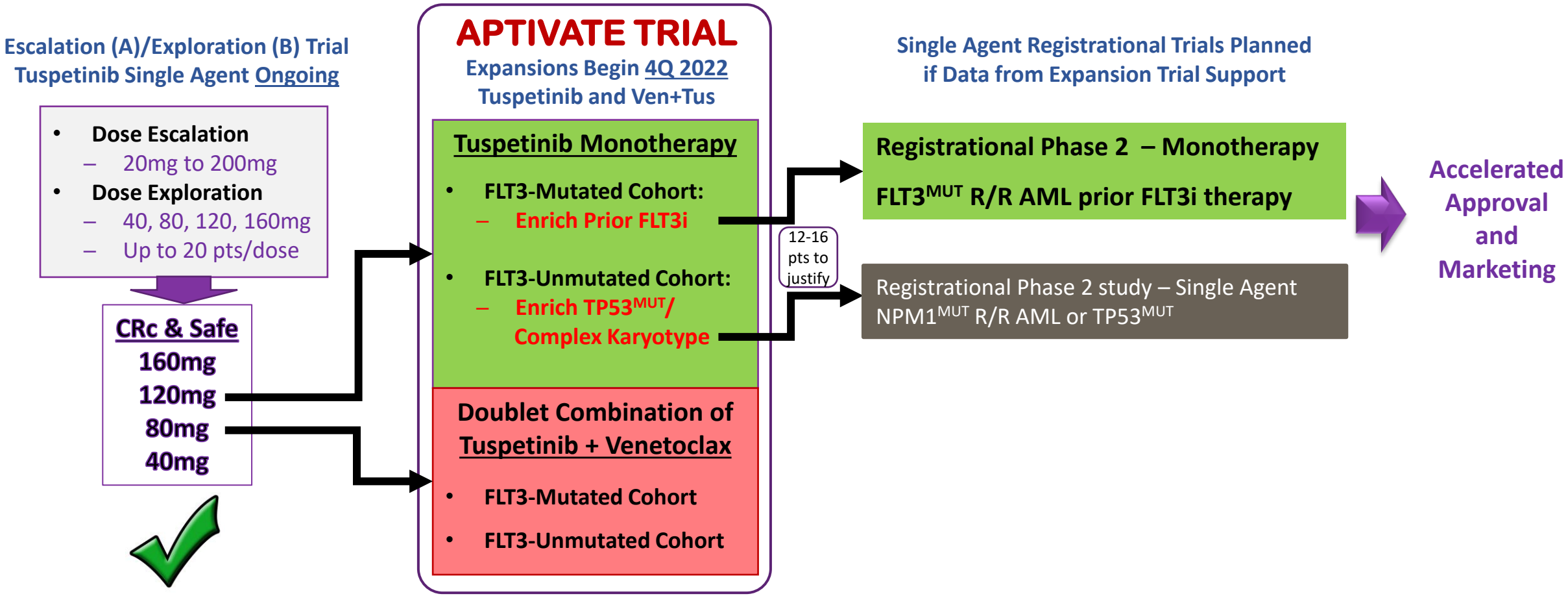

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Escalation (A)/Exploration (B) Trial Tuspetinib Single Agent Ongoing

- **Dose Escalation**
  - 20mg to 200mg
- **Dose Exploration**
  - 40, 80, 120, 160mg
  - Up to 20 pts/dose

CRc & Safe
160mg
120mg
80mg
40mg

APTIVATE TRIAL

Expansions Begin 4Q 2022
Tuspetinib and Ven+Tus

Tuspetinib Monotherapy

- **FLT3-Mutated Cohort:**
  - Enrich Prior FLT3i
- **FLT3-Unmutated Cohort:**
  - Enrich $TP53^{MUT}$/ Complex Karyotype

Doublet Combination of Tuspetinib + Venetoclax

- **FLT3-Mutated Cohort**
- **FLT3-Unmutated Cohort**

Single Agent Registrational Trials Planned if Data from Expansion Trial Support

Registrational Phase 2 – Monotherapy

$FLT3^{MUT}$ R/R AML prior FLT3i therapy

12-16 pts to justify

Registrational Phase 2 study – Single Agent
$NPM1^{MUT}$ R/R AML or $TP53^{MUT}$

Accelerated Approval and Marketing

Drug Combination Trials to Support Usage of 239 with Other Agents in AML Populations

Triplet Combo Phase 2-3 Randomized Study
1L unfit AML: HMA/VEN vs. Tus/HMA/VEN + maint
1L fit AML, FLT3-WT: Chemo vs. Tus/Chemo + maint

Doublet Combo Phase 2 Randomized Study
R/R AML in 2L, FLT3 mutant – Tus vs. Tus/VEN vs. GILT

- **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)
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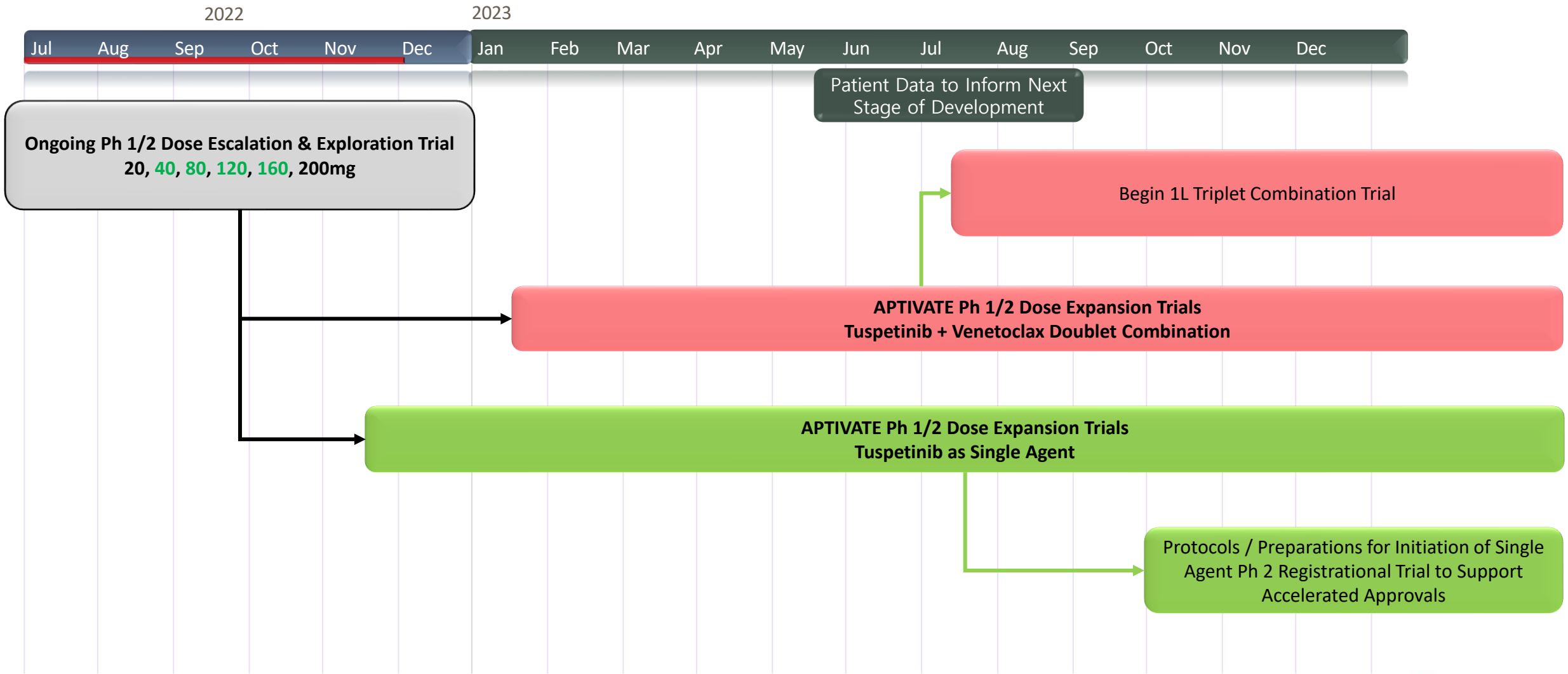
Tuspetinib Planned Clinical Development Timeline, Clinical Data Release and Potential Value Driving Milestones



Data from 2022 ASH Annual Meeting

Tuspetinib Daily Oral Treatment for AML : Highlights of ASH 2022

- **Orphan Drug & Fast Track Designation**
- **ASH 2021: 5 CRc and 1 PR reported**
- **ASH 2022: 4 CRc and 3 PR emerged thus far**
- **Highly Favorable Safety and Broad Therapeutic Window**
  - None of typical toxicities observed with other TKIs
  - Spanning the 40, 80, 120 and 160 mg dose levels
- **Significant Bone Marrow Leukemic Blast Reductions in FLT3+ and FLT3-WT Patients Across Dose Levels**
- **Key Response in Mutationally-defined Populations**

FLT3-WT	4 of 21 (19%) + new CRi
FLT3+	8 of 21 (38.1%)
FLT3+/NPM1+	4 of 6 (66.7%)
FLT3+ with prior FLT3i	3 of 11 (27.3%)
N/K-RAS+	3 of 8 (37.5%)

- **CRs Among Patients with Diverse Adverse Mutations**
  - RAS, NPM1, MLL, TP53, FLT3, DNMT3A, RUNX1, IDH
  - FLT3+ Patients failed by prior FLT3i
- **APTIVATE Expansion Trial is Active and Enrolling**
  - Monotherapy to support **SINGLE ARM PHASE 2 ACCELERATED APPROVAL**
  - Combine with venetoclax to position for doublets and triplets in earlier line patients
- **Commercial Potential >$1B**
  - **TKI of CHOICE for TRIPLET COMBINATION** to Place 1L Patients Unfit/Fit/FLT3+/FLT3-WT in MRD-Negative CR
  - **TKI of CHOICE for MAINTAINENANCE THERAPY** to Keep Patients Long Term in MRD-Negative CR
  - **SUPERIOR FLT3 INHIBITOR** to Treat FLT3+ Patients who Failed Prior FLT3 Inhibitors

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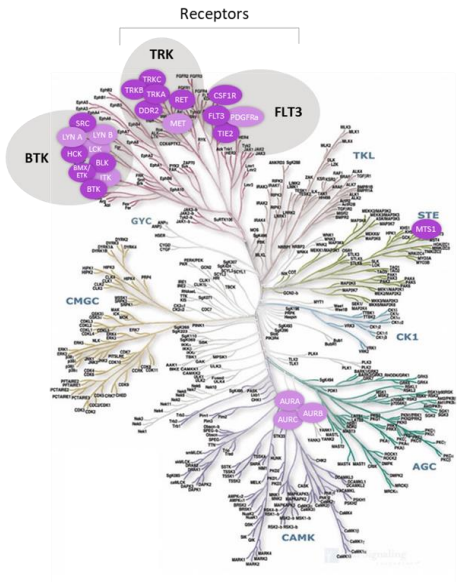
Luxeptinib

Oral Lymphoid & Myeloid Kinase Inhibitor

Luxeptinib
Proven Clinical Activity but Needs Greater Exposures

Luxeptinib Selectively & Potently Inhibits Myeloid & Lymphoid Kinases

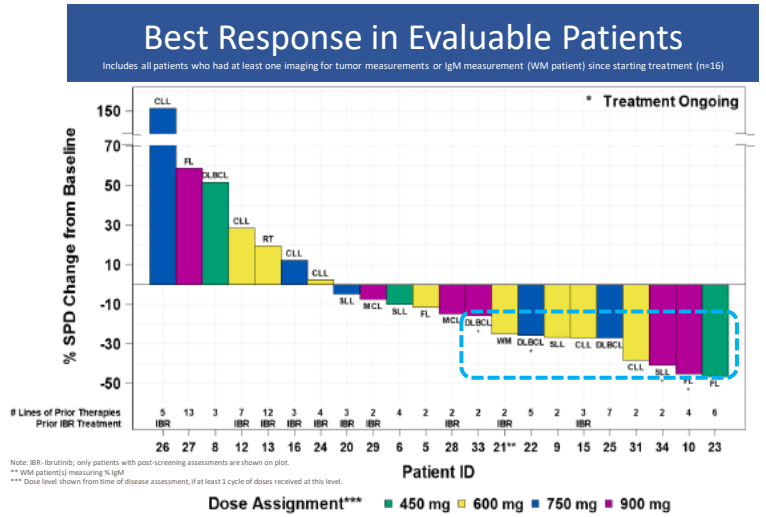


Phase 1a/b
R/R B-cell leukemias/lymphomas

36 Patients dosed

Antitumor Activity in Diverse B-cell Cancers

- Multiple patients experienced meaningful tumor shrinkage
- Complete metabolic responses and extended time on Tx



Phase 1a/b
R/R AML and MDS

29 Patients dosed

MRD-negative CR in FLT3+ AML Patient

- Observed MRD- CR at 450mg BID dose level
- Heavily pretreated AML patient, failed by prior treatments with chemotherapy / FLT3i / 2 HSCT
- Atypically high plasma exposure levels
- Demonstrates active against R/R AML

Data from 2022 ASH Annual Meeting

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Luxeptinib
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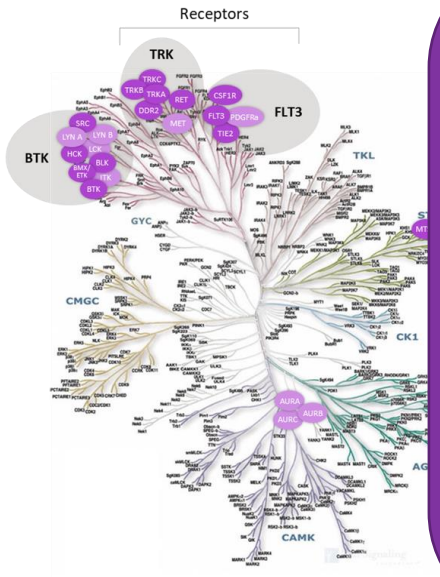

Phase 1a/b
R/R B-cell leukemias/lymphomas

- Preliminary report of a **DLBCL** patient who achieved a **Complete Response (CR)** as determined via biopsy and imaging at the end of Cycle 22 with 900mg BID dosing of the original G1 formulation.
- This patient achieved a Complete Metabolic Response (CMR) at Cycle 11.
- **Demonstrates Lux is also active on lymphoid malignancies.**

R/R AML and MDS

29 Patients dosed

Antitumor Activity in Diverse B-cell Cancers

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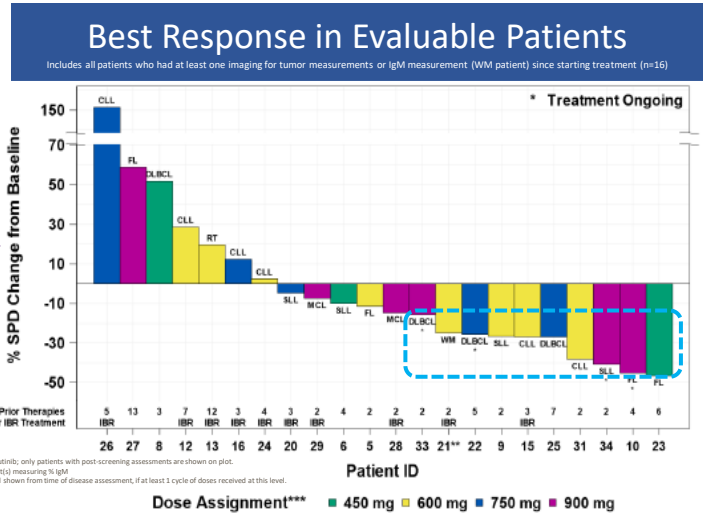

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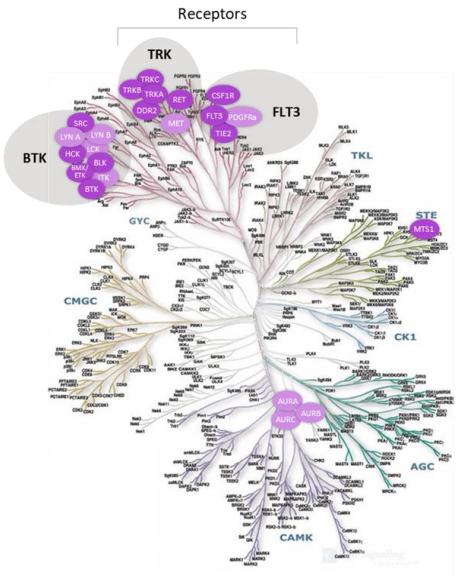

Phase 1a/b
R/R B-cell leukemias/lymphomas

36 Patients dosed

- **To date 65 R/R patients dosed**
- **Limited absorption of original G1 formulation hampered Lux's overall clinical effectiveness**

Phase 1a/b
R/R AML and MDS

29 Patients dosed

Antitumor Activity in Diverse B-cell Cancers

- Multiple patients experienced meaningful tumor shrinkage
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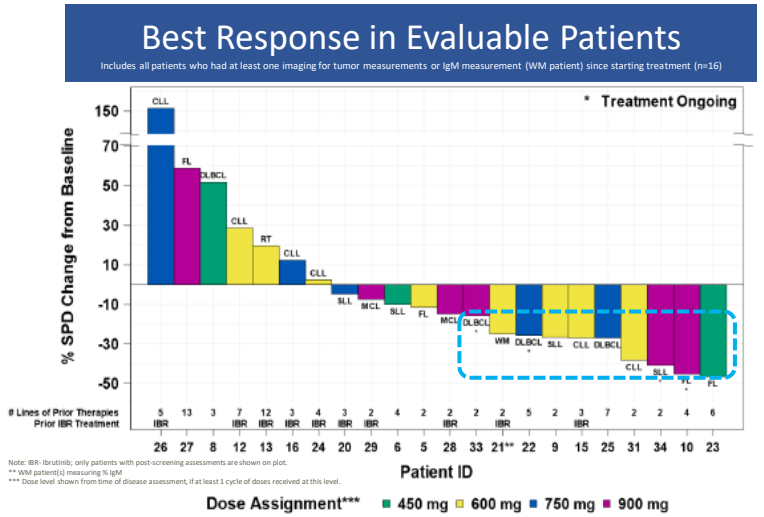

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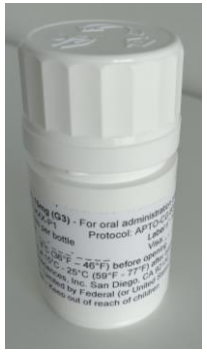

Luxeptinib Moving Forward with Generation 3 (G3) Formulation

Single Dose PK in 20 Patients During Q1 2022 → Continuous Dosing in Patients During Q4 2022

- **G3 Self Emulsifying Formulation Developed Over 2 Years**
  - Designed for more rapid absorption (early Tmax), more efficient absorption (use lower doses), longer retention (longer $t_{1/2}$), greater accumulation (higher steady state levels)
  - Demonstrated up to 30-fold increase in absorption in rodents and dogs
- **Demonstrated up to 30-fold Increase in Absorption in Rodents and Dogs**
- **Tested Single Dose of G3 at Five Dose Levels for PK Profile in 20 AML & B-cell Cancer Patients**
- **PK Modeling Predicted an Approx. 18-fold Improvement in Bioavailability and Earlier Tmax**
  - Modeling **predicts steady state** with **50mg G3 Q12h is equivalent to 900mg G1 Q12h (18-fold)**
- **Commenced Continuous Dosing with G3 → 3x3 Dose Escalation Study (expect 6-9 months to assess)**
  - Expect 9-15 patients will determine if G3 is safe and achieves desired exposures to deliver clinical responses
  - Potential to develop for AML, B-cell cancers, inflammation, autoimmunity, allergy, immuno-oncology
- **Luxeptinib Active Against AML & B-Cell Cancers → Expect G3 to Deliver Higher Exposures and Responses**

Data from 2022 ASH Annual Meeting

Naval G. Daver, M.D.
Associate Professor in the Department of Leukemia at the University of Texas MD Anderson Cancer Center

Global Lead Investigator for Tuspetinib Phase 1/2 Trial

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Q&A SESSION

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THANK YOU