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Aptose Biosciences is a precision oncology company developing oral targeted agents to treat hematologic malignancies

Acute myeloid leukemia, AML Myelodysplastic syndromes, MDS

(Nasdaq: APTO; TSX: APS)

Aptose Investment Highlights

Tuspetinib (TUS) lead agent: Once daily, oral, kinase inhibitor designed to selectively suppress a handful of kinases that drive key oncogenic signaling pathways operative in AML

Mechanistic Precision

SYK FLT3WT/MUT KITMUT JAK1/2 RSK1/2



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(Nasdaq: APTO; TSX: APS)



Tuspetinib (TUS) lead agent: Ideal drug for combination therapies in AML

- AML treatment strategies quickly shifting to combination therapies
- Combination therapies deliver greatest commercial and medical impact
 - Represent 98% of tuspetinib commercial forecasts
 - Projected faster accruals and earlier regulatory approvals
 - Can deliver higher response rates and more durable responses
- TUS/VEN/HMA ideal combination therapy planned for 1L AML
- TUS/VEN clinical responses in R/R AML with Prior-VEN failure
 - Presents accelerated approval path for TUS/VEN in R/R AML
- Annual commercial forecast > \$2.5 Bn for AML and HR-MDS

Up to \$25M Keystone and \$7M Hanmi capital investments

Value-driving clinical milestones during 4Q 2023



Review Clinical Path and Findings that Support Tuspetinib Combination Strategy

EOP1 Meeting with FDA

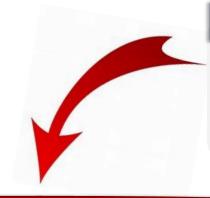


- RP2D = 80mg once daily
- All approval paths remain available



Dose Escalation Ph 1/2 Trial in R/R AML

- Demonstrated single agent efficacy
- Established "contribution of component" that TUS brings to combination therapy
- Favorable safety and tolerability



APTIVATE Expansion Trial in R/R AML

- TUS or TUS/VEN doublet
- TUS/VEN safe and highly active → including Prior-VEN failure subgroup that is difficult-to-treat

Finding Differentiates TUS/VEN Doublet from Other Therapies

- TUS/VEN impressive Response Rate in Prior-VEN AML
- High unmet need | Dismal response to salvage therapy
- 90%+ R/R AML patients entering our APTIVATE trial
- Enables a clear Accelerated Approval path



Why is Prior-VEN Failure R/R AML Such a High Unmet Medical Need?

Vast majority of VEN-failure patients (2L & 3L+) have no approved or effective experimental options

Prior-VEN Failure R/R AML Patients

Most AML Patients in US will receive Venetoclax and many ultimately fail Results in high-risk biology and broadly resistant mutation patterns

Fraction of Patients Receive Salvage Therapy Monotherapies or off label/experimental combinations¹

Many Transition to Supportive Care or Hospice Too unfit for salvage therapy or no available options¹

Salvage Therapy | Dismal response rates and brief OS

- Retrospective Report¹: **Prior-VEN as frontline** responded to **salvage** therapy with a **4% CR rate**
- Retrospective Report²: **Prior-VEN as frontline** responded to **targeted** therapy with a **15% CR rate** (FLT3i or IDHi)
- Retrospective Report³: **Prior-VEN as salvage** responded to **targeted** therapies with a **6% CR rate** (FLT3i or IDHi)

TUS/VEN doublet achieves responses in Prior-VEN failure patients

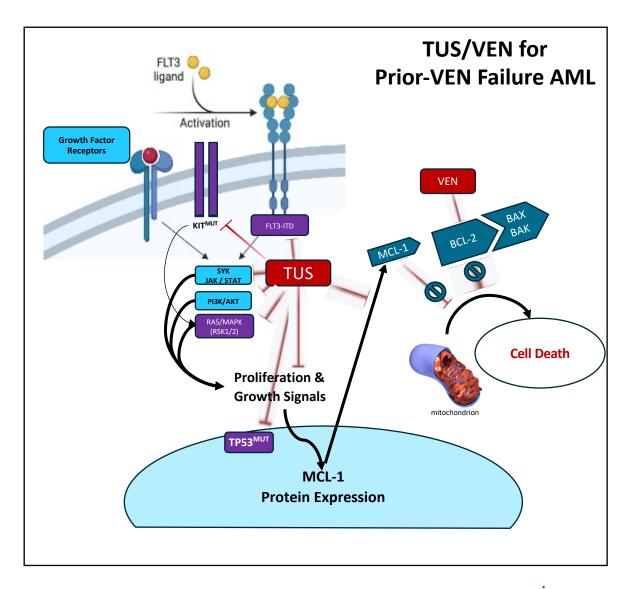
- TUS/VEN is well tolerated, once daily oral, and convenient therapy
- TUS/VEN has unique mechanism to treat Prior-VEN Failure patients



Amannis and colleagues, Outcomes with molecularly targeted agents as salvage therapy following frontline venetoclax + hypomethylating agent in adults with acute myeloid leukemia: A multicenter retrospective analysis. Letter to the Editor, Leukemia Research 2023;131:107331 ³Bewersforf et al., Efficacy of FLT3 and IDH1/2 inhibitors in patients with acute myeloid leukemia previously treated with yenetoclax, Leukemia Research 2022; 122; 106942.

Mechanism of Action for TUS/VEN on Prior-VEN Failure AML

- BCL-2 Overexpression blocks cell death
- Venetoclax Targets BCL-2
 - **VEN inhibits BCL-2** and enables cell death
 - VEN alone has very modest activity in AML
 - **VEN enables** other drugs to work better
- Venetoclax Resistance is Complex
 - KIT, Ras/MAPK, FLT3 mutations promote signaling
 - **TP53 mutations** prevent cell cycle arrest
 - MCL-1 overexpression blocks cell death
 - **VEN cannot overcome MCL-1** blocking cell death
- TUS/VEN Doublet Mechanism
 - TUS inhibits kinase-driven abnormal signaling
 - TUS overcomes TP53^{MUT} with clinical responses
 - TUS reduces MCL-1 protein expression
 - **VEN inhibits BCL-2 block** on cell death
 - TUS/VEN combine to kill AML cells





APTIVATE: TUS/VEN Delivers Clinical Responses in Prior-VEN Failure R/R AML

Snapshot of Preliminary Observations as of August 1st, 2023 Very early in the treatment of these patients – Provide updates in October

R/R AML Patients Dosed with TUS/VEN Doublet

- 15 pts dosed with TUS/VEN at 01Aug2023
 - 14 of 15 failed Prior-VEN therapy
 - ->90% of patients placed on study in the U.S.
 have failed prior VEN therapy
- 10 of 15 reached evaluable stage at 01Aug2023
 - 9 of 10 evaluable had failed Prior-VEN therapy

Patient Subgroup Among 10 Evaluable Patients	CRc Responses
Prior-VEN	44% (4 of 9)
FLT3-WT	43% (3 of 7)
FLT3-MUT	67% (2 of 3)
No Prior-Ven	100% (1 of 1)
Evaluable	50% (5 of 10)

Positioned to treat the greatest number of patients and with the greatest medical needs

- Potential to treat R/R AML FLT3-WT (> 70% AML population) | Not just FLT3-MUT
- Potential to treat R/R AML who previously failed VEN | Rising need in U.S. and ROW



CRc

CR

CRh

CRp

CRi

[•] Efficacy Evaluable with TUS/VEN combo therapy: Completed two planned bone marrow assessments, achieved objective response, or demonstrated disease progression at/after 1st response assessment. Certain patients still on study have not yet reached the efficacy evaluable criteria and may become evaluable in the future (n=3). Not evaluable if withdrew from trial prior to meeting efficacy evaluable criteria (n=2).

Composite CR (CRc; includes CR, CRh, CRi and CRp)

Tuspetinib Commercial Potential

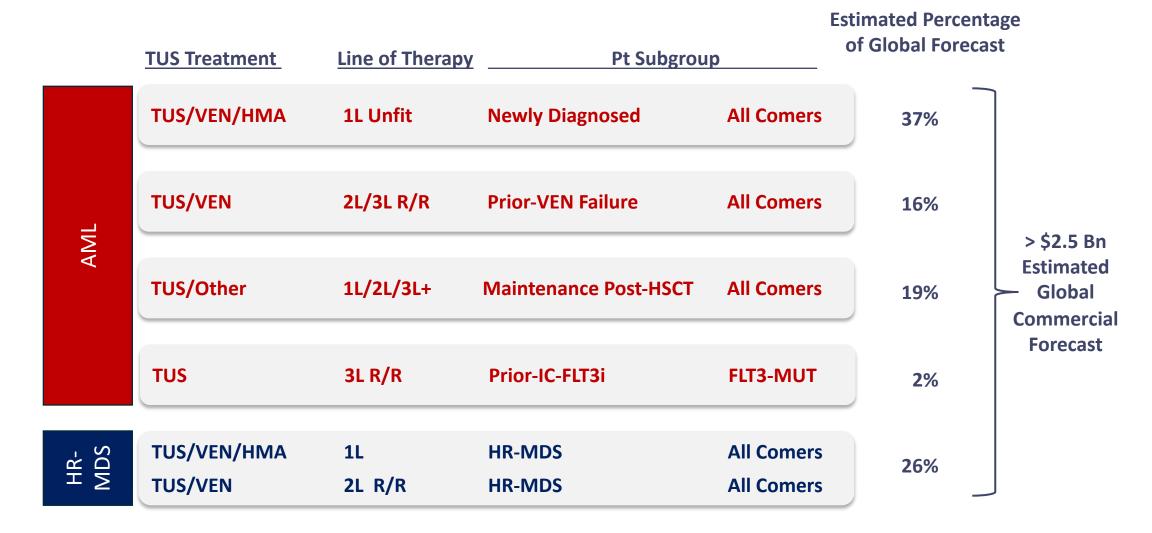
AML Patient Needs

Commercial Opportunities

Accelerated Approval Registrational Trials



Tuspetinib Potential Annual Sales can Exceed \$ 2.5 Bn by 2035 Primary Commercial Opportunities Inclusive of AML and Higher Risk MDS





Rationale and Strategy for Targeting Specific Commercial Opportunities

Highest Priority Opportunity: TUS/VEN Doublet may serve AML patients who failed Prior-VEN therapy

- Fastest path to approval represents our immediate focus for development and commercialization
- Need emerging as more AML patients receive venetoclax and fail with highly refractory disease
- We believe TUS/VEN treatment of Prior-VEN AML can be developed on an accelerated approval pathway
- TUS/VEN Doublet serves as a steppingstone to the TUS/VEN/HMA Triplet

Greatest Commercial Opportunity: TUS/VEN/HMA Triplet may serve as 1L therapy for newly diagnosed AML

Potential to address the medical needs of the greatest number of patients

Longer Term Opportunity: TUS Alone or with other agents may serve as maintenance therapy following HSCT

Long term continuous dosing after AML patients achieve CRs or receive HSCT may help prevent relapse

Accelerated Approval Path via Single Arm Trial: TUS may serve 3L+ patients with no approved therapies

Monotherapy may treat specific AML subgroups with high-risk mutations or who failed prior-IC-FLT3i

Expansion Opportunity: TUS Combinations may serve HR-MDS patients (R/R and 1L HR-MDS)

Rationale: TUS single agent responses in AML patients with wildtype FLT3 and MDS-like genotypes



Generating Data to Support Clinical Development and Registrational Plans

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



FDA EOP1

Dose Escalation

• 20mg to 200mg

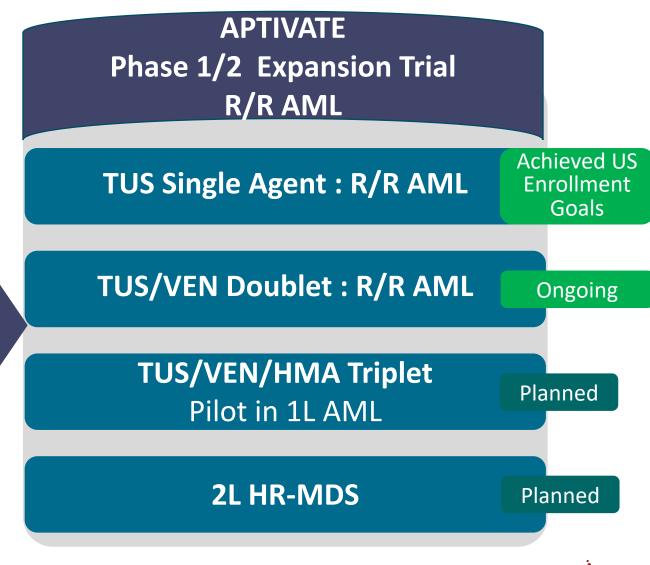
Dose Exploration

- 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

Safe and Well Tolerated





Tuspetinib Single Agent Clinical Trial

Single Agent Dose Escalation Phase 1/2 Clinical Trial in Patients with R/R AML

Successfully Completed

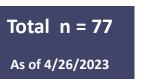


Tuspetinib Single Agent Phase 1/2 study in R/R AML

Dose escalation & dose exploration successfully completed

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

- Extensive dose exploration to address Project Optimus: 77 patients dosed over 6 dose levels
- Clinical Responses (CRs) achieved at 4 dose levels (40, 80, 120, 160mg) with no DLT
- CRs in patients with highly adverse genetics, including mutated TP53 and RAS and FLT3WT
- Favorable safety and tolerability with no concerns of myelosuppression in remission, QTc, muscle destruction, differentiation syndrome, discontinuations

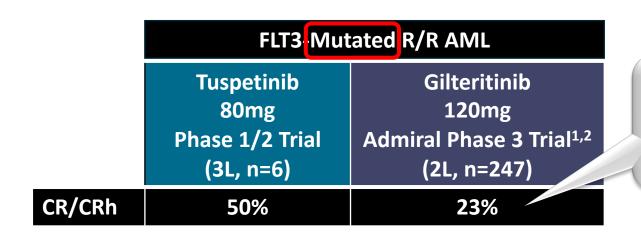




Tuspetinib Single Agent Response Rates Compare Favorably to Gilteritinib FLT3i

Tuspetinib is More than a FLT3 Inhibitor (SYK, FLT3WT/MUT, KITMUT, JAK1/2, RSK1/2)

Compare RP2D of Each □No Prior Venetoclax Therapy □FLT3-Mutated and FLT3-Wildtype



FLT3 Mutated R/R AML

Tuspetinib is more effective relative to gilteritinib Phase 3 Admiral data

Tuspetinib 80mg Phase 1/2 Trial (2L, n=8) CR/CRh R/R AML Gilteritinib 120mg Phase 1b Trial³ (2L, n=14) 0%

FLT3-Wildtype R/R AML

- Tuspetinib is more effective than gilteritinib
- Important data that unlock the potential for TUS to treat additional 70-75% of the AML population (FLT3^{WT}) not available to gilteritinib



¹Pulte, and Pazdur and colleagues, FDA Approval Summary: Gilteritinib for Relapsed or Refractory Acute Myeloid Leukemia with a FLT3 Mutation. Clinical Cancer Research 2021;27(13): 3515 ²Gilteritinib US package insert May 2019

³Perl and colleagues, 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;18(8):1061.

Tuspetinib Single Agent is Clinically Safe and Broadly Active in R/R AML **Findings Position Tuspetinib for Combination Therapies**

- Achieved single agent responses in heavily pre-treated and elderly R/R AML patients
 - Responses across diverse subgroups with adverse genetics (TP53^{MUT}, RAS^{MUT}, NPM1^{MUT}, FLT3^{MUT/WT})
- RP2D established as 80mg once daily for single agent administration
 - Single agent activity superior to gilteritinib in FLT3-MUT and FLT3-WT patients
 - Potential to treat FLT3-WT patients, representing 70-75% of AML population not accessible to gilteritinib
- Single agent responses establish contribution of component for TUS in combination therapies
- Excellent safety and tolerability profiles predict TUS will be safe to combine with other agents in combination cocktails without overlapping toxicities
 - No concerns of myelosuppression in remission, QTc, muscle destruction, differentiation syndrome
 - Avoids discontinuations and many of the typical toxicities observed with other drugs for AML



Tuspetinib APTIVATE Trial

Ongoing APTIVATE Expansion Trial in Patients with R/R AML

TUS Single Agent → Achieved Enrollment Goals

TUS/VEN Doublet → Continuing to Enroll

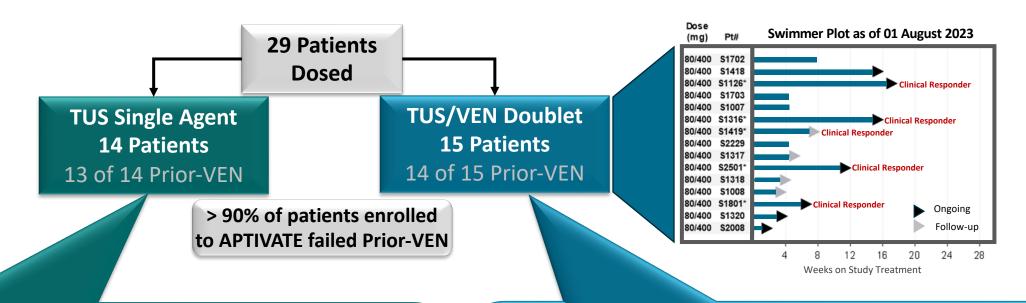
Composite CR (CRc; includes CR, CRh, CRi and CRp)



Efficacy Evaluable with TUS/VEN combo therapy is achieved when patients have completed two planned bone marrow assessments, achieved objective response, or demonstrated disease progression at /after 1st response assessment

Certain patients are not yet evaluable because they are still on study but and have not yet reached the efficacy evaluable criteria but may become evaluable in the future (n=3). Patients are not evaluable if they withdrew from the trial prior to meeting efficacy evaluable criteria (n=2).

APTIVATE Study: Patient Enrollment Snapshot as of 01 August 2023



TUS Single Agent

- APTIVATE Trial: 6 Eval. Pts with Prior-VEN: RR 18% (1 CRp)
- Dose Esc. Trial: 12 Pts with No Prior-VEN: RR 42% (5 CR/CRh)¹
- Against Prior-VEN AML patients, TUS single agent is as good or better than other drugs, but is more active in AML patients with No Prior-VEN
- Explains "questions regarding dose response" in Dose Escalation Trial. Dose responsive through 80mg. Above 80mg (120mg, 160mg), most patients enrolled were Prior-VEN: different patient population enrolled at higher doses that is less responsive

TUS/VEN Doublet

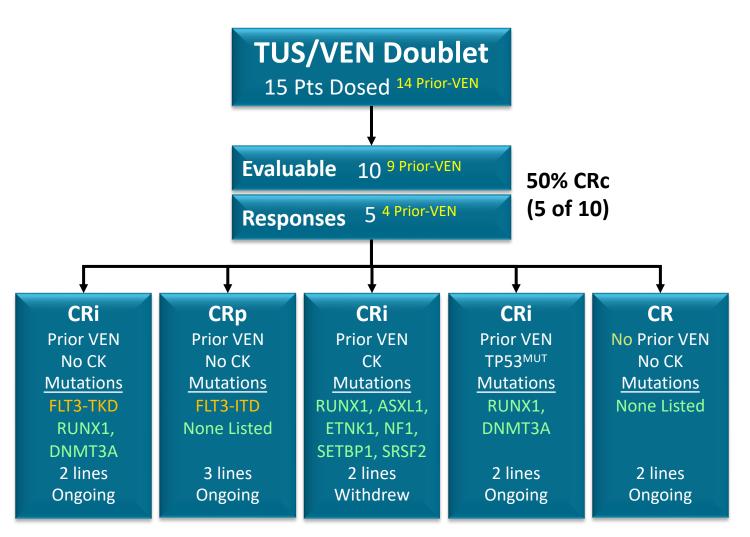
Learned TUS/VEN remarkably active in Prior-VEN AML

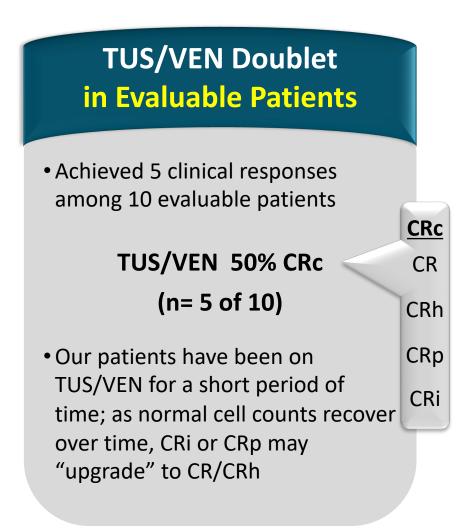
- VEN alone is not active and not used in Prior-VEN failure patients
- This demonstrates responses with TUS/VEN are due to doublet, not VEN
- Early responses in difficult-to-treat patients drove high investigator enthusiasm for TUS/VEN doublet
- Going forward, we will focus enrollment of APTIVATE patients to the TUS/VEN doublet



APTIVATE TRIAL: R/R AML Patients Received TUS/VEN

As of 01 August 2023



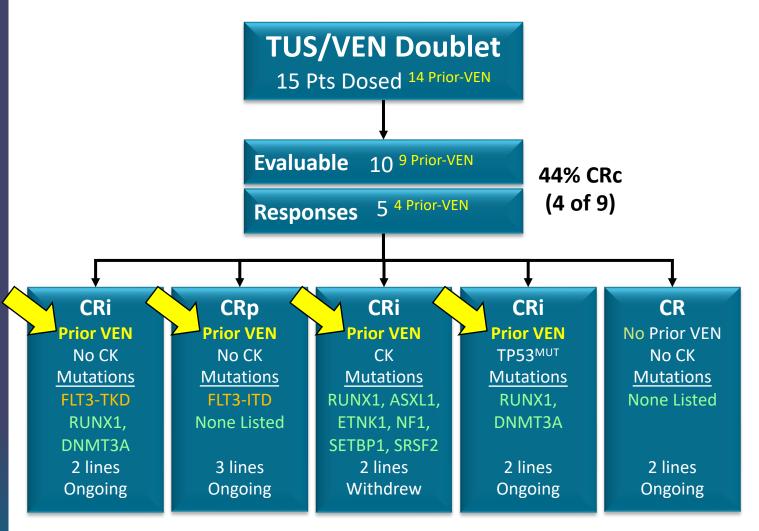


- Efficacy Evaluable with TUS/VEN combo therapy is achieved when patients have completed two planned bone marrow assessments, achieved objective response, or demonstrated disease progression at/after 1st response assessment.
- Certain patients are not yet evaluable because they are still on study but and have not yet reached the efficacy evaluable criteria but may become evaluable in the future (n=3). Patients are not evaluable if they withdrew from the trial prior to meeting efficacy evaluable criteria (n=2). Composite CR (CRc; includes CR, CRh, CRi and CRp)
- Patients received 2-5 prior lines of therapy | IC is Intensive Chemotherapy | CK is Complex Karyotype
- Evaluable patients: 9 of 10 Prior-VEN | 2 of 10 Prior-FLT3i | 7 of 10 Prior-IC | 2 of 10 Prior-HSCT



APTIVATE TRIAL: TUS/VEN Doublet for R/R AML with Prior-VEN Failure

As of 01 August 2023



TUS/VEN Doublet for Prior-VEN AML

 Salvage therapy expects responses in <10% of Prior-VEN failure patients

TUS/VEN 44% CRc (n= 4 of 9)

 $(n=2 FLT3^{MUT}; n=2 FLT3^{WT})$

- As normal cell counts recover over time, CRi or CRp may "upgrade" to CR/CRh
- TUS/VEN offers solution for Prior-VEN patients and a potential accelerated approval path for tuspetinib
- Efficacy Evaluable with TUS/VEN combo therapy is achieved when patients have completed two planned bone marrow assessments, achieved objective response, or demonstrated disease progression at/after 1st response assessment.
- Certain patients are not yet evaluable because they are still on study but and have not yet reached the efficacy evaluable criteria but may become evaluable in the future (n=3). Patients are not evaluable if they withdrew from the trial prior to meeting efficacy evaluable criteria (n=2). Composite CR (CRc; includes CR, CRh, CRi and CRp)
- Patients received 2-5 prior lines of therapy | IC is Intensive Chemotherapy | CK is Complex Karyotype
- Evaluable patients: 9 of 10 Prior-VEN | 2 of 10 Prior-FLT3i | 7 of 10 Prior-IC | 2 of 10 Prior-HSCT



CRc

CR

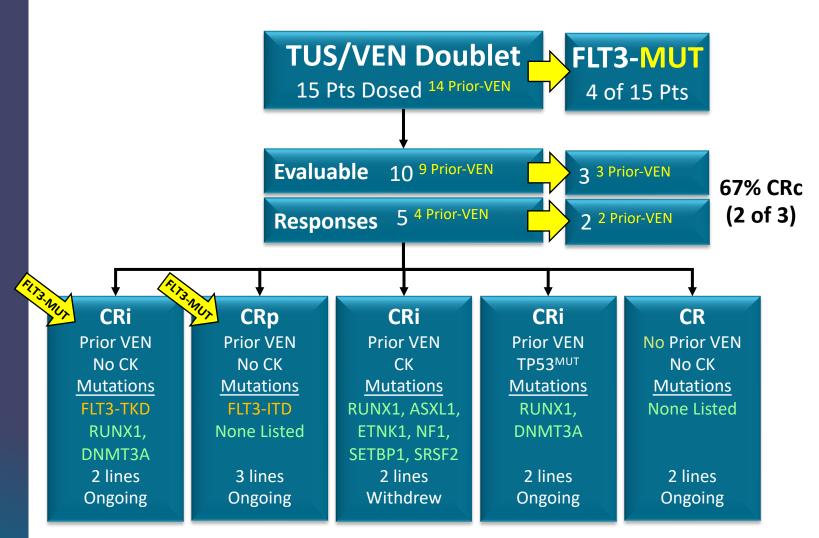
CRh

CRp

CRi

APTIVATE TRIAL: TUS/VEN Doublet for R/R AML with FLT3-Mutated

As of 01 August 2023



TUS/VEN Doublet for FLT3-MUT AML

 R/R AML with Mutated FLT3 respond favorably to TUS/VEN

> TUS/VEN 67% CRc (n= 2 of 3)

 $(1 \text{ FLT3}^{TKD}; 1 \text{ FLT3}^{ITD})$

TUS inhibits WT & mutant forms
 of FLT3 kinase, as well as JAK1/2,
 SYK, RSK1/2, mutant forms of KIT,
 TAB1-TAK1, SKT10 to suppress
 key oncogenic pathways in AML

- Efficacy Evaluable with TUS/VEN combo therapy is achieved when patients have completed two planned bone marrow assessments, achieved objective response, or demonstrated disease progression at/after 1st response assessment.
- Certain patients are not yet evaluable because they are still on study but and have not yet reached the efficacy evaluable criteria but may become evaluable in the future (n=3). Patients are not evaluable if they withdrew from the trial prior to meeting efficacy evaluable criteria (n=2). Composite CR (CRc: includes CR. CRh. CRi and CRp)
- Patients received 2-5 prior lines of therapy | IC is Intensive Chemotherapy | CK is Complex Karyotype
- Evaluable patients: 9 of 10 Prior-VEN | 2 of 10 Prior-FLT3i | 7 of 10 Prior-IC | 2 of 10 Prior-HSCT



TUS/VEN Responses in FLT3-Mutated R/R AML with Prior-VEN Failure TUS/VEN Response Rates Compare Favorably to VEN/Gilt

TUS is More Than a FLT3 Inhibitor

CR/CRi (CRc) in FLT3-Mutated AML		
TUS/VEN APTIVATE Prior-VEN (n= 2 of 3)	VEN/Gilt Phase 1b Trial ¹ Prior-VEN (n= 22 of 56)	
67%	39%	

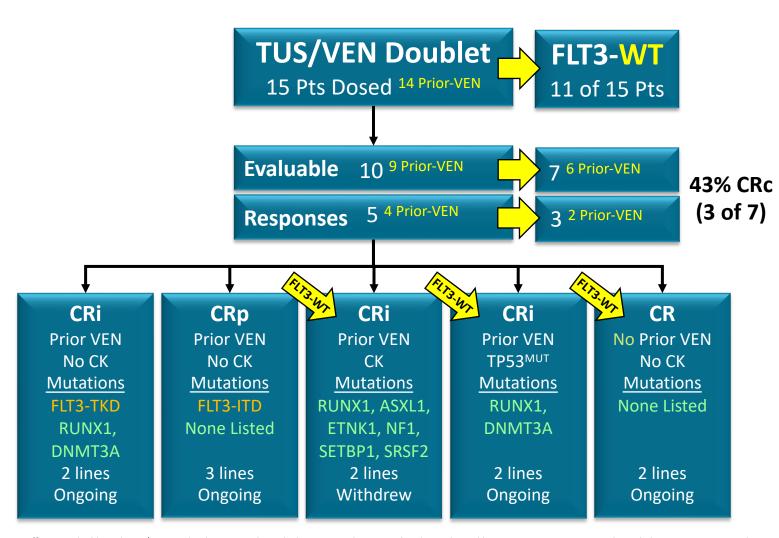
FLT3-Mutated/Failed Prior-VEN

- TUS/VEN doublet compares favorably to GILT/VEN
- Safety is the "secret sauce" for TUS
- TUS has superior safety profile over Gilteritinib
- TUS/VEN offers a safer therapeutic solution for FLT3-mutated AML with Prior-VEN Failure
- Believe VEN/Gilt will not be as competitive due to its safety profile



APTIVATE TRIAL: TUS/VEN Doublet for R/R AML with FLT3-Wildtype

As of 01 August 2023



TUS/VEN Doublet for FLT3-WT AML

 R/R AML with Wildtype FLT3 are not offered a targeted therapy

TUS/VEN 43% CRc (n= 3 of 7)

- Reminder: FLT3-WT is 70-75% of AML population
- No other agents in development addressing this population
- Substantial market potential for TUS/VEN in FLT3-WT AML
- Efficacy Evaluable with TUS/VEN combo therapy is achieved when patients have completed two planned bone marrow assessments, achieved objective response, or demonstrated disease progression at/after 1st response assessment.
- Certain patients are not yet evaluable because they are still on study but and have not yet reached the efficacy evaluable criteria but may become evaluable in the future (n=3). Patients are not evaluable if they withdrew from the trial prior to meeting efficacy evaluable criteria (n=2). Composite CR (CRc; includes CR, CRh, CRi and CRp)
- Patients received 2-5 prior lines of therapy | IC is Intensive Chemotherapy | CK is Complex Karyotype
- Evaluable patients: 9 of 10 Prior-VEN | 2 of 10 Prior-FLT3i | 7 of 10 Prior-IC | 2 of 10 Prior-HSCT



TUS/VEN Responses in FLT3-Wildtype R/R AML with Prior-VEN Failure VEN/Gilt is Not Active in FLT3-WT/Prior-VEN Population

TUS is More Than a FLT3 Inhibitor

CR/CRi (CRc) in FLT3-Wildtype AML Who Failed Prior-VEN			
TUS/VEN APTIVATE (n= 2 of 6)	VEN/Gilt Phase 1b Trial ¹ (n= 0 of 5)		
33%	0%		

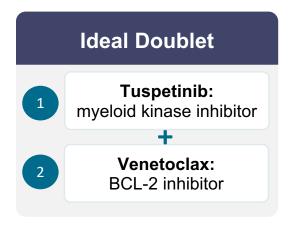
FLT3-WT & Failed Prior-VEN

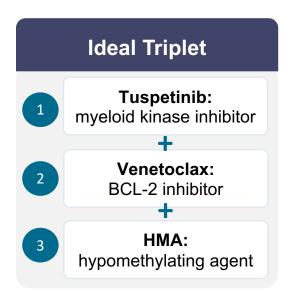
- TUS/VEN achieved 33% CRc
 - Add, the "secret sauce" → Strong safety
- TUS/VEN offers a safe therapeutic solution for AML patients with FLT3-WT/Prior-VEN Failure
- VEN/Gilt not active in this AML population, and caused prolonged cytopenia and DILI
 - Believe VEN/Gilt will not be competitive

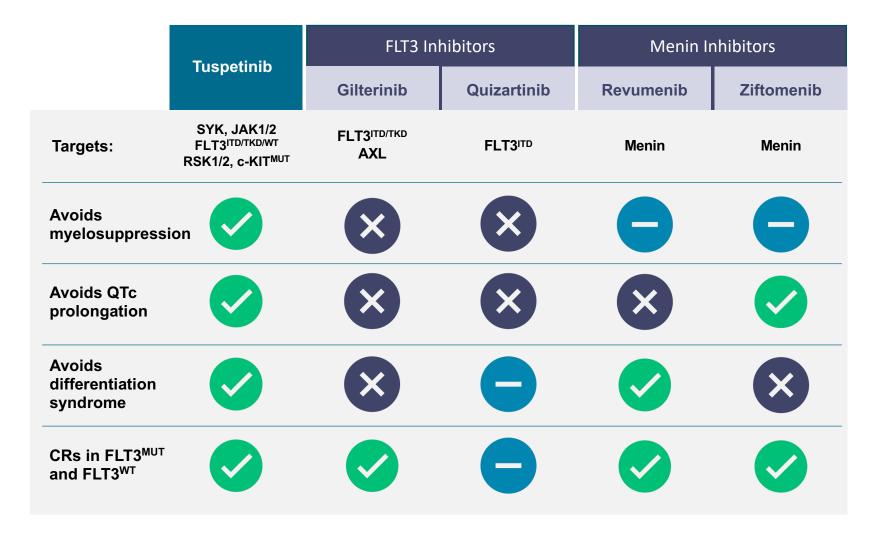


Tuspetinib ideal for combination therapy to treat 1L AML and R/R AML

TUS Combination Therapies Offer > \$2.5 Bn Commercial Opportunities



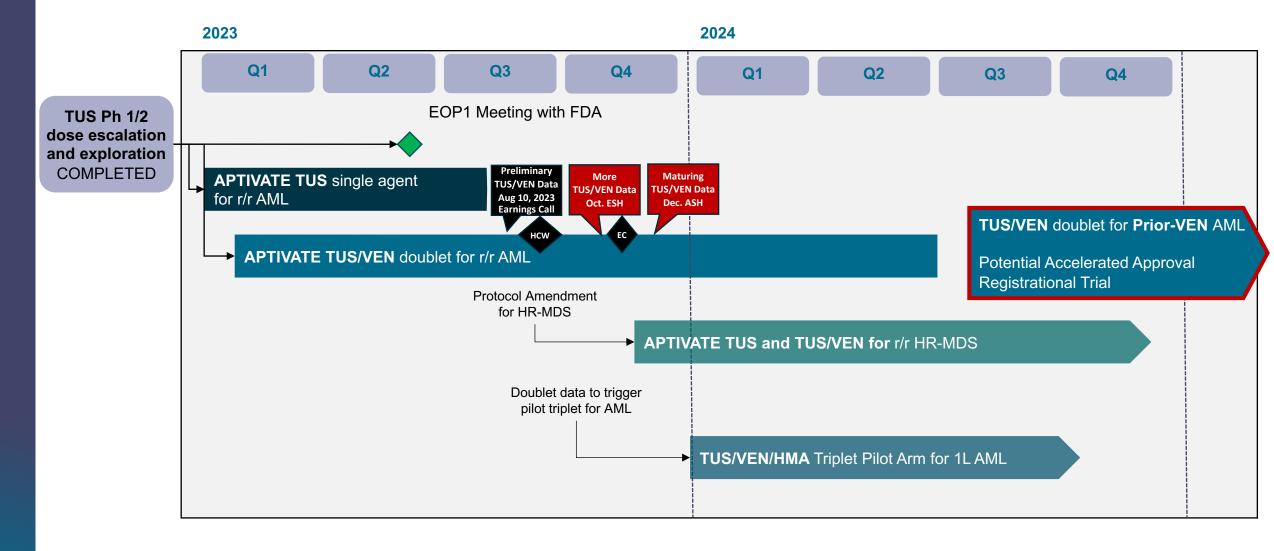






Our Immediate Plan: Move TUS/VEN to Accelerated Approval Registrational Trial

- 2L AML (failed 1L VEN/HMA and no approved targeted agents available) | 3L AML (failed 1L VEN/HMA and failed approved targeted agents in 2L)
- High enthusiasm from investigators, as competing off-label regimens likely have greater toxicity and more narrow populations than a TUS/VEN regimen





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Acute myeloid leukemia, AML Myelodysplastic syndromes, MDS

(Nasdaq: APTO; TSX: APS)



Tuspetinib safety, convenience, and breadth of activity make it the ideal drug for combination therapies in AML

- AML treatment strategies quickly shifting to combination therapies
- Combinations provide greatest commercial and patient impacts
- TUS/VEN/HMA triplet ideal therapy for frontline AML
- TUS/VEN achieved CRs in "high need" Prior-VEN AML
- Forecast > \$2.5 Bn market potential with AML and HR-MDS

Plan to deliver value-driving clinical milestones Q4 2023

Pursuing TUS/VEN Accelerated Approval in Prior-VEN AML

Key Activities and Upcoming Events

- Advancing partnering discussions
- Planning to expand into HR-MDS
- Planning TUS/VEN/HMA Pilot in 1L AML
- Release updated Doublet data : ESH (Oct)
- Release maturing Doublet data: ASH (Dec)
- Release news flow at November Earnings Call



