ENABLE: UPDATED EFFICACY AND SAFETY RESULTS OF ELVN-001, A NOVEL SELECTIVE ATP-COMPETITIVE INHIBITOR OF BCR::ABL1, IN PATIENTS WITH PREVIOUSLY TREATED CP-CML

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EHA 2026: June 11-14, 2026; Stockholm, Sweden

Disclosures

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Research Grant	Novartis, Sanofi, Incyte, Enliven, Ascentage, Abbvie, Pfizer
Consultant	Novartis, Sanofi, Takeda, Ascentage, Abbvie, Daiichi-Sankyo, Astellas, Jazz
Speakers Bureau	N/A
Honoraria	Novartis, Sanofi, Ascentage, Jazz
Employee	N/A
Shareholder	N/A

ELVN-001: A Highly Selective ATP-Competitive Inhibitor of BCR::ABL1

ELVN-001 was designed to address key unmet challenges in CML

Potency without Off-Target Toxicity[1]

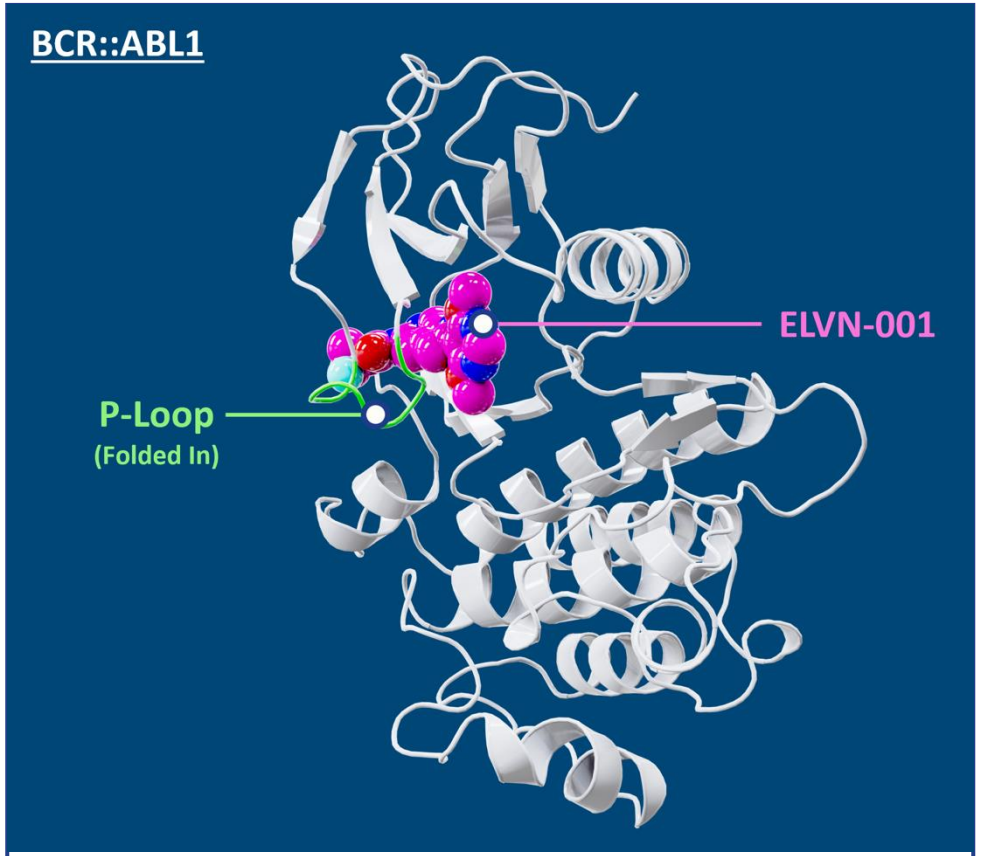
- ELVN-001 delivers **potent** inhibition of BCR::ABL1 with **high ABL1 selectivity:** >100-fold selectivity against >99% of 370 kinases; no inhibition of KIT, VEGFR2, PDGFR, or SRC

Resistance[2,3]

- ELVN-001 showed activity against T315I and the emerging class of mutations associated with resistance to allosteric inhibition
- Not a P-gp or BCRP substrate or inhibitor

Administration Limitations[4,5]

- Once daily administration of ELVN-001 with or without food
- Potential for concomitant administration with CYP3A4 substrates or inhibitors and proton pump inhibitors



ELVN-001 has a unique P-loop folded-in binding mode

ATP, adenosine triphosphate; BCR::ABL1, breakpoint cluster region-Abelson leukemia virus 1; BCRP, breast cancer resistant protein; P-gp, P-glycoprotein

[1]Lee H, et al. Int J Hematol. 2021; [2]Hegedus, et al. Clin Transl Sci. 2022; [3]Braun T, et al. Cancer Cell. 2020; [4]Osorio S, et al. Ann Hematol. 2018; [5]Cheng F, et al. Crit Rev Oncol Hematol. 2024

ELVN-001: Differentiated by its Selective ABL1 Inhibition

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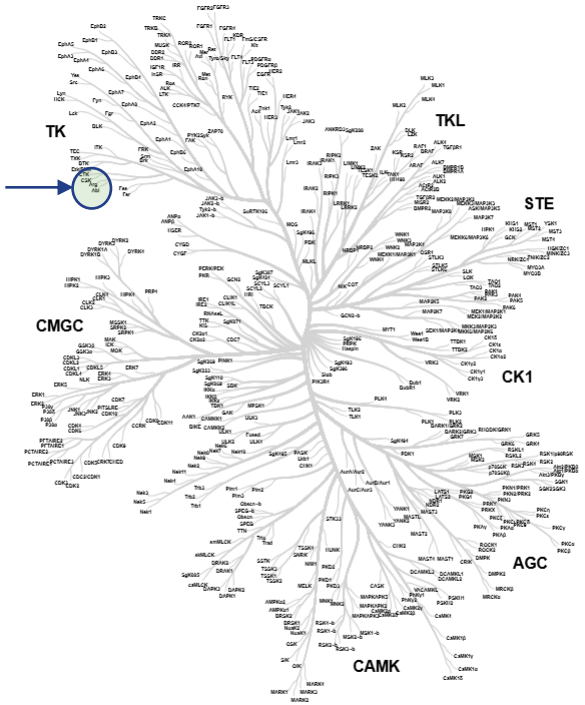
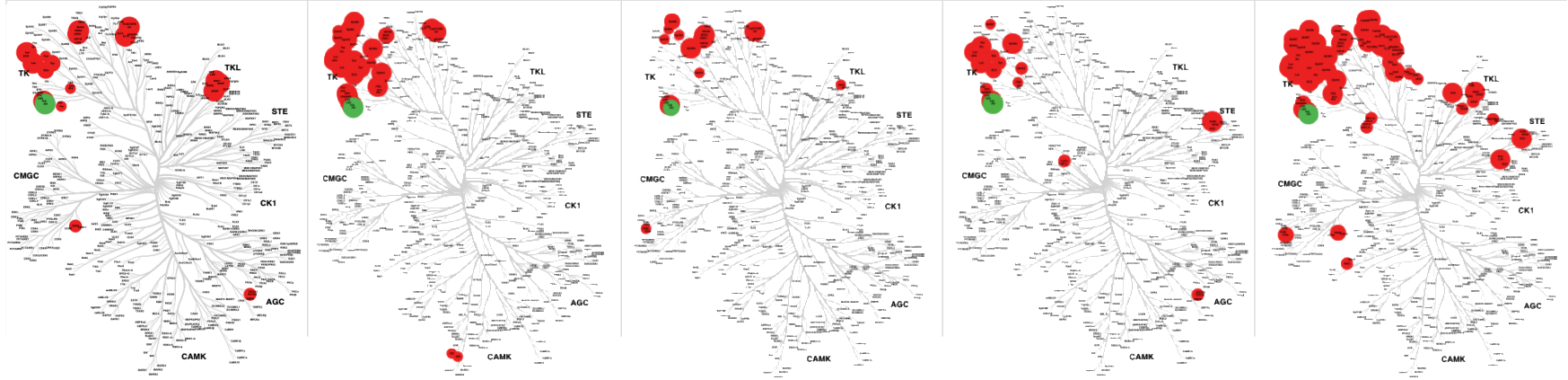
ELVN-001	Imatinib	Dasatinib	Nilotinib	Bosutinib	Ponatinib
ABL1	Also inhibits: KIT, CSFR-1, PDGFR	Also inhibits: SRC family, KIT, PDGFR	Also inhibits: KIT, PDGFR, CSFR-1, DDR-1, hERG channel	Also inhibits: SRC family	Also inhibits: KDR, FGFR, KIT, RET, FLT3, PDGFR





ELVN-001 provides greater selectivity than available ATP inhibitors[a], with potential for better tolerability

[a]Each of these active site TKIs was profiled at 30x its respective ABL1 IC_{50} value against a panel of 377 protein kinases in biochemical assays with 100 mM ATP concentration in the screen (Reaction Biology) (Metz KS et al. Cell Systems. 2018).

ELVN-001: Phase 1 Trial Design and Status

Key Eligibility Criteria:

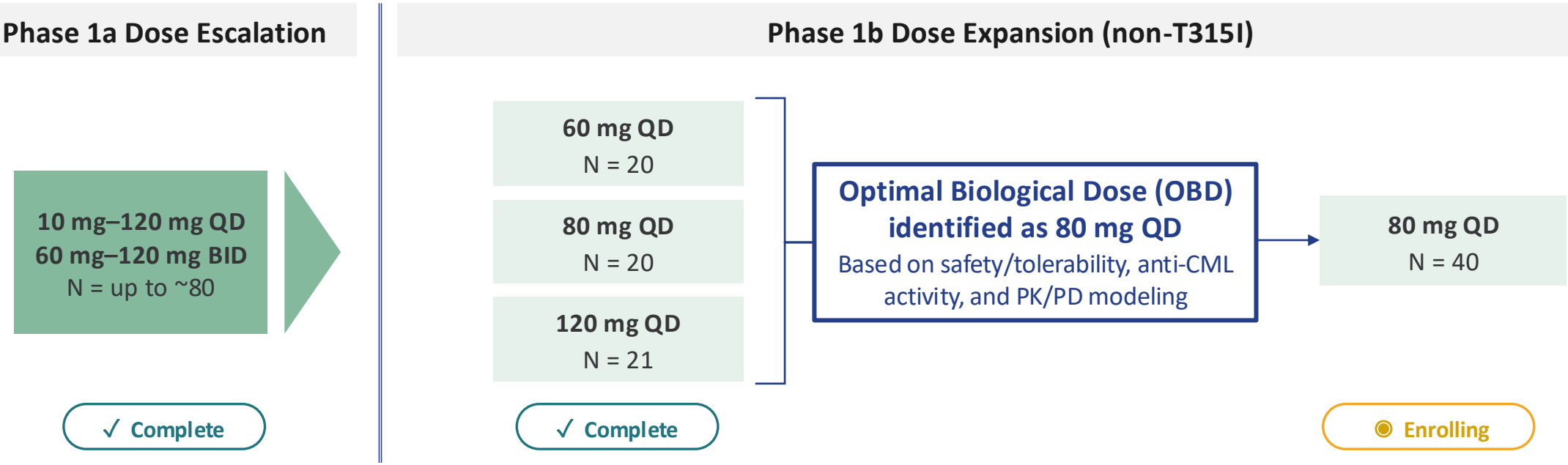
- Chronic phase CML
- Failed, intolerant to, or not a candidate for available therapies known to be active for treatment of their CML
- Typical or atypical transcripts

Primary Endpoints

- Incidence of DLTs, AEs, clinically significant laboratory and ECG abnormalities

Key Secondary Endpoints

- Molecular response by central qPCR
- PK parameters



Phase 1 is ongoing (NCT05304377). AE, adverse event; DLT, dose-limiting toxicity; ECG, electrocardiogram; BID, twice daily; OBD, optimal biological dose; CML, chronic myeloid leukemia; PD, pharmacodynamics; PK, pharmacokinetics; QD, once daily; qPCR, quantitative polymerase chain reaction.

Patient Demographics and Baseline Characteristics

Parameter	All Patients (N = 161[a])	80 mg QD (Phase 1b) (N = 49)
Median age in years (range)	59 (19–82)	57 (19–82)
Typical BCR::ABL1 transcript (e13a2/e14a2), n (%)	150 (93%)	47 (96%)
Baseline BCR::ABL1 transcript[b] ≤0.1%	26 (17%)	8 (17%)
>0.1% – 1%	37 (25%)	11 (23%)
>1% – 10%	28 (19%)	10 (21%)
>10%	50 (33%)	10 (21%)
Baseline BCR::ABL1 mutation (Sanger), n (%)	39 (24%)	5 (10%)
T315I mutation	12 (7%)	n/a
Mutations associated with resistance to allosteric inhibition	13 (8%)	2 (4%)
Other mutations	9 (6%)	3 (6%)

[a] Includes 3 re-enrolled patients (158 individual patients)

Parameter	All Patients (N = 161[a])	80 mg QD (Phase 1b) (N = 49)
Median **lines** of prior TKI therapy, n (range)	4 (1–10)	3 (1–9)
Median number of prior **unique** TKIs, n (range)	3 (1–7)	3 (1–6)
1–2 prior, n (%)	46 (29%)	19 (39%)
3 prior, n (%)	39 (24%)	11 (22%)
4 prior, n (%)	37 (23%)	11 (22%)
≥ 5 prior, n (%)	37 (23%)	7 (14%)
Prior asciminib or ponatinib at any time, n (%)		
Asciminib[b]	100 (62%)	27 (55%)
Ponatinib	60 (37%)	13 (27%)
Reason for discontinuation of last TKI, n (%)[c]		
Lack of efficacy	99 (61%)	25 (51%)
Lack of tolerability	51 (32%)	20 (41%)

[b] Most received asciminib in late line and the majority discontinued asciminib due to lack of efficacy
[c] Unknown/other in 9 patients (all patients) and 3 patients (80 mg QD)

Majority of patients received ≥ 3 prior TKIs (70%) and prior ponatinib and/or asciminib (72%)

Data cutoff: 10 March 2026

Patient Disposition: Majority of Patients Remain on Study

Disposition	All Patients (N = 161)	80 mg QD (Phase 1b) (N = 49)
Median duration of exposure, weeks (range)	35 (0.1–156)	16.1 (0.3–86.7)
Ongoing, n (%)	123 (76%)	40 (82%)
Discontinued, total n (%)	38 (24%)	9 (18%)
Lack of efficacy	21 (13%)	1 (2.0%)
Adverse event	10 (6.2%)	3 (6.1%)
Death	1 (0.6%)	1 (2.0%)
Other[a]	6 (3.7%)	4 (8.2%)

[a] Protocol violation, investigator decision, and consent withdrawal

- No patients progressed to blast phase
- Death was due to post-operative complication (not related to ELVN-001)

Overall, 146 person-years of exposure and 118 patients treated at doses ≥ 80 mg QD

At 80 mg QD in phase 1b:

- 82% of patients remain on study
- Current median duration of exposure of 16 weeks (cohort actively enrolling)
- Low rate of discontinuation due to adverse events

Data cutoff: 10 March 2026.

ELVN-001 had Favorable Safety and Tolerability

- **Wide therapeutic window**
  - 80 mg BID determined to be MTD:
    - 2 patients with DLT at 120 mg BID (one Grade 3 hallucination in patient with history of hallucinations and one Grade 3 myalgia)
  - Low incidence of AOEs*:
    - 7 patients (4.4%) with any grade; 3 (1.9%) with Grade 3, all with CV disease/risk factors incl. prior nilotinib and/or ponatinib
- **Safety of 80 mg QD similar to overall safety; determination of optimal biological dose based on PK/PD modeling**

Most Common TEAEs (by Preferred Term), n (%)	All Patients (N = 158 Safety Analysis Set)		80 mg QD (N = 62 Safety Analysis Set)	
	Any	≥ Grade 3	Any	≥ Grade 3
Any TEAE	142 (90%)	53 (34%)	51 (82%)	15 (24%)
Hematologic TEAEs ≥ 5%				
Thrombocytopenia[a]	23 (15%)	10 (6.3%)	10 (16%)	4 (6.5%)
Neutropenia[a]	11 (7.0%)	10 (6.3%)	1 (1.6%)	0
Non-hematologic TEAEs ≥ 10%				
Lipase increased	35 (22%)	9 (5.7%)[b]	13 (21%)	3 (4.8%)[b]
Fatigue	28 (18%)	2 (1.3%)[b]	7 (11%)	1 (1.6%)[b]
Headache	24 (15%)	1 (0.6%)[b]	11 (18%)	1 (1.6%)[b]
Arthralgia	22 (14%)	2 (1.3%)[b]	10 (16%)	1 (1.6%)[b]
Myalgia	22 (14%)	1 (0.6%)[b]	7 (11%)	0
Nausea	19 (12%)	0	8 (13%)	0
Diarrhea	18 (11%)	0	6 (9.7%)	0
Amylase increased	16 (10%)	0	5 (8.1%)	0

[a] Grouped terms: platelet count decreased/thrombocytopenia and neutrophil count decreased/neutropenia
[b] Grade 3 only

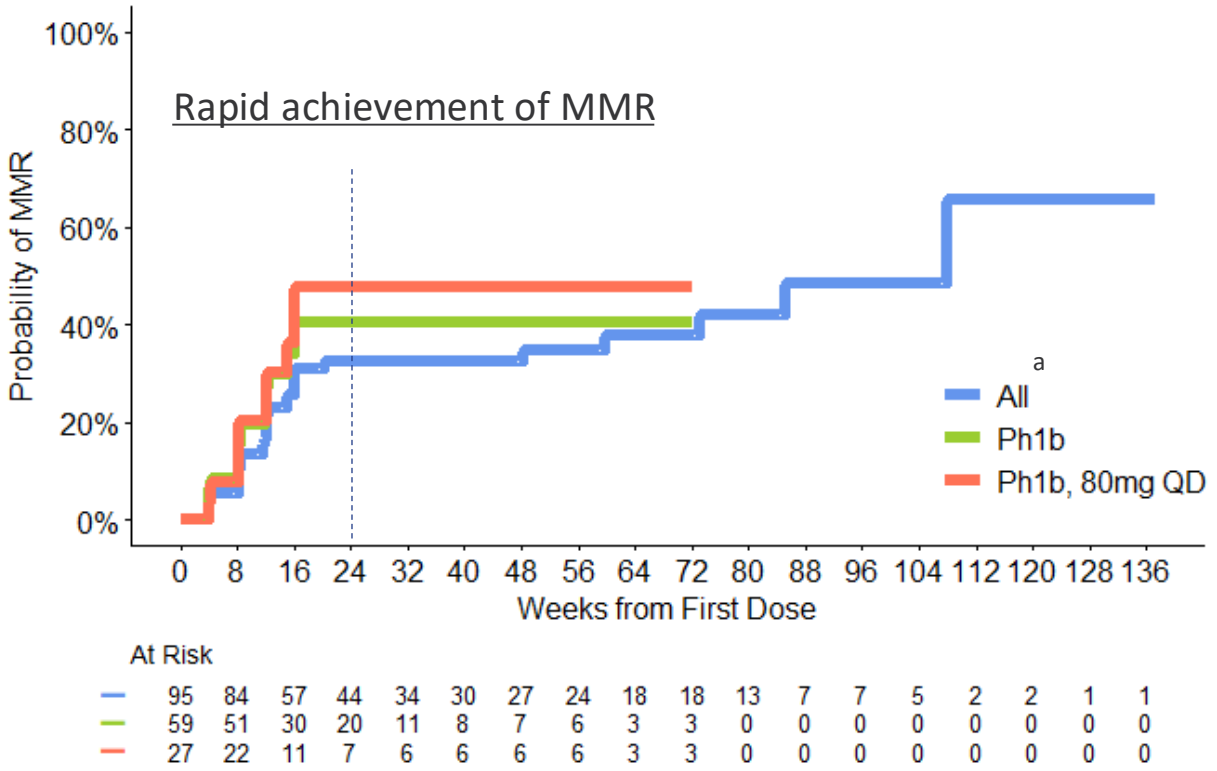
Data cutoff: 10 Mar 2026.
TEAE, treatment-emergent adverse event. *AOEs (arterial occlusive events) identified by MedDRA. TEAE of hypertension, any grade, reported in 5.7% of patients,1.9% Grade 3.

Encouraging Anti-CML Activity in Phase 1b

Key Efficacy Milestones by Week 24 for Phase 1b

	Total QD (Phase 1b) (N = 90)	80 mg QD (Phase 1b) (N = 49)
Median exposure (weeks)	28.0 (0.3-86.7)	16.1 (0.3-86.7)
MMR (*BCR::ABL1* ≤ 0.1%)		
Overall MMR	37/69 (54%)	17/28 (61%)
MMR achieved	21/53 (40%)	10/21 (48%)
MMR maintained	16/16 (100%)	7/7 (100%)
MR2 (*BCR::ABL1* ≤ 1%)		
MR2 achieved	19/33 (58%)	9/13 (69%)
DMR (*BCR::ABL1* ≤ 0.01%)		
DMR achieved	14/64 (22%)	8/27 (30%)

Cumulative Incidence of MMR in Patients Not in MMR at Baseline



[a]Patients enrolled to phase 1a were allowed to increase the dose if certain criteria were met

Data cutoff: 10 Mar 2026.

DMR, deep molecular response; MMR, major molecular response; NOTE: Patients were included if they had baseline typical *BCR::ABL1* transcript, and postbaseline assessment of *BCR::ABL1* transcript at 24 weeks or achieved MMR/≤1% within 24 weeks or discontinued treatment before 24 weeks without achieving MMR/≤1%. For patients with MMR/≤1% at baseline, only postbaseline assessments beyond 70 days were included in the analysis.

All Patients in Phase 1b had Improved or Stable MR Category

Change in *BCR::ABL1* Transcript in Patients Evaluable for MMR by Week 24 (N = 69)

Improvement in MR category
No category change
Worsening in MR category

BCR::ABL1 transcript (%) by Week 24	*BCR::ABL1* transcript (%) at baseline					
	≥MR4.5 ≤0.0032 (N = 4)	**MR4** > 0.0032 to 0.01 (N = 1)	**MR3** > 0.01 to 0.1 (N = 11)	> 0.1 to 1 (N = 21)	> 1 to 10 (N = 15)	> 10 (N = 17)
≥MR4.5 ≤0.0032	4	1	4	5	2	
MR4 > 0.0032 to 0.01			1	1	1	
MR3 > 0.01 to 0.1			6	6	4	2
> 0.1 to 1				9	4	5
> 1 to 10					4	3
> 10						7

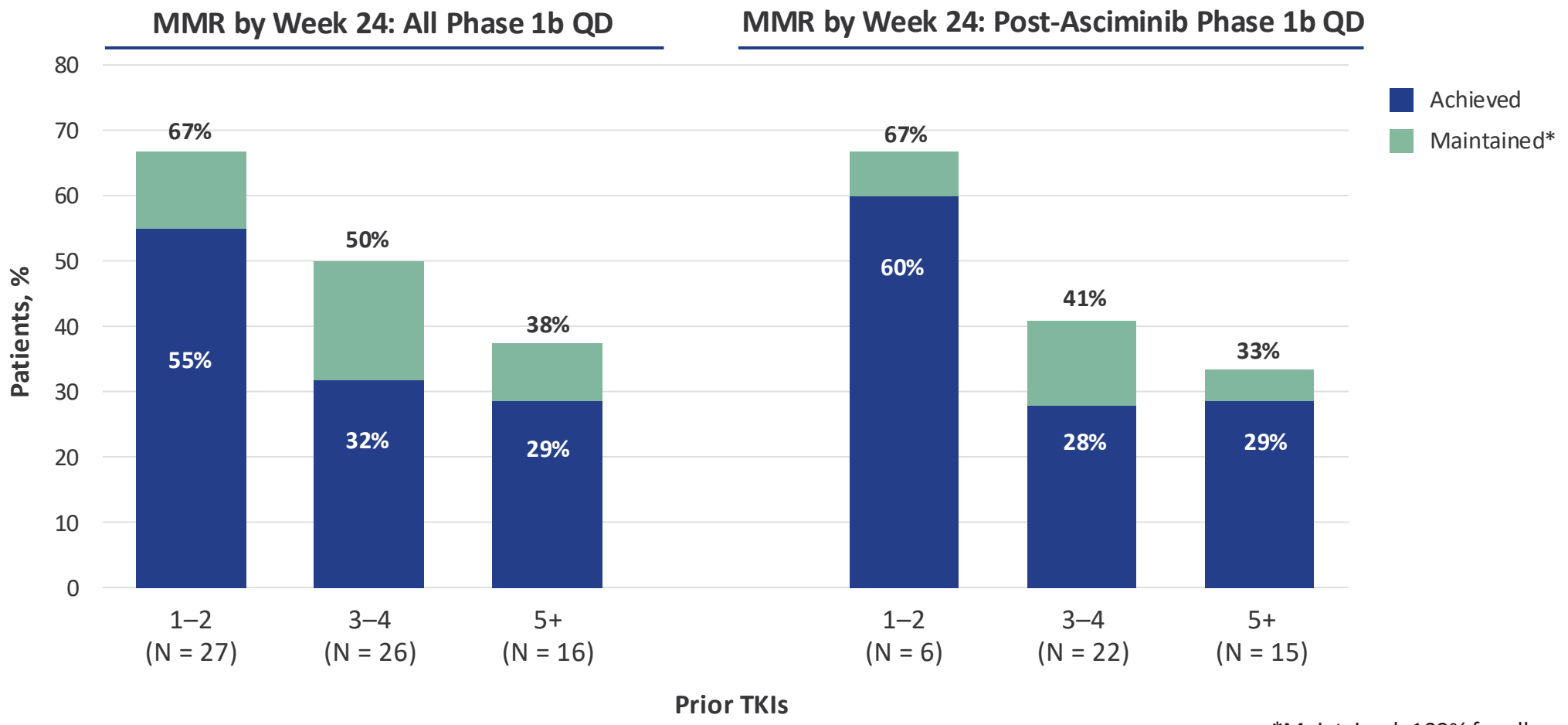
In subgroup with baseline transcript >10%:

59% (10/17) had improved MR category

Data cutoff: 10 Mar 2026.

NOTE: Evaluable patients had baseline typical BCR::ABL1 transcript without T315I mutation and post-baseline assessment of BCR::ABL1 transcript at 24 weeks or achieved MMR within 24 weeks or discontinued treatment before 24 weeks without achieving MMR. For patients with MMR at baseline, only post-baseline assessments beyond 70 days were included in the analysis.

Encouraging MMR Rates Across Lines of Therapy and After Asciminib Failure



*Maintained: 100% for all groups

Data cutoff: 10 Mar 2026.

NOTE: Analysis by number of prior TKIs done with prior *unique* TKIs. Evaluable patients had baseline typical BCR::ABL1 transcript without T315I mutation and post-baseline assessment of BCR::ABL1 transcript at 24 weeks or achieved MMR within 24 weeks or discontinued treatment before 24 weeks without achieving MMR. For patients with MMR at baseline, only post-baseline assessments beyond 70 days were included in the analysis.

Conclusions

ELVN-001 showed favorable safety and tolerability with longer follow-up

- Low rate of discontinuations due to TEAEs
- The safety profile is consistent with ELVN-001's selectivity for ABL1
- No evidence of increased cardiovascular toxicity to date

The Optimal Biological Dose was determined to be 80 mg QD based on safety, efficacy, PK/PD

Encouraging anti-CML activity continued to be observed

- At the OBD of 80 mg QD in Phase 1b: 61% overall MMR with 48% achieving MMR by Week 24
- MR stable or improved in all patients enrolled in Phase 1b
- Encouraging MMR rates even in heavily pretreated patients and after asciminib failure

Phase 3 ENABLE-2 pivotal trial is expected to initiate in the second half of 2026

ELVN-001, an ATP-competitive BCR::ABL1 TKI with high selectivity for ABL1, demonstrated favorable safety and efficacy profile at biologically active doses

Acknowledgments

Thank you

to all investigators and site staff, and to the patients and their families for their participation in the study

This study was funded by Enliven Therapeutics, Inc.