

# **TERN-701 Phase 1 CARDINAL Study** Initial Data from Dose Escalation

NASDAQ: TERN

**December 3, 2024** 

## **Forward-Looking Statements and Disclaimers**

This presentation contains forward-looking statements about Terns Pharmaceuticals, Inc. (the "Company," "we," "us," or "our") and its industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including but not limited to statements regarding beneficial characteristics and potential therapeutic effects of our product candidates and compounds, projections of market potentials and industry trends, discussions of timelines and expectations related to our product candidates and clinical trials, including with respect to potential trial design, milestones and the availability of data, as well as information about the Company objectives or other prospects, and plans, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. The Company has based these forward-looking statements largely on its current expectations, estimates, forecasts and projections about future events and financial trends that it believes may affect its financial condition, results of operations, business strategy and financial needs.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although the Company believes that it has a reasonable basis for each forward-looking statement contained in this presentation, it cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or will occur at all. These risks are not exhaustive. For a detailed discussion of the risk factors that could affect our actual results, please refer to the risk factors identified in our Securities and Exchange Commission ("SEC") reports, including but not limited to our Annual Report on Form 10-K for the year ended December 31, 2023. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

This presentation discusses product candidates that are investigational only and have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied. Data presented for our product candidates and other agents are not based on head-to-head trials and are based on publicly available data, which include cross-trial and/or cross-phase data and information.

- Opening Remarks / Amy Burroughs, CEO
- CARDINAL Interim Phase 1 Data / Emil Kuriakose, CMO
- Closing Remarks / Amy Burroughs
- Management Q&A / Amy Burroughs, Emil Kuriakose, Mark Vignola, CFO



#### Chronic Myeloid Leukemia (CML) is a Chronic and Well-Established Indication, Yet an Unmet Need Still Exists

# In 2024, CML therapies represented a ~\$5B market opportunity

- ~10K new cases diagnosed in the United States, annually<sup>1</sup>
- U.S. prevalence is expected to triple by 2040<sup>2</sup>
- Majority of patients will take TKI therapy for life<sup>3</sup>

Approximately 40% switch therapy by five years due to intolerance and/or resistance<sup>4</sup>

- Chronic use of 1G, 2G active-site TKIs are associated with multiple AEs due to off target effects<sup>4</sup>
- First approved allosteric, asciminib, is superior to prior generation TKIs<sup>5,6</sup> and has opened up a new class
- There remains opportunity to continue to improve on efficacy, safety, tolerability and ease of use for these patients who are on lifelong therapy

American Cancer Society. (Jan 2024) Key Statistics for Chronic Myeloid Leukemia, (Aug 2024).
 Jabbour E, Kantarjian H. Am J Hematol. (Sep 2022);97(9):1236-1256.
 Bower H., et al. Journal of Clinical Oncology (Aug 2016);34(24):2851-7.
 Novartis ASCO 2024 Investor Event.
 Hughes TP et al. N Engl J Med. 2019;381(24):2315-2326.
 Hochhaus A, et al. N Engl J Med. Published online 2024 May 31.
 first generation; 2G: second generation; AE: adverse events; TKI: tyrosine kinase inhibitors



#### Allosteric TKIs Represents the Next Generation of CML Medicines, with Superior Therapeutic Potential Over Active-Site TKIs

#### **CML Drug Development by Decade**



#### **Opportunity for Next Generation, Allosteric BCR-ABL Inhibitors**<sup>1</sup>





# **TERN-701** has Early Signs of Differentiation from Asciminib and Opportunity to Achieve a Best-in-Class Profile

	TERN-701 Differentiation Matrix					
	Preclinical <sup>1,2</sup>	Early Clinical (Ph1) <sup>3</sup>	Late Clinical (Pivotal)#			
Potency ≥ asciminib		— N/A —	— N/A —			
Once-daily (QD) dosing						
Lack of food effect						
Potential for improved efficacy & safety		Early, encouraging data from				
Potential for simplified label (QD across mutations, improved DDI)						

DDI: drug-drug interactions; N/A: not applicable; Ph: phase

# Featured opportunities for TERN-701 are not based on late-stage clinical data and are potential differentiation points that Terns is exploring.

Note: No head-to-head study has been conducted with TERN-701 against asciminib or any other drug or product candidate. Differences exist in study designs and conditions, and caution should be exercised when comparing data across studies. Data and comparisons are shown for illustrative purposes only.



<sup>1.</sup> Zhou et al. ASPET 2023. TERN-701 Preclinical Poster.pdf. 2. Data on File. 3. Anderson et al. SOHO 2024. TERN-701 FE Poster.pdf



## **CARDINAL Interim Phase 1 Data**

Emil Kuriakose, MD CMO



#### TERN-701 Dose Escalation Interim Data Show Compelling Clinical Activity and Encouraging Safety

- Early, promising safety and efficacy profile in a small number of difficult to treat patients (n=15)<sup>1</sup>
  - Compelling molecular responses in heavily pre-treated patients with high baseline transcripts, and decreases in BCR::ABL1 in the majority of response evaluable patients
  - Highly encouraging cumulative MMR rate of 50%<sup>2</sup>
  - No DLTs, AE-related treatment discontinuations, or dose reductions
  - Robust and continuous coverage over target efficacious exposures at all dose levels
- As of today, 19 patients enrolled in the study with at least three patients enrolled in all escalation cohorts
- Plan to initiate dose expansion in 1H25

 N=15 as of October 28, 2024 data cut-off
 5 of 10 non-T315i mutation patients with 3 or more months of treatment and/or MMR or better at baseline AE: adverse event; DLT: dose limiting toxicities; MMR: major molecular response



#### CARDINAL is a Multicenter Global Phase 1 Study of TERN-701 in Patients with Relapsed/Refractory Chronic Phase CML

#### Dose escalation has enrolled rapidly and is near completion

**CARDINAL** Study Population

Chronic phase **2L+** CML patients w/wo BCR::ABL1 mutations who have had:

 Treatment failure / suboptimal response to <u>></u>1 2G-TKI

OR

- Treatment failure / suboptimal response / intolerance to any ≥2 activesite TKIs
- Prior asciminib allowed



Endpoints For Part 1

- Primary: Safety/tolerability
- Secondary: PK, Efficacy



• Secondary: Safety/tolerability, PK

**‡RDE**: recommended dose for expansion will be selected following a Part 1 interim analysis

\*Dose 1 expected to be  $\geq$  160mg. Dose 2 targeted be a dose level > 160 mg QD with sufficiently non-overlapping exposures and comparable safety to Dose 1 2C TKI: deactivity allocities and comparable safety to Dose 1

2G-TKI: dasatinib, nilotinib or bosutinib; PK: pharmacokinetics; TKI: tyrosine kinase inhibitor

#### Efficacy and Safety Assessments in the CARDINAL Study

#### **Efficacy Measures**

- Molecular response assessed centrally evaluating change in BCR-ABL (IS) transcript levels from baseline
- Hematologic response in patients with hematologic relapse at baseline

#### **Safety Assessments**

- Dose limiting toxicities
- Treatment emergent hematologic and nonhematologic AEs
- Serious adverse events
- Dose discontinuations and reductions



1. Wang R et al. Medicine (Baltimore). 2019 Apr;98(15):e15222. 2. Saussele S et al. Leukemia. 2018 May;32(5):1222-1228. 3. Shah NP et al. Journal of the National Comprehensive Cancer Network 2024, 22(1), 43-69. 4. Talpaz M et al. Cancer. 2018 Apr 15;124(8):1660-1672. AEs: adverse events; IS: international standard; MR: molecular response

# Enrolled Patients Have Heavily Pretreated Relapsed/Refractory CML with High Disease Burden

- High baseline disease burden
  - 60% with baseline BCR::ABL1 >1%
  - 73% without baseline MMR
  - 20% with BCR::ABL1 resistance mutation
- Heavily pre-treated population
  - Median 4 prior TKIs
  - 80% had  $\geq$  3 therapies
  - 47% had prior ponatinib
  - 40% had prior asciminib
- Of asciminib pre-treated patients
  - 1 treatment failure in a remote prior line
  - 5 had asciminib immediately before TERN-701
    - 1 treatment failure
    - 1 suboptimal response with intolerance\*
    - 3 intolerant\*

	Baseline Disease Status	CARDINAL (N=15)			
	Baseline BCR::ABL1				
К	> 10%		40%		
MN	> 1% to 10%		20%		
ž	> 0.1% to 1%	13%			
MR	> 0.01% to 0.1%	20%			
≥ ^I	< 0.01%	7%			
	Median prior TKIs (range)	Z	4 (1-6)		
	≥ 3 prior lines	80% 47%			
	Prior ponatinib				
	Prior asciminib		40%		
	PCDuADI 1 mutations	T315I	13%		
	DUR. ADL'I INUTATIONS	F317L	7%		



### Meaningful Activity in Refractory Patients with High BCR::ABL1

3-month median treatment duration; 14 of 15 patients remain on treatment



1. Defined as having a baseline BCR::ABL1 transcript and at least two post-baseline BCR-ABL transcript levels (centrally assessed)

\* hematologic relapse

Asc?: prior asciminib; CHR: complete hematologic response; Mut: mutation; MR2: at least a 2-log reduction (i.e., BCR::ABL1<sup>IS</sup> ≤ 1%); MR4: at least 4-log reduction (i.e., BCR::ABL1<sup>IS</sup> ≤ 0.01%); Tx: treatment; TKI #: number of prior TKIs

# Highly Encouraging Cumulative MMR Rate of 50% (5/10)

TERN-701 improved or maintained categorical response in all patients without T315I mutation

	Baseline BCR::ABL1							
Post-treatment BCR::ABL1	<b>MR5</b> ≤0.001 (n=0)	<b>MR4.5</b> >0.001 to 0.0032 (n=0)	MR4 >0.0032 to 0.01% (n=1)	MR3 (MMR) >0.01 to 0.1% (n=3)	<b>MR2</b> >0.1 to 1% (n=0)	<b>MR1</b> >1 to 10% (n=2)	>10% (n=4)	
<b>MR5</b> ≤0.001								
<b>MR4.5</b> >0.001 to 0.0032								
<b>MR4</b> >0.0032 to 0.01%			1				1	
<b>MR3 (MMR)</b> >0.01 to 0.1%				3				
<b>MR2</b> >0.1 to 1%						1		
<b>MR1</b> >1 to 10%						1		
>10%							3	

Categorical BCR::ABL1 (IS) response shift in non-T315Im patients with > 3 months of treatment and/or > MMR at baseline

Table includes response evaluable patients without T315Im with  $\geq$  3 months of treatment with corresponding 3-month transcript level reported at visit cutoff,  $\geq$  MMR at baseline, or treatment discontinuation at any time

# 88% of Patients with Baseline Transcript > 1% Have Decreases in BCR::ABL1 Levels on Treatment

- 8 response evaluable patients had baseline transcript >1%
  - 6 had baseline transcript >10%
  - 4 had prior asciminib and 3G TKI\*
- 88% (7/8) have decrease in BCR::ABL1 and continue treatment as of data cut-off
- One discontinuation due to loss of response after >50% decline in BCR::ABL1 in 6L patient with T315I mutation



\*3G TKI= ponatinib/olverembatinib/ELVN-001; # Baseline transcript >50%

## **TERN-701 Early Molecular Response Data are Trending Favorably**

Encouraging 3-month MMR in non-T315Im CML in a more refractory patient population than asciminib Ph1

• At 3 months, TERN-701 shows:

Pacolino PCD

- 1/4\* with BCR::ABL1 >10% achieves DMR; 4/4 have decrease in transcript with treatment ongoing
- 1/2 with BCR::ABL1 >1-10% achieves MR2 post-asciminib; 2/2 have decrease in transcript with treatment ongoing
- Asciminib showed <5% and <10% MMR at 3 months in patients without T315Im with BCR::ABL1 >10% and >1-10%, respectively

### Incidence of MMR in non-T315I mutant CP CML in asciminib Phase 1



Daseline DCRADLI	
>10% (N=41)	<5%
>1-10% (N=21)	<10%

\* 4 response-evaluable patients without T315I mutation and baseline transcript >10%

Note: No head-to-head study has been conducted with TERN-701 against asciminib or any other drug or product candidate. Differences exist in study designs and conditions, and caution should be exercised when comparing data across studies. Data and comparisons are shown for illustrative purposes only; CP: chronic phase; DMR: deep molecular response; MMR: major molecular response; MR2: at least a 2-log reduction (i.e., BCR::ABL1<sup>IS</sup> ≤ 1%) Mauro MJ, et al. Leukemia. 2023 May;37(5):1048-1059. Supplemental Material.

Acciminih MMD at

Time to MMR (weeks)

ΓERNS

#### **TERN-701 Deepens Response in Patient with Suboptimal Response** to Asciminib

#### MR2 in 4L patient treated with 2G TKI, 3G TKI and asciminib with baseline BCR::ABL1 >1%



MR1: at least 1-log reduction; MR2: at least a 2-log reduction (i.e., BCR::ABL1<sup>IS</sup> ≤ 1%); cycle = 28 days

#### **TERN-701 Achieves Rapid Deep Molecular Response in 5L Refractory Patient**

MR4 in patient treated with imatinib and all 2G TKIs with loss of response to bosutinib and baseline transcript >10%



#### TERN-701 Achieves Robust Target Coverage Over Mutated and Non-Mutated BCR::ABL1 Variants with Once Daily Dosing



Steady state PK for 400 mg not available as of data cut-off date  $C_{ave} = C_{average}$ ; PK: pharmacokinetics

In vitro IC<sub>90</sub> values corrected for plasma protein binding

\* denotes myristoyl mutations or mutations indicated in resistance to allosteric inhibition of BCR::ABL1

#### **Emerging Safety Data for TERN-701 are Highly Encouraging**

- ✓ No dose limiting toxicities (DLTs)
- No AE-related treatment discontinuations or dose reductions
- ✓ No  $\geq$  Grade 3 treatment-related AEs
- ✓ No treatment-related SAEs
- ✓ No clinically meaningful changes in LFTs, amylase, or lipase
- ✓ No clinically meaningful changes in blood pressure, ECG, or other vitals



### **No Concerning Safety Signals for Hematologic Adverse Events**

Majority of treatment-emergent hematologic adverse events are low grade No hematologic DLTs or treatment related AEs > Grade 2

#### Hematologic Treatment-Emergent Adverse Events

Parameter SOC/PT n (%)	160 (N	mg QD I=7)	320 mg QD (N=5)		400 mg QD (N=3)		All patients (N=15)	
	All grade	≥ Grade 3	All grade	≥ Grade 3	All grade	≥ Grade 3	All grade	≥ Grade 3
Thrombocytopenia	2 (29%)	0	2 (40%)	0	0	0	4 (27%)	0
Anemia	1 (14%)	0	2 (40%)	1 (20%)*	0	0	3 (20%)	1 (7%)
Neutropenia	1 (14%)	0	3 (60%)	1 (20%)*	0	0	4 (27%)	1 (7%)
Thrombocytosis	0	0	2 (40%)	0	0	0	2 (13%)	0

\* Neither grade  $\geq$  3 event was considered related to TERN-701

AEs: adverse events; DLT: dose limiting toxicities; G: grade; SOC: system organ class; PT: preferred term; QD: once-daily



### No Concerning Safety Signals for Non-Hematologic Adverse Events

Majority of non-hematologic treatment-emergent adverse events are low grade No non-hematologic DLTs or treatment related AEs > Grade 2

#### **Non-Hematologic Treatment-Emergent Adverse Events in > 1 Patient**

Parameter SOC/PT n (%)	ا 160 (N	mg QD I=7)	320 mg QD (N=5)		400 mg QD (N=3)		All patients (N=15)	
	All Grade	≥ Grade 3	All Grade	≥ Grade 3	All Grade	≥ Grade 3	All Grade	≥ Grade 3
Nausea	1 (14%)	0	1 (20%)	0	1 (33%)	0	3 (20%)	0
Headache	3 (43%)	0	0	0	0	0	3 (20%)	0
Dizziness	1 (14%)	0	1 (20%)	0	0	0	2 (13%)	0
Fatigue	1 (14%)	0	1 (20%)	0	0	0	2 (13%)	0
Oedema peripheral	1 (14%)	0	1 (20%)	0	0	0	2 (13%)	0

AEs: adverse events; DLTs: dose limiting toxicities; PT: preferred term; QD: once-daily; SOC: system organ class

#### Incidence of Dose Limiting Toxicities (DLTs) for TERN-701 Trending Lower than Asciminib Phase 1

#### Both Phase 1 studies assessed DLTs during first 28 days of treatment

Asciminib Dose	Dose Limiting Toxicities		TERN-701 Dose	Dose Limiting Toxicities	
40 mg BID	Grade 3 lipase elevation (n=2)		160 mg QD	No DLTs	
80 mg BID	Grade 2 myalgia & arthralgia (n=1)				
150 mg BID	Grade 3 acute coronary syndrome (n=1)		320 mg QD	No DLTs	
	Grade 3 clinical pancreatitis (n=1)				
200 mg QD Grade 3 lipase elevation (n=1)		400 mg QD	No DLTs		
	Grade 3 abdominal pain (n=1)				
200 mg BID	Grade 3 bronchospasm (n=1)		500 mg QD	Undergoing evaluation	

#### **TERN-701 Emerging Data Support Potential Best-in-Class Profile**

- Emerging data from the first 3 dose levels of TERN-701 Ph1 dose escalation (n=15) show<sup>1</sup>
  - Clinically effective exposures achieved at starting dose of 160 mg QD and above
  - Compelling responses in patients with high disease burden and poor response on prior 2G/3G TKIs and asciminib
  - Well tolerated with no DLTs, no dose reductions or AE-related discontinuations across all doses evaluated
- Deepening responses in patients with non-T315Im CML post-asciminib suggests TERN-701 doses 
   <u>> 160 mg</u>
   may achieve more effective target coverage compared to the approved asciminib dose
- On track to initiate dose expansion in 1H25, which will generate more mature efficacy data including longer term MMR rates expected in 4Q25



# **CARDINAL**

Terns would like to acknowledge and thank the trial participants, investigators and CARDINAL study team – thank you!





# **Closing Remarks**

Amy Burroughs, CEO



# Robust Clinical Data Generated Across Multiple Clinical Studies of TERN-701 Supports Efficient Full Development

CARDINAL dose expansion start in 1H25; additional efficacy data in 4Q25



#### **Phase 3 Registrational Trial**

Evaluating multiple options for pivotal trial(s) including frontline and second line patients

Phase 3 Monotherapy Frontline CML patients

Phase 3 Monotherapy 2L+ CML patients



## TERN-701 Has Broad Anticipated Opportunity Across 1L and 2L+

\$5 billion current CML market opportunity poised for expansion with increasing addressable patient population



Addressable market to expand as U.S. CML prevalence is expected to triple by 2040<sup>3</sup>

1. Novartis ASCO Investor Event | June 2, 2024; 2. Novartis R&D Investor Event | November 28, 2023; 3. Jabbour E, Kantarjian H. Am J Hematol. (Sep 2022);97(9):1236-1256 G7: Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States; Dx: diagnosed



# **TERN-701 Has Early Signs of Differentiation from Asciminib and Opportunity to Achieve a Best-in-Class Profile**

	TERN-701 Differentiation Matrix					
	Preclinical <sup>1,2</sup>	Early Clinical (Ph1) <sup>3</sup>	Late Clinical (Pivotal)#			
Potency ≥ asciminib		— N/A —	— N/A —			
Once-daily (QD) dosing						
Lack of food effect						
Potential for improved efficacy & safety		Early, encouraging data from				
Potential for simplified label (QD across mutations, improved DDI)						

DDI: drug-drug interactions; N/A: not applicable; Ph: phase

# Featured opportunities for TERN-701 are not based on late-stage clinical data and are potential differentiation points that Terns is exploring.

Note: No head-to-head study has been conducted with TERN-701 against asciminib or any other drug or product candidate. Differences exist in study designs and conditions, and caution should be exercised when comparing

data across studies. Data and comparisons are shown for illustrative purposes only.

<sup>1.</sup> Zhou et al. ASPET 2023. TERN-701 Preclinical Poster.pdf. 2. Data on File. 3. Anderson et al. SOHO 2024. TERN-701 FE Poster.pdf

#### Terns Pipeline: Broad Rights to Multiple Wholly-owned Opportunities Targeting Serious Diseases





## **Management Q&A**

Amy Burroughs, CEO Emil Kuriakose, CMO Mark Vignola, CFO





# **Appendix**



31

#### TERN-701 Showed Robust Tumor Growth Inhibition with High Tumor Drug Levels in CML Mouse Models

TERN-701 showed robust tumor growth inhibition in KCL-22 mouse xenograft at low doses TERN-701 achieved robust and prolonged target coverage in leukemic cells in mouse model



#### TERN-701 Doses in CARDINAL Study are Associated with Potent Pharmacodynamic Inhibition of BCR::ABL1 Signaling

**Clinical doses in CARDINAL achieve exposures with** 



All error bars represent the SEM \*\*\*p<0.001.

BID: twice (two times) a day; PD: pharmacodynamic; QD; once-daily

**TERN-701 3mg/kg dose potently inhibits** 

#### TERN-701 PK Data from Adult Healthy Volunteer Study Supports Once-daily Dosing Without Regard to Food

Dosing with or without food is a key differentiator within the allosteric BCR-ABL class

**Favorable TERN-701 Pharmacokinetic Profile** 

- Linear PK with approximately dose proportional increase in exposure from 40-400mg<sup>1</sup>
- Median half-life of 8-14 hours supporting QD dosing



1. Across single dose TERN-701 range of 20 mg to 400 mg

2. TERN-701 80 mg dose; asciminib (40mg) change in exposure (ΔAUC<sub>inf</sub>) from fed relative to fasted was (62%)

3. Effective plasma IC90 for the native BCR-ABL KCL-22 cell line

#### No TERN-701 Food Effect

 No clinically significant difference in TERN-701 exposure (AUC) when dosed fasted or with a high-fat meal<sup>2</sup>

