

## **Company Overview**

NASDAQ: TERN

March 2024

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Developing small-molecule medicines, with clinically validated mechanisms of action, to address oncology and metabolic diseases with large unmet medical need

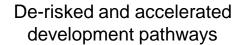
### Terns Investment Highlights and Strategic Approach

## Each of Terns' molecules meet the following strategic criteria:

- ✓ Oral, small molecule compounds
- ✓ Clinically validated mechanisms with opportunities to improve
- Indications with high unmet needs

#### Oncology







Optionality for in-house full development



Complementary with other assets

#### Metabolic



Large markets with multiple ways to win (e.g., combinations)



Opportunity to create near-term value before seeking partnership

#### **Top Shareholders**











#### **Strong Balance Sheet**

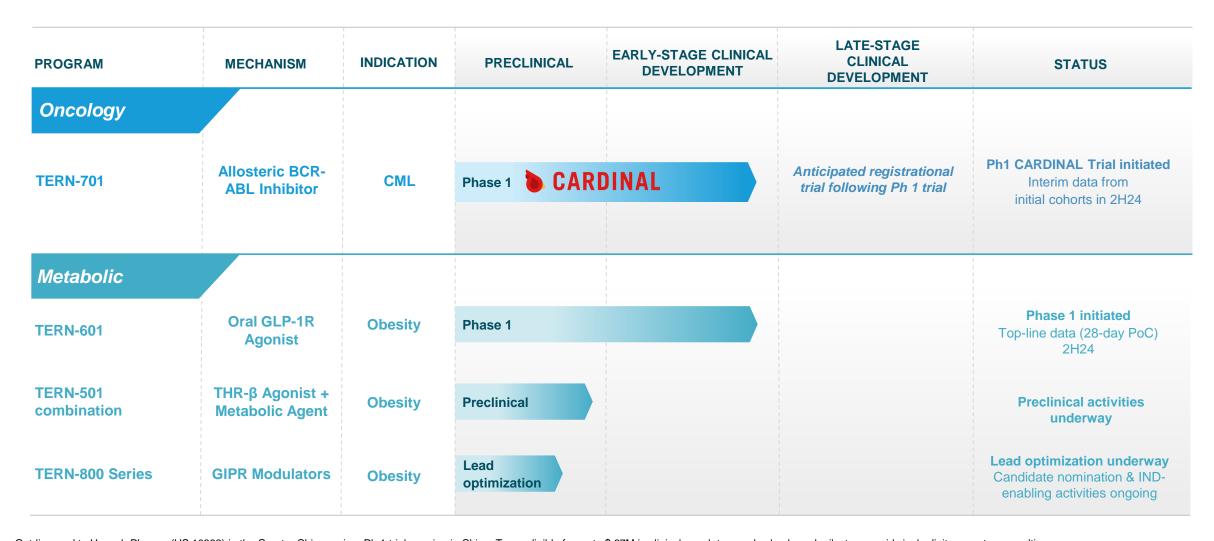
Cash of \$263M<sup>1</sup> expected to provide runway into 2026







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







## **TERN-701**

# Allosteric BCR-ABL TKI for Chronic Myeloid Leukemia

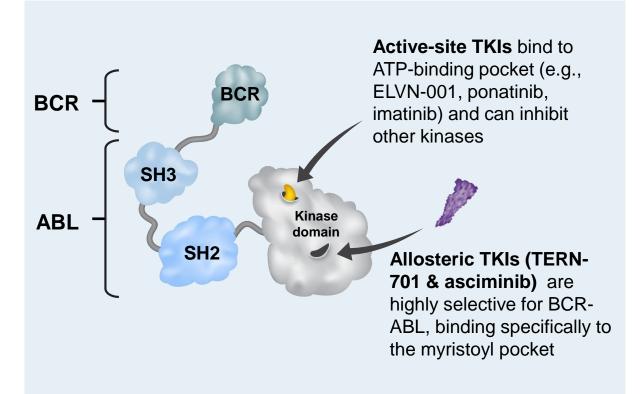
Allosteric TKIs have significant efficacy improvement over active-site TKIs

- CML is an orphan indication supporting a ~\$5B market with need for multiple agents and with limited allosteric competition
- TERN-701 Phase 1 clinical trial (CARDINAL) is progressing; interim data from initial cohorts in 2H24

### Allosteric TKI: an Improved Approach for CML Treatment

TERN-701 is an internally-developed allosteric TKI with an expected profile > asciminib

#### Active BCR-ABL1 → Cell proliferation / reduced apoptosis



Inactive BCR-ABL1 → Cell death

- CML is a chronic, orphan indication with a sizeable market (>\$5B) and a need for multiple agents
- People with CML can live for decades with life-long treatment, but switching therapies is common (e.g., due to intolerance), necessitating new therapies that are safe, efficacious and well-tolerated
- Allosteric TKIs have shown ~2x efficacy improvement over older standard-of-care active-site TKIs and are better tolerated, with a relative lack of competition in the class
- **Blockbuster expectations** for 1<sup>st</sup> approved allosteric TKI, asciminib: label in 3L CML expected to expand into 1L
- Phase 1 CARDINAL trial progressing with site activations globally and study-eligible subjects being identified by investigators

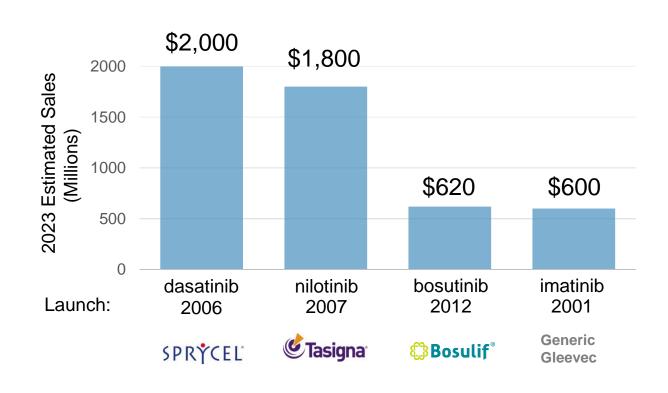


## CML is a Sizeable Market With Need for Multiple Agents

CML is a chronic, orphan indication with:

- > ~9,280 new cases being diagnosed in the U.S. in 2024<sup>1</sup>
- U.S. CML prevalence today is ~110K and is expected to <a href="mailto:triple">triple</a> by 2040, driven by improved survival<sup>2,3</sup>
- Patients responding to treatment have a life expectancy almost the same as the general population and live decades with their disease requiring life-long treatment<sup>4</sup>

## Current Standard of Care Active-Site TKIs represent a ~\$5B Market<sup>5</sup>



<sup>.</sup> Cancer.org Key Statistics for Chronic Myeloid Leukemia, 2. Huang et al Cancer 2020; 3. Jabbour, Kantarjian, AJH 2020; 4. Bower et al., Journal of Clinical Oncology 2016; 5. Factset estimates (Note: 2023E ponatinib sales of ~\$160M)

## Frequent Switching Occurs Between TKIs, Most Commonly Due to Intolerance

~40% of people started on a TKI switch to an alternative TKI¹

- Reasons to switch may include<sup>2</sup>:
  - side effects / intolerance
  - co-morbidity
  - inadequate response
  - drug-drug interaction

Physicians are seeking additional novel therapies that are safe, efficacious and well-tolerated

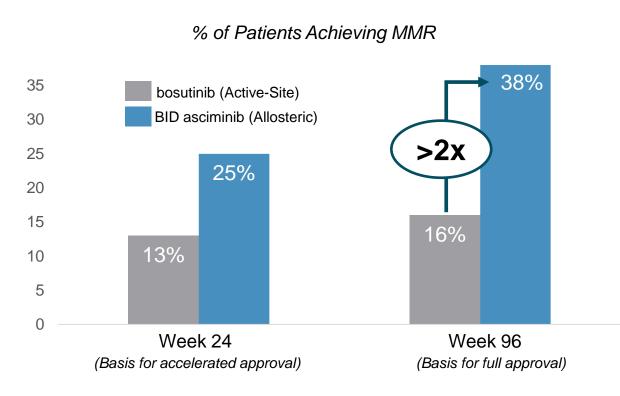
### The Only Approved Allosteric TKI for CML has Shown a Benefit Over 2<sup>nd</sup> Gen Active-site TKIs, Leading to Blockbuster Expectations

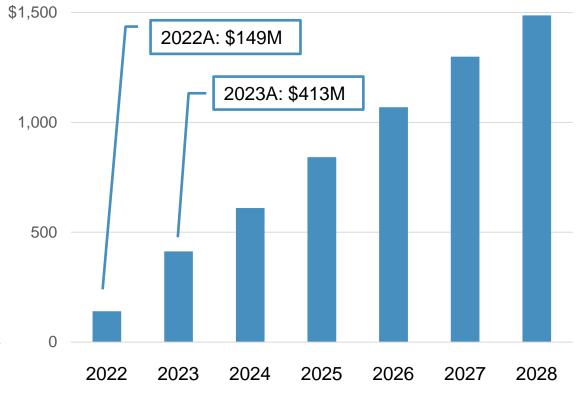
- Asciminib showed >2x improvement in MMR in 3L patients over 96 weeks<sup>1</sup> in Phase 3
- Asciminib also had a ~3x lower discontinuation rate

than bosutinib over 96 weeks<sup>2</sup>



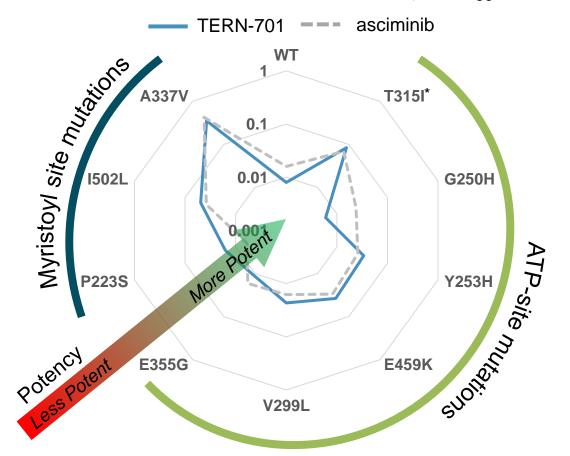






## TERN-701 Potency Suggests Anti-Tumor Activity Comparable to asciminib; With Opportunities to Differentiate

#### *In vitro* BCR-ABL Inhibition (μM IC<sub>50</sub>)





In non-clinical assays, **TERN-701 demonstrated a similar profile to asciminib**including high potency against:

- wild type BCR-ABL, and
- most-common mutations occurring in patients treated with active-site TKIs



**TERN-701** could have optimized dosing & fewer drug-drug interactions vs asciminib

## **Asciminib (Scemblix) Has Multiple Limitations that Represent Opportunities for TERN-701**

TERN-701 has potential to be the best-in-class allosteric inhibitor, building on the advantages of asciminib with potential for simpler, more optimized dosing



#### IMPORTANT SAFETY INFORMATION AND INDIC

HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use

SCEMBLIX® (asciminib) tablets, for oral Initial U.S. Approval: 2021

SCEMBLIX is a kinase inhibitor indicated for the treatment of adult patients

· Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs). (1)

This indication is approved under accelerated approval based on major molecular response (MMR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a

- . Ph+ CML in CP with the T315I mutation. (1)
  - --- DOSAGE AND ADMINISTRATION
- Recommended Dosage in Ph+ CML in CP: 80 mg orally once daily or 40
- Recommended Dosage in Ph+ CML in CP with the T315I Mutation: 20 mg orally twice daily. (2.2)
- Avoid food for at least 2 hours before and 1 hour after taking SCEMBLD
- . Swallow tablets whole. Do not break, crush, or chew the tablets. (2.5) ---DOSAGE FORMS AND STRENGTHS-
- Film-coated tablets: 20 mg and 40 mg (3) -- CONTRAINDICATION

-WARNINGS AND TRECAUTIONS-

 Myelosuppression: Severe thrombocytopenia and neutropenia events may occur. Monitor complete blood counts regularly during therapy and manage

- · Hypersensitivity: May cause hypersensitivity reactions. Monitor for signs and symptoms and initiate appropriate treatment as clini
- <u>Cardiovascular Toxicity</u>: Cardiovascular toxicity may occur. Mon and symptoms. Initiate appropriate treatment as clinically indicate
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of eproductive potential of the potential risk to a fetus and to use eff contraception. (5.6, 8.1, 8.3)

#### ....ADVERSE REACTIONS

Most common adverse reactions (≥ 20%) are upper respiratory tract infections, musculoskeletal pain, fatigue, nausea, rash, and diarrhea. Most common laboratory abnormalities (> 20%) are platelet count de triglycerides increased, neutrophil count decreased, hemoglobin decr creatine kinase increased, alanine aminotransferase increased, lipase

To report SUSPECTED ADVERSE REACTIONS, contact No Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800 1088 or www.fda.gov/medwatch.

- Strong CYP3A4 Inhibitors: Closely monitor for adverse rea concomitant use of SCEMBLIX at 200 mg twice daily. (7.1)
- Itraconazole Oral Solution Containing Hydroxypropyl-β-cyclodextrin Avoid concomitant use of SCEMBLIX at all recommended doses. (7.1)
- Certain Substrates of CYP3A4: Closely monitor for adverse reactions during concomitant use of SCEMBLIX at 80 mg total daily dose. Avoid use of SCF ABLIX at 200 mg twice daily. (7.2)
- Substrates of CYP2C9: Avoid concomitant use of SCEMBLIX at all
- 80 mg total daily dose: If unavoidable, reduce the CYP2C9 substrate dosage as necessary, (7.2) 200 mg twice daily: If unavoidable, consider alternative therapy
- with non-CYP2C9 substrate. (7.2)
- . Certain P-gp Substrates: Closely monitor for adverse reactions during use of SCEMBLIX at all recommended doses

#### **Dosage and Administration:**

- Multiple doses for different BCR-ABL variants
- Requires BID dosing in many clinical settings
- 3-hour fasting requirement (2-hours before, 1hour after)

#### **Warnings and Precautions:**

- Pancreatic toxicity
- Cardiovascular toxicity

#### **Drug Interactions:**

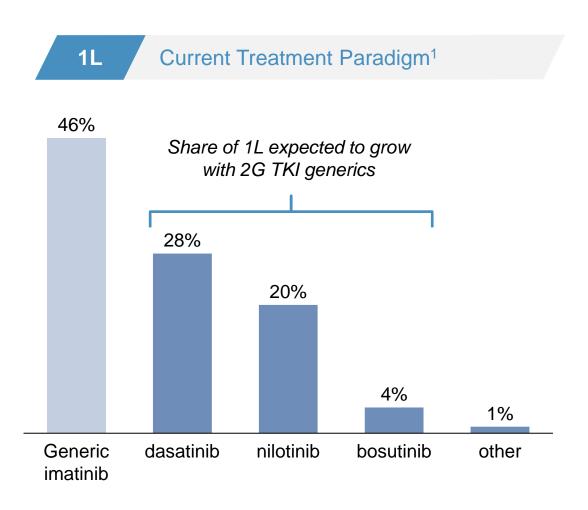
- CYP3A4 inhibitors/substrates
- CYP2C9 substrates
- P-qp substrates



## **Exploring Opportunities for TERN-701 to be a Differentiated Allosteric Inhibitor for CML Patients**

Comparison of Allosteric BCR-ABL TKIs	TERN-701 Opportunities	asciminib (Scemblix)
Anticipated full development in 2L	✓	-
Dose-optimization for improved target coverage, efficacy	✓	-
Once-daily dosing across BCR-ABL mutational spectrum	✓	=
Simpler label for prescribers (e.g., Improved DDI profile w.r.t. statins, SSRIs, macrolide antibiotics, benzodiazepines, antihypertensives)	✓	_

## Treatment Paradigm in CML Expected to Evolve, Providing a Unique Opportunity for TERN-701 in the 2L Setting



#### 1L/2L Future Paradigm

- 2G TKI use in 1L expected to grow as these drugs become generic in the coming years
- Patients will require new 2L options:
  - 1<sup>st</sup> gen imatinib is unlikely effective to sequence after a 2<sup>nd</sup> gen TKI (das / nil / bos)
  - Expected increase in intolerance with growing share of 2<sup>nd</sup> gen TKIs in 2L
- Results in an opportunity for TERN-701 as an optimized allosteric inhibitor in 2L

### Phase 1 CARDINAL Trial Design, Interim Data Expected in 2H24

Starting dose appears safe and clinically active based on emerging early clinical data from partner's ongoing Phase 1 trial in China

#### **TERN-701**

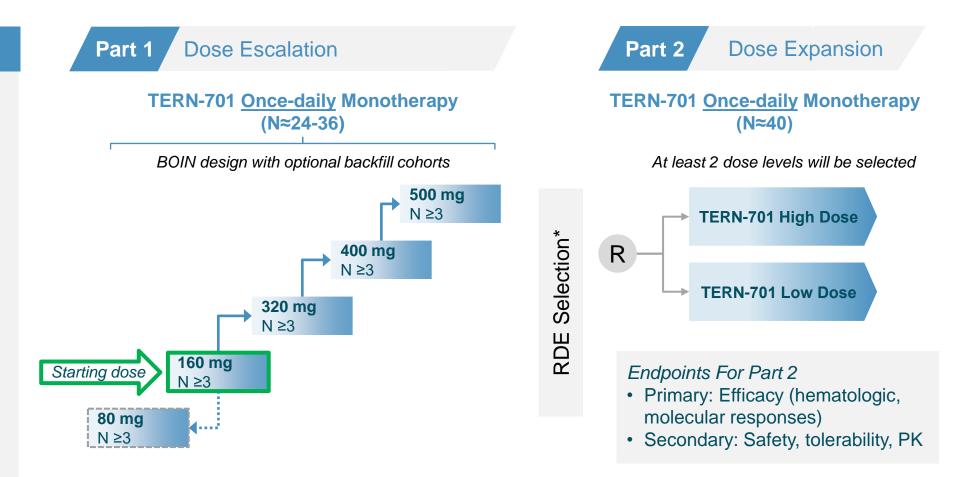
#### CARDINAL Trial Design

#### **Population**

- CP **2L and 3L** CML patients
- Treatment failure / suboptimal response to at least one prior 2nd gen active-site TKI† (i.e., 2L)
- Intolerance on current TKI (including asciminib)

#### **Endpoints For Part 1**

- Primary: Safety and tolerability
- Secondary: PK, efficacy (BCR-ABL transcript level Δ)



Patients may continue therapy beyond primary endpoint measures, through the end of study

### Next Steps for TERN-701 in CML: Interim Ph1 Data in 2H24

Anticipated Pivotal Trial Following Phase 1 CARDINAL Trial

#### 1H24

Phase 1 Global ~1-2 yrs\*



- CARDINAL trial is progressing
- Interim data from initial cohorts expected in 2H24

Phase 3 Registrational Trial 2-3 years\*

Evaluating multiple options for pivotal trial(s) including 2L and frontline patients:







### **Our Approach for Metabolic**

Focused on the discovery and development of oral, small molecule candidates within established MoAs for building future, best-in-class oral combination therapies for the treatment of obesity



## **TERN-601**

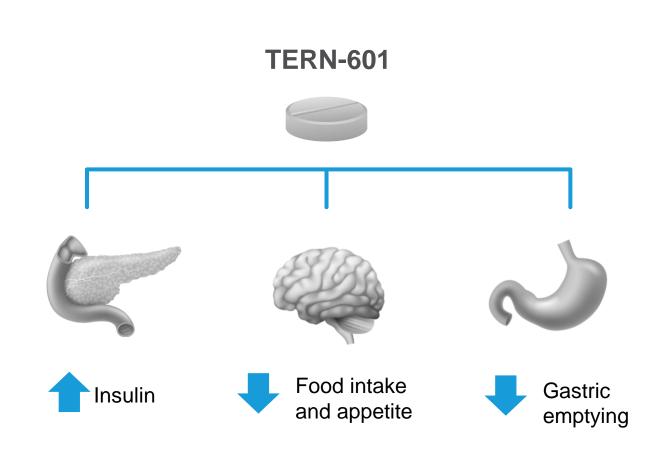
# Oral GLP-1 Agonist with Differentiated Profile for Obesity

- Small molecule (nonpeptide) with oral oncedaily dosing
- Suitable for combination and co-formulation
- Ph 1 top-line data (28day proof of concept) expected in 2H24

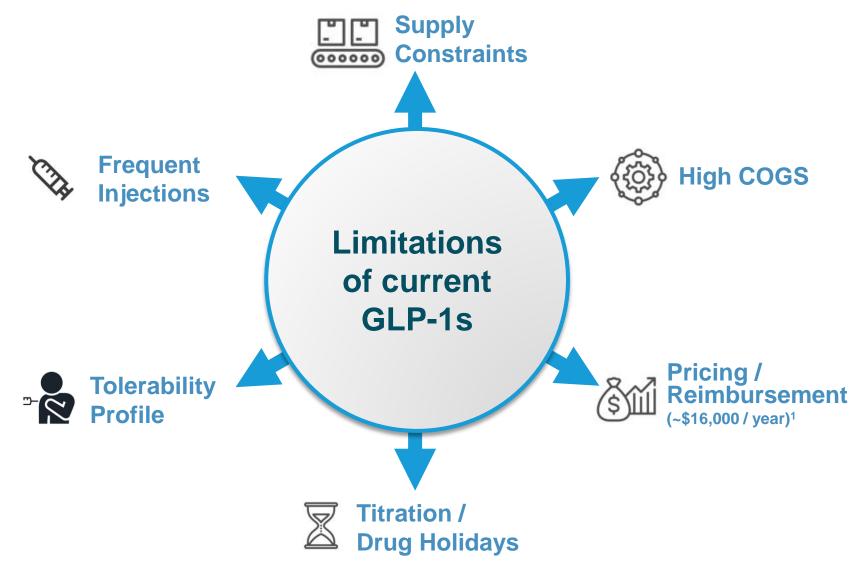
## **GLP-1 Background and Terns' Early Discovery Approach**

GLP-1 has demonstrated broad metabolic benefits in obesity and Type 2 Diabetes

- Oral GLP-1 agonists have demonstrated efficacy on weight loss, HbA1c over 28-days<sup>1</sup>, but are limited by dosing/tolerability
- Terns' GLP-1 agonist program focused on:
  - Potent, safe and effective small molecule (non-peptide) with oral once-daily dosing
  - Suitable for combination / co-formulation
  - Applicability to obesity and other indications
- Phase 1 clinical trial initiated; top-line data (28-day PoC) expected in 2H24



## Oral, Small-Molecule GLP-1s May Address Limitations of Current Injectable GLP-1s



### **TERN-601 Program Initiated with Proof-of-Concept Trial**

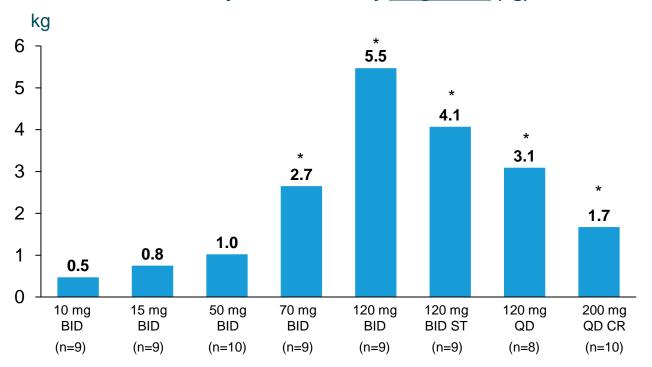
Top-line data (body weight loss over 28-days) anticipated in 2H24

**TERN-601** Single Ascending Dose Multiple Ascending Dose Part 1 Part 2 Ph 1 Trial Design **TERN-601 Once-daily Monotherapy TERN-601 Once-daily Monotherapy**  $(N \approx 40-48)$ (N≈ 72) **Population**  Healthy adults with obesity or overweight Up to 6 SAD cohorts, 30 mg starting dose (N=8 per cohort) **Endpoints**  Primary: Safety and Top-line 28-day Up to 6 MAD cohorts tolerability weight loss data (N=12 per cohort) expected in 2H24 Secondary / exploratory: PK, Δ in body weight over 28-Initial cohorts characterize PK Subsequent 28-day dose titration and tolerability to optimize cohorts (≥3 cohorts) to assess days, etc. starting dose for titration cohorts weight loss

## Oral, Small Molecule GLP-1RAs Can Demonstrate Proof of Concept Weight Loss in Trials as Short as 1 Month

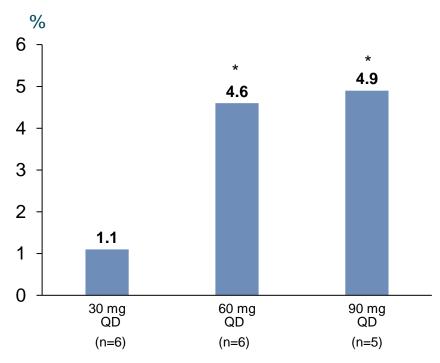
#### danuglipron 28-day Phase 1 Results

#### Placebo-adjusted mean body weight loss (kg)



#### GSBR-1290 28-day Phase 1b Results

#### Placebo-adjusted mean body weight loss (%)





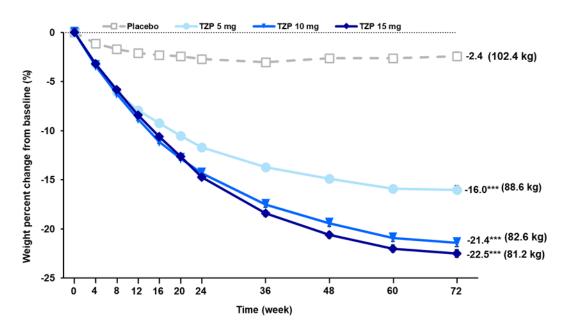
## **TERN-800 Series**

- Exploring GIPR agonist and antagonist molecules that can be combined with GLP-1s
- Candidate nomination and IND-enabling activities ongoing
- Focused on potential first-in-class oral GIPR modulators

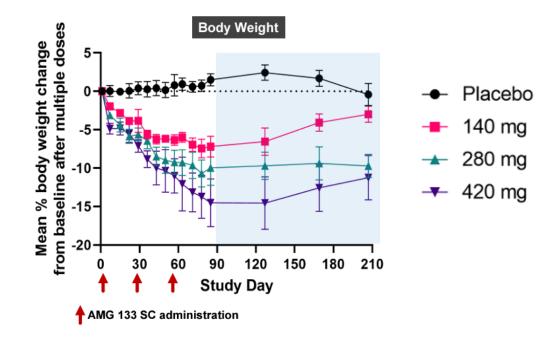
## GIPR Modulators Have Shown High Potential in Weight Loss (~15% - ~20%)

Terns discovery efforts are underway for both GIPR antagonism & agonism approaches with potential to combine with oral GLP-1

**tirzepatide**, a GLP-1 / GIPR *agonist*, showed ~20% mean weight loss over 72 weeks:



**AMG-133**, a GLP-1 agonist / GIPR *antagonist*, also showed significant weight loss up to 150 days:



# TERN-800 Series is Underway: GIPR Leads Identified, Exploring Both Agonist and Antagonist Approaches

Lead optimization efforts ongoing



- Combining internal chemistry expertise with external synthesis teams to develop initial set of '800 series compounds based on improving known scaffolds
- Supplementing efforts with computational approach to virtually screen 9 billion compounds in silico to identify additional GIPR modulators
- Focused on modulators that can be combined with GLP-1s



## **TERN-501**

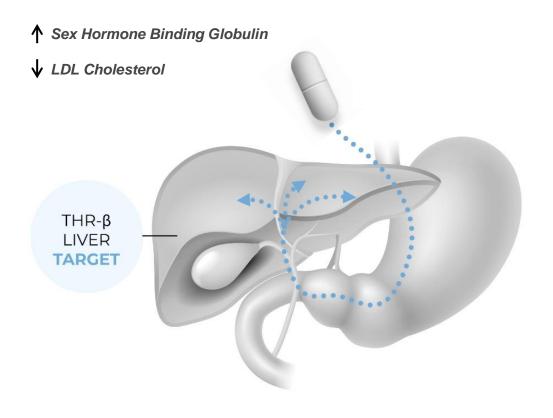
## Highly-Selective THR-β Agonist

- Potential best-in-class THR-β agonist on efficacy and tolerability based on Phase 2 clinical data
- Emerging superior profile for combinations with GLP-1s to enhance weight loss and metabolic health
- Evaluating opportunities to further develop TERN-501 as a partner therapy for cardiometabolic disease

**TERN-501** 

### **TERN-501: A Differentiated THR-β Agonist**

THR-β regulates key aspects of energy metabolism (e.g., fatty acid & lipid synthesis, liver fat removal through fatty acid oxidation)



Other THR-β agonists face limitations with off-target effects, unpredictable PK, or need for CYP metabolism

• TERN-501 was screened for a differentiated, potentially best-in-class profile:

- High β/α selectivity  $\rightarrow$  low dose, broad therapeutic window, low CV side effects and improved efficacy
- ▶ Better gastrointestinal profile vs peer molecules → improved tolerability
- Predictable PK, once-daily dosing with low drug-drug interaction potential → attractive partner for combinations
- Positive top-line DUET results announced August 2023: compelling profile of efficacy, tolerability & combinability vs peers

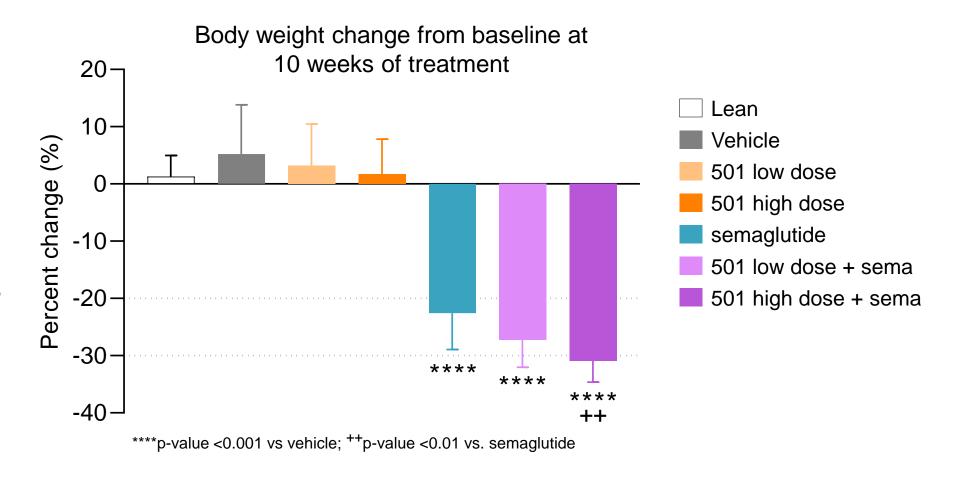
### **TERN-501 Has Best-in-Class Potential**

Comparison of THR-βs	TERN-501	Resmetirom	VK2089	ALG-055009	ASC41
Class Leading Liver Fat Reductions	✓	-	<b>√</b> -	?	-
Once-Daily Dosing	✓	<b>√</b>	?	<b>√</b>	<b>√</b>
Safe/Efficacious @ Low Dose	✓	_	?	-	-
High THR-β / α Selectivity	✓	<b>√</b>	-	✓	-
Combinability (Linear, Non-variable PK)	<b>√</b>	_	_	✓	_
Not Metabolized by CyP	✓	_	-	<b>√</b>	-
Lack of Cardiovascular AEs	<b>✓</b>	<b>√</b>	-	<b>√</b>	<b>√</b>
Lack of Central Thyroid Effects	✓	<b>√</b>	-	-	-
Lack of GI Adverse Events	✓	_	<b>√</b>	-	<b>√</b>
Total Score	9	4	2	5	3

## Non-clinical Data Suggests TERN-501 May Augment Weight Loss Effects of GLP-1R Agonist

Preliminary data in diet-induced obese (DIO) NASH mice1; study remains ongoing

- Semaglutide induces significant body weight loss after 10-weeks of treatment
- TERN-501
  significantly enhances
  body weight loss effects
  of semaglutide



# Combination of GLP-1 and THR-β Has the Potential to Improve Multiple Metabolic Disorders

Potential Beneficial Effects of Simultaneously Targeting Multiple Pathways Involved in Weight Control and Metabolism

Terns is uniquely positioned to develop an oral GLP-1 + THR-β combination

### **GLP-1R agonism**

Weight loss & CV benefits

- + Improved glycemic control

+ Weight loss

+ Insulin sensitivity

++ Liver fat reduction

++ Potential additive
/ synergistic
metabolic benefits

### THR-β agonism

Potential metabolic benefits

- + Improvements in lipids e.g., LDL, HDL, VLDL, TG, ApoB and Lp(a)
- + Reduction in liver fat and fibrosis
- + Potentially improved energy efficiency













## Conclusions

Strong Balance Sheet Multiple upcoming milestones

## **Strong Financial Position Supports Upcoming Milestones**



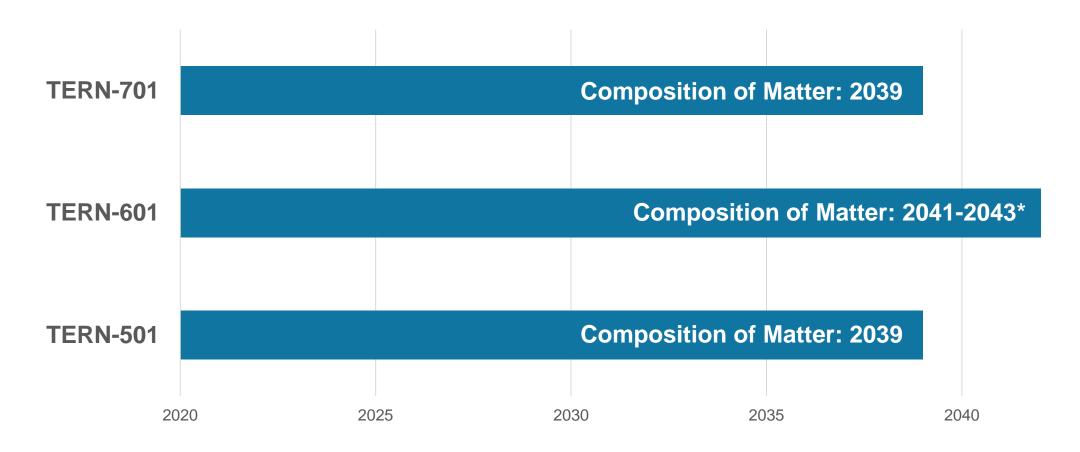
## **Key Completed and Upcoming Milestones**

Multiple clinical milestones expected across Terns' pipeline



### **Terns: Robust Intellectual Property**

In addition to patents, 5-year NCE exclusivity (plus 30 month stay) expected to apply after approval Patent applications cover polymorphs, drug product formulation and combo approach



### Mission. Vision. Core Values.

### **MISSION**

To advance transformative medicines that address serious diseases

#### **VISION**

To pioneer significant innovations across the lifecycle of drug development



**Trust**: empowered and accountable to do the right thing

**Evolve**: learning and growing from our successes, failures and changes in the environment

**Respect**: celebrating the diversity of our backgrounds, opinions and experiences

**Nurture**: fostering internal and external relationships

Soar: aiming high and being your best



## **Appendix**

## CARDINAL Design Features Multiple Differentiation Opportunities for TERN-701 in the CML Landscape

#### Improved ability to dose optimize TERN-701

- Starting dose that appears safe and clinically active
- Opportunity to efficiently develop TERN-701 as a dose-optimized allosteric inhibitor for CML

#### Inclusion of 2L chronic phase CML patients

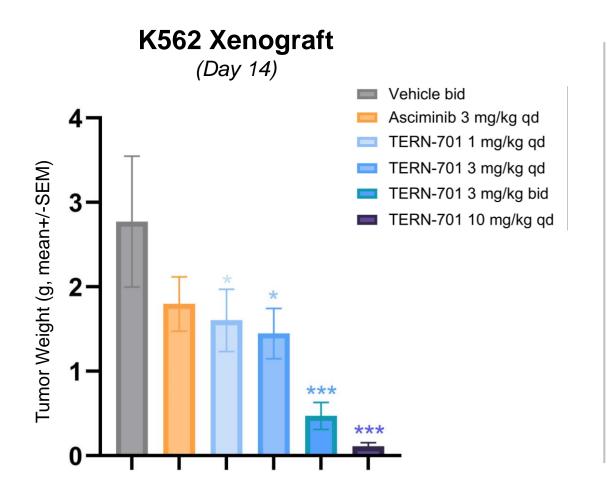
- Better positions Terns to move directly to a 2L (or earlier line) pivotal study
- No allosteric inhibitor currently approved for 2L CML patients

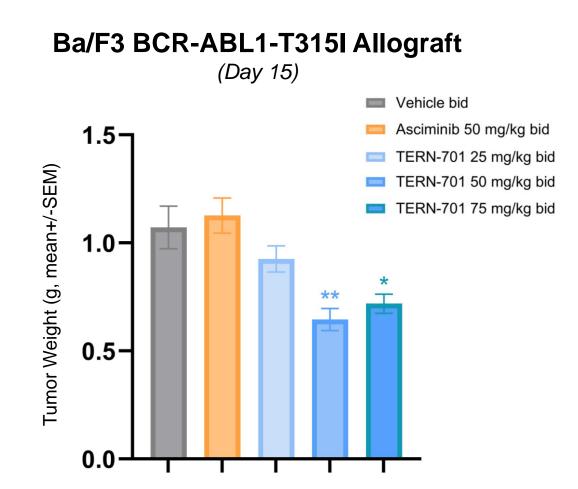
#### Allosteric MoA excitement

- High interest given limited allosteric inhibitor treatment options
- Reduced competition for trial enrollment

Opportunities
for TERN-701 to
be uniquely
positioned →
Initial data
expected in
2H24

## TERN-701 Showed a Greater Anti-Tumor Effect vs. asciminib in Non-clinical Models of CML





Source: ASPET TERN-701 poster

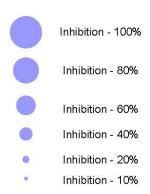
**TERNS** 

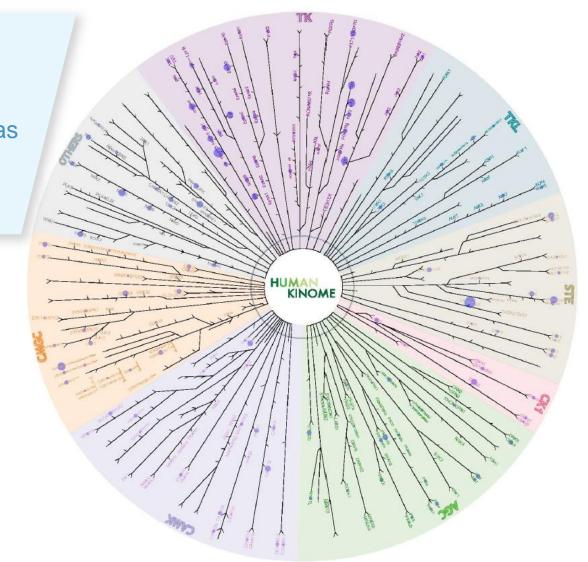
## TERN-701 Also Demonstrated High Selectivity on a Broad Kinase Panel, Suggesting Reduced Potential for Off-Target Activity

**TERN-701** was assessed at 1 μM against a panel of 375 kinases

No kinase, including wild-type ABL1, was observed to be inhibited by >50% → reduced potential for TERN-701 off-target activity

#### Dot Size by Percent Inhibition





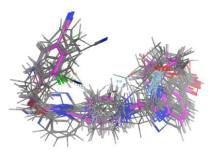
## Terns' Proprietary Model Predicts New GLP-1RA Molecular Activity with Greater Accuracy than Physics-based Evaluations

#### **Terns' Discovery Approach for GLP-1**

Begin with original reference molecule...



2 ... overlay with GLP-1 molecules with known EC<sub>50</sub> (half maximal effective concentration) data and active site binding properties...



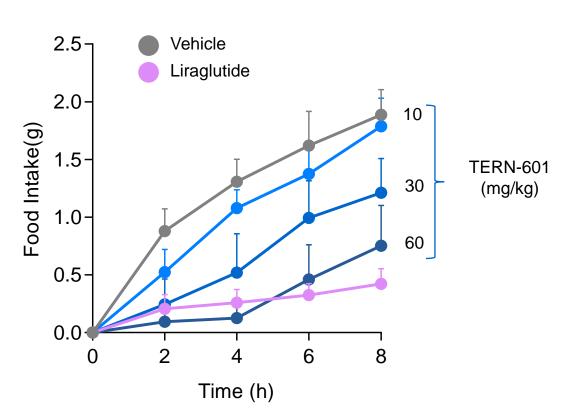
... to build a 3D QSAR model (Terns' proprietary screening tool)



- Terns' GLP-1 scaffolds are designed using our proprietary
   3D QSAR model of the GLP-1 receptor
  - Using QSAR, Terns' medicinal chemistry team can predict new GLP-1R molecular activity with greater accuracy than physics-based evaluations
- Screened 20,000+ molecular permutations to identify suitable small-molecule scaffolds with potentially improved properties relative to other GLP-1s
- Terns has synthesized multiple compounds targeting GLP-1R that exhibit varying degrees of ligand bias towards cAMP and β-arrestin
- Our lead molecule, TERN-601, is a potent GLP-1R agonist partially biased towards cAMP generation

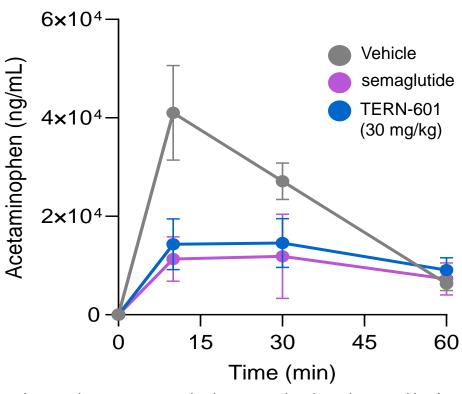
### TERN-601 Reduced Food-intake & Slowed Gastric Emptying in Humanized GLP-1R Mice

#### Cumulative food-intake



Food intake was measured in fasted mice treated with TERN-601 (10, 30, 60 mg/kg, PO) or liraglutide (0.3 mg/kg, SQ), with food available ad libitum 15 minutes post dose. Data presented as mean ±SD (n = 10/group).

### Gastric emptying

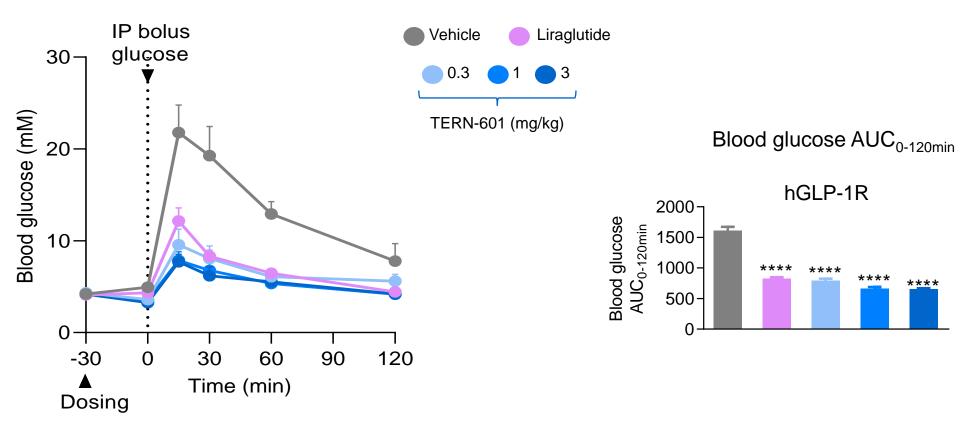


Gastric emptying was assessed using acetaminophen pharmacokinetics as a marker in fasted mice given TERN-601 (30 mg/kg, PO) or semaglutide (10 nmole/kg, SQ), followed by acetaminophen (APAP, 100 mg/kg) and glucose (2 g/kg).

Acetaminophen levels in plasma were measured at various time points by LC-MS/MS. Data presented as mean ±SD APAP plasma concentration (n = 5/group)

## TERN-601 Demonstrated Similar Activity to Peptide Control on Glucose Tolerance in Humanized GLP-1R mice

### Intraperitoneal glucose tolerance test (IPGTT) in hGLP-1R mice

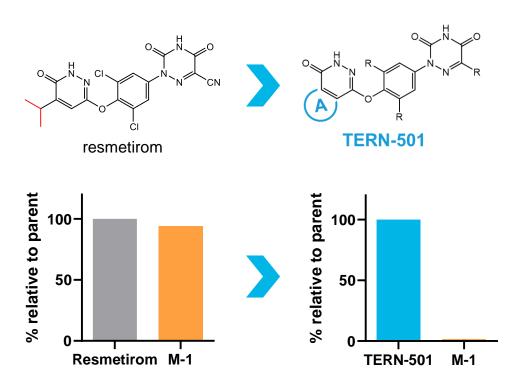


Fasted hGLP1R and WT mice received TERN-601 (0.3, 1, 3 mg/kg, PO) or liraglutide (0.3 mg/kg, SQ) before glucose challenge (2 g/kg IP) and blood glucose was monitored for 120 minutes. Data presented as mean  $\pm$ SD (n = 5-7/group) ns= not significant; \*\*\*\*p<0.0001 vs. Vehicle.

### **TERN-501 Improved PK & THR-β Selectivity**

#### Differentiated and excellent candidate for co-formulation

#### **TERN-501: Improved Pharmacokinetics**



#### **TERN-501: Improved THR-**β ratio

