



# TERNs

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PHARMACEUTICALS

## Company Overview

NASDAQ: TERN

**April 2024**

# Forward-Looking Statements and Disclaimers

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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



De-risked and accelerated development pathways



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

## 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

PROGRAM	MECHANISM	INDICATION	PRECLINICAL	EARLY-STAGE CLINICAL DEVELOPMENT	LATE-STAGE CLINICAL DEVELOPMENT	STATUS
<b>Oncology</b>						
TERN-701	Allosteric BCR-ABL Inhibitor	CML	Phase 1 		Anticipated registrational trial following Ph 1 trial	Ph1 CARDINAL Trial initiated Interim data from initial cohorts in 2H24
<b>Metabolic</b>						
TERN-601	Oral GLP-1R Agonist	Obesity	Phase 1			Phase 1 initiated Top-line data (28-day PoC) 2H24
TERN-501 combination	THR-β Agonist + Metabolic Agent	Obesity	Preclinical			Preclinical activities underway
TERN-800 Series	GIPR Modulators	Obesity	Lead optimization			Lead optimization underway Candidate nomination & IND-enabling activities ongoing

Out-licensed to Hansoh Pharma (HS 10382) in the Greater China region; Ph 1 trial ongoing in China; Terns eligible for up to \$ 67M in clinical, regulatory and sales-based milestones, mid single digit percentage royalties on net sales; certain milestones are subject to the availability of additional data and future funding  
PoC: Proof of concept



# TERN-701

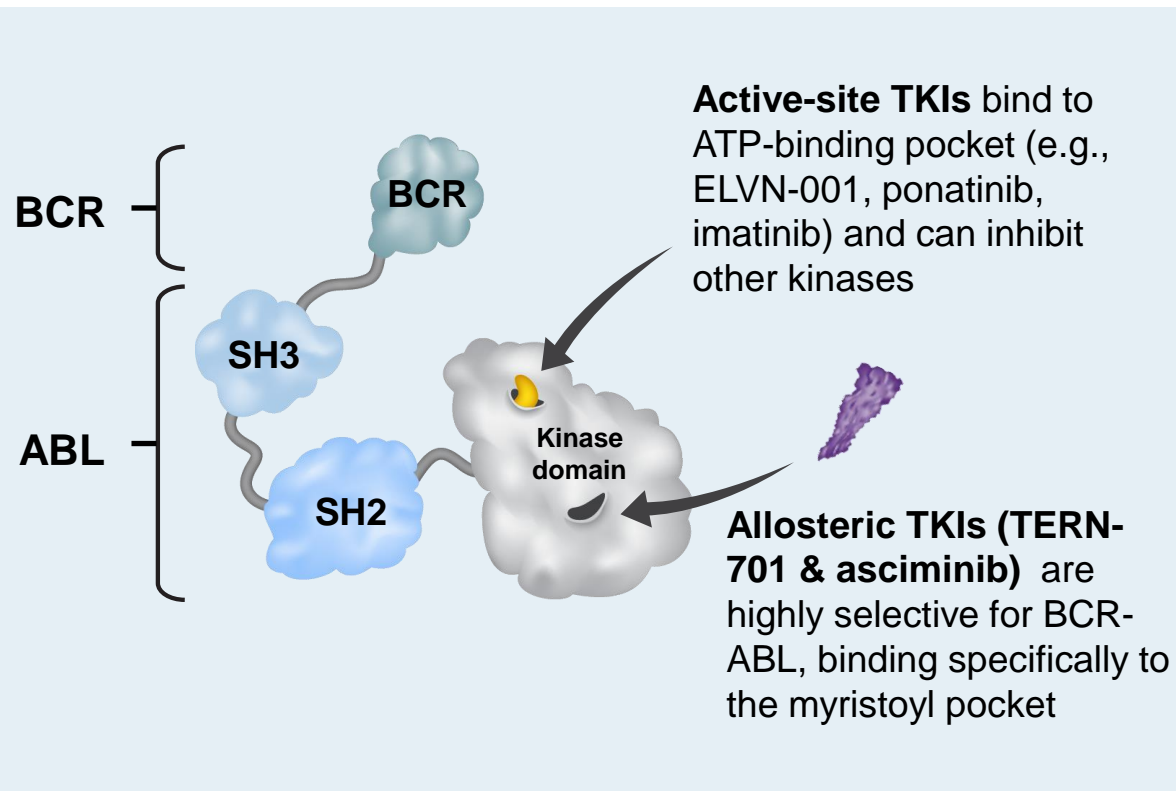
## Allosteric BCR-ABL TKI for Chronic Myeloid Leukemia

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- Allosteric TKIs have significant efficacy improvement over active-site TKIs
- CML is a \$5B orphan indication with need for multiple agents and limited allosteric competition
- TERN-701 Phase 1 trial (CARDINAL) progressing; interim data in 2H24

*TERN-701 is an internally-developed allosteric TKI with an expected profile  $\geq$  asciminib*

Active BCR-ABL1  $\rightarrow$  Cell proliferation / reduced apoptosis



Inactive BCR-ABL1  $\rightarrow$  Cell death

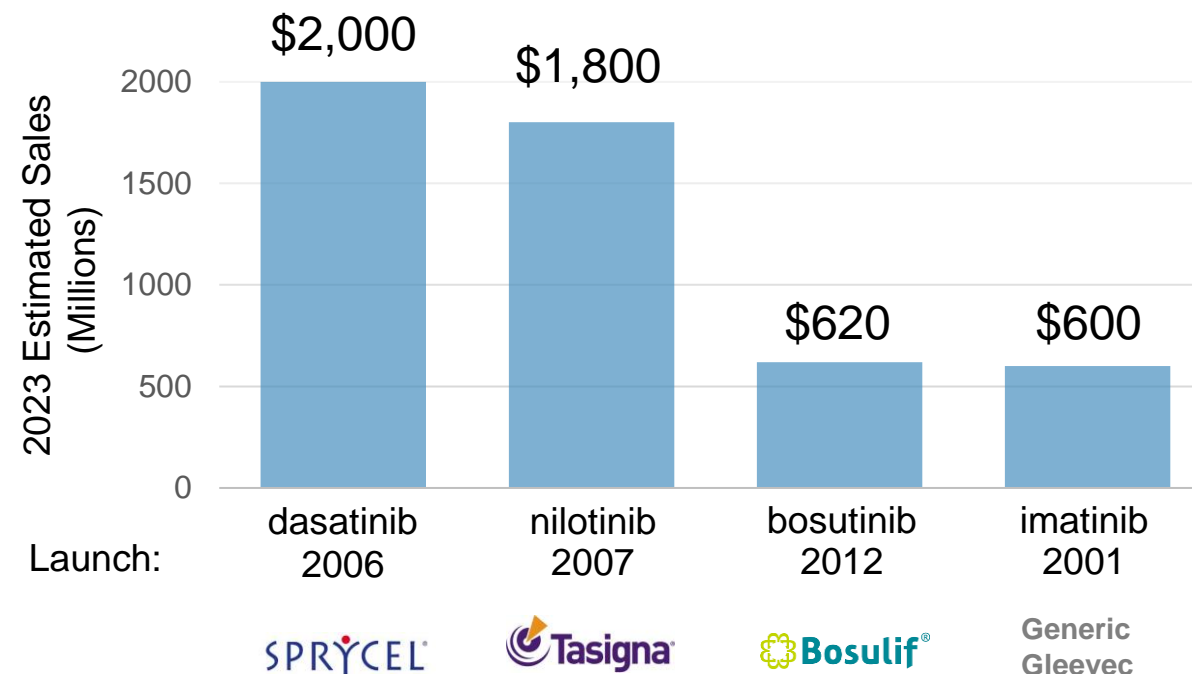
- CML is a **chronic, orphan indication** with a **sizeable market (>\$5B)** and a need for **multiple agents**, driven by lifelong treatment and frequent switching
- **Allosteric** TKIs have shown  $\sim 2x$  efficacy improvement over older standard-of-care active-site TKIs and are better tolerated, 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
- TERN-701 is the **only other allosteric** in development with the potential to differentiate from asciminib in **efficacy and ease of use** (e.g., food effect)
- **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 **triple** 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>



1. 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

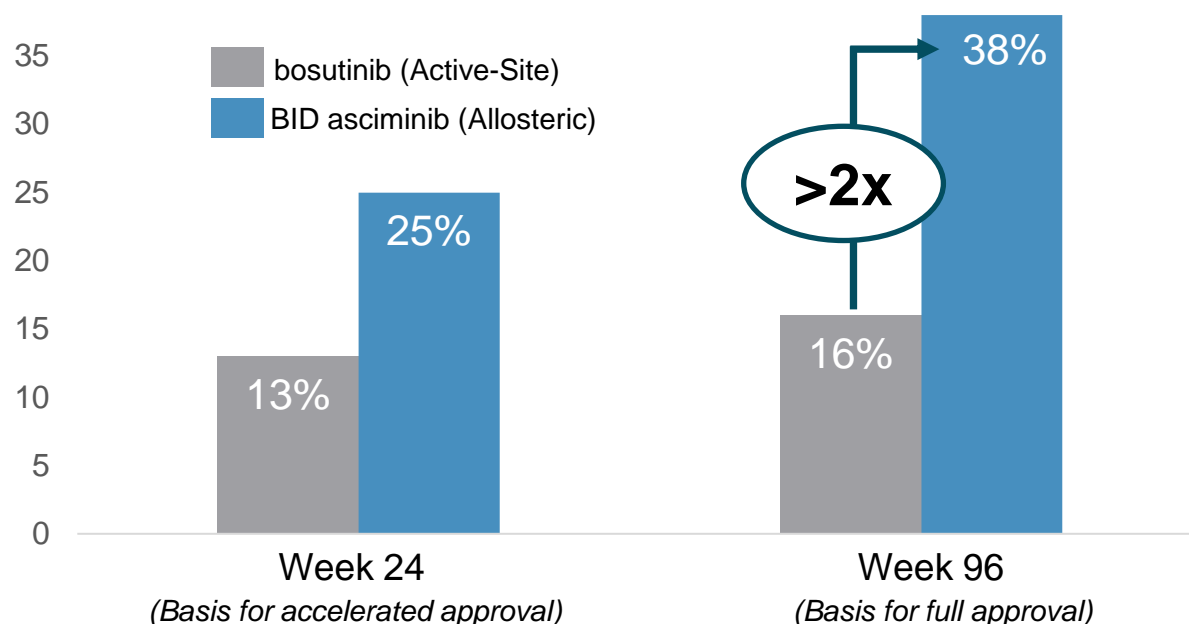
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- ~40% of people started on a TKI switch to an alternative TKI<sup>1</sup>
- Reasons to switch may include<sup>2</sup>:
  - side effects / intolerance
  - co-morbidity
  - inadequate response
  - drug-drug interaction
- Physicians are seeking additional novel therapies that are **safe, efficacious** and **well-tolerated**

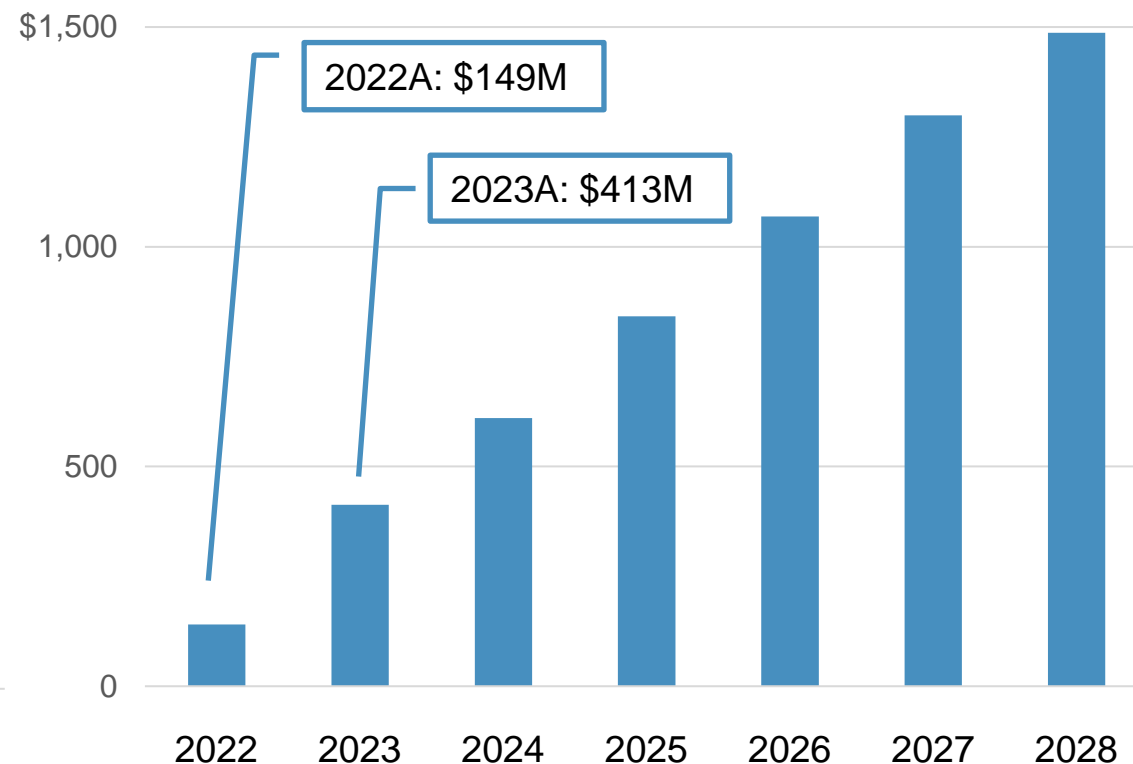
# The Only Approved Allosteric TKI for CML has Shown a Benefit Over 2<sup>nd</sup> Gen Active-site TKIs, Leading to Blockbuster Expectations

- 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>
- Analysts expect asciminib to rapidly approach **blockbuster sales**

% of Patients Achieving MMR



Consensus Sales Estimates (\$mm)<sup>3</sup>



Note: 3L: 3<sup>rd</sup> line; BID: twice-daily; MMR: major molecular response; Scemblix has 3L+ U.S. market share of NBRx 43%, TRx 22% as of 4Q23 (NVS 4Q23 Earnings)

1. [Scemblix Prescribing Information](#) 2. (8% asciminib vs 26% bosutinib) 3. Estimates from EvaluatePharma; may include sales beyond 3L setting

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

*TERN-701 has the potential to be a differentiated BCR-ABL inhibitor with advantages over asciminib, including more convenient dosing to improve treatment options and quality of life for people living with CML*

**SCSEMBLIX®**  
(asciminib) 20 mg, 40 mg tablets

**IMPORTANT SAFETY INFORMATION AND INDICATIONS**

**HIGHLIGHTS OF PRESCRIBING INFORMATION**  
These highlights do not include all the information needed to use SCSEMBLIX safely and effectively. See full prescribing information for SCSEMBLIX.

**SCSEMBLIX® (asciminib) tablets, for oral use**  
Initial U.S. Approval: 2021

**INDICATIONS AND USAGE**  
SCSEMBLIX is a kinase inhibitor indicated for the treatment of adult patients with:

- 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 confirmatory trial(s).
- 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 mg twice daily. (2.1)
- Recommended Dosage in Ph+ CML in CP with the T315I Mutation:** 200 mg orally twice daily. (2.2)
- Avoid food for at least 2 hours before and 1 hour after taking SCSEMBLIX. (2.5)
- 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)

**CONTRAINDICATIONS**

None. (4)

**WARNINGS AND PRECAUTIONS**

- Myelosuppression:** Severe thrombocytopenia and neutropenia events may occur. Monitor complete blood counts regularly during therapy and manage by treatment interruption or dose reduction. (2.4, 5.1)
- Hypersensitivity:** May cause hypersensitivity reactions. Monitor patients for signs and symptoms and initiate appropriate treatment as clinically indicated. (5.4)
- Cardiovascular Toxicity:** Cardiovascular toxicity may occur. Monitor patients with history of cardiovascular risk factors for cardiovascular and symptoms. Initiate appropriate treatment as clinically indicated and symptoms. (5.5)
- Embryo-Fetal Toxicity:** Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective 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. (6) Most common laboratory abnormalities (≥ 20%) are platelet count decreased, triglycerides increased, neutrophil count decreased, hemoglobin decreased, creatine kinase increased, alanine aminotransferase increased, lipase increased, and amylase increased. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

**DRUG INTERACTIONS**

- Strong CYP3A4 Inhibitors:** Closely monitor for adverse reactions during concomitant use of SCSEMBLIX at 200 mg twice daily. (7.1)
- Itraconazole Oral Solution Containing Hydroxypropyl-β-cyclodextrin:** Avoid concomitant use of SCSEMBLIX at all recommended doses. (7.1)
- Certain Substrates of CYP3A4:** Closely monitor for adverse reactions during concomitant use of SCSEMBLIX at 80 mg total daily dose. Avoid use of SCSEMBLIX at 200 mg twice daily. (7.2)
- Substrates of CYP2C9:** Avoid concomitant use of SCSEMBLIX at all recommended doses.
  - 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 concomitant use of SCSEMBLIX at all recommended doses. (7.2)

## Dosage and Administration:

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

## Warnings and Precautions:

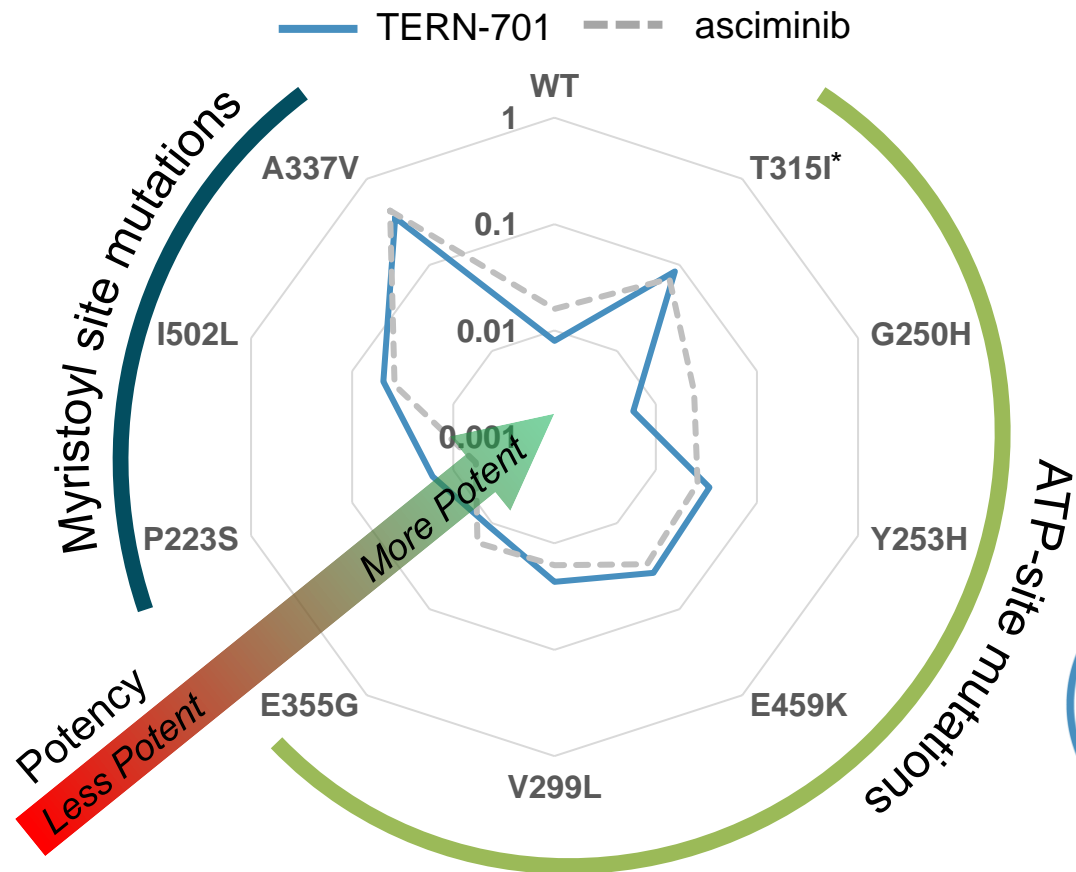
- Pancreatic toxicity
- Cardiovascular toxicity

## Drug Interactions:

- CYP3A4 inhibitors/substrates
- CYP2C9 substrates
- P-gp substrates

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

*In vitro* BCR-ABL Inhibition ( $\mu\text{M IC}_{50}$ )



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 & easier use vs asciminib

Note: WT (wild-type) and BCR-ABL mutations were evaluated in an ABL auto-phosphorylation assay  
 \* T315i mutation was evaluated in a cell proliferation assay

# TERN-701 PK Supports Once-daily Dosing Without Regard to Food

TERN-701

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

## Favorable TERN-701 Pharmacokinetic Profile

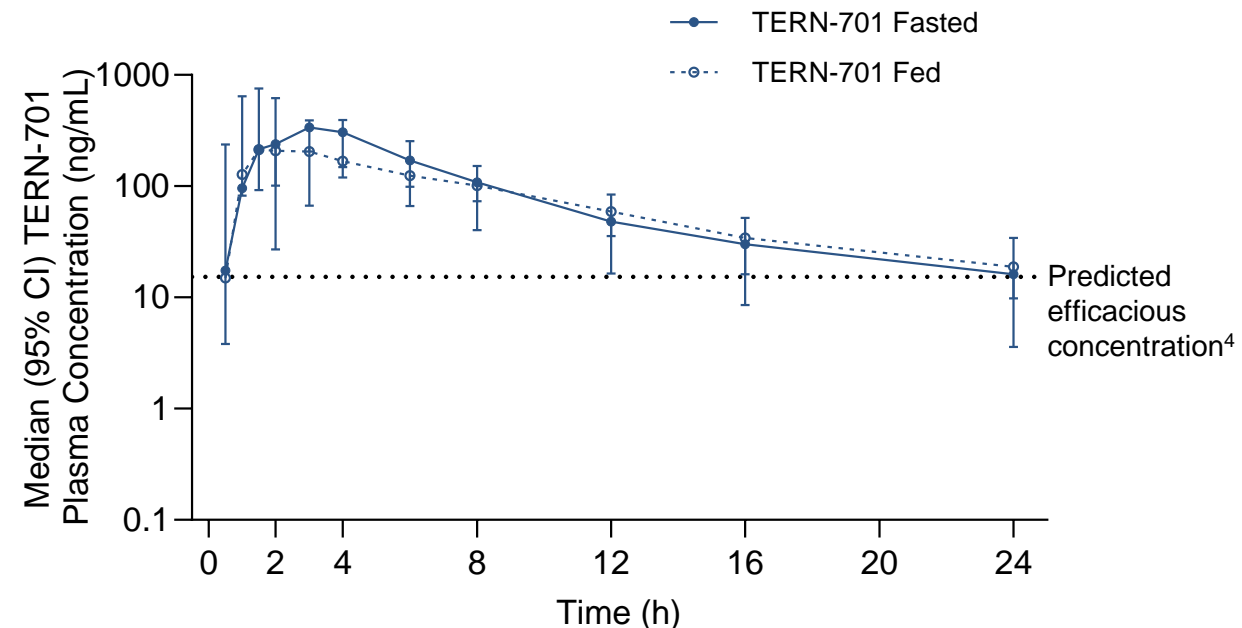
- Linear PK with approximately **dose proportional increase in exposure**<sup>1</sup>
- Median half-life of **8-12 hours supporting QD dosing**

## Consistent PK Across Populations

- PK profile of TERN-701 in Western healthy volunteers were **generally consistent** with that observed in the Phase 1 clinical study in Chinese CML patients<sup>2</sup>

## No TERN-701 Food Effect

- **No clinically significant difference in TERN-701 exposure (AUC)** when dosed fasted or with a high-fat meal<sup>3</sup>



1. Across single dose TERN-701 range of 20 mg to 160 mg  
2. Phase 1 study evaluating same doses led by Hansoh, Terns' corporate partner in China  
3. TERN-701 80 mg dose; asciminib (40mg) change in exposure ( $\Delta AUC_{inf}$ ) from fed relative to fasted was (62%)  
4. Effective plasma IC90 for the native BCR-ABL KCL-22 cell line

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)

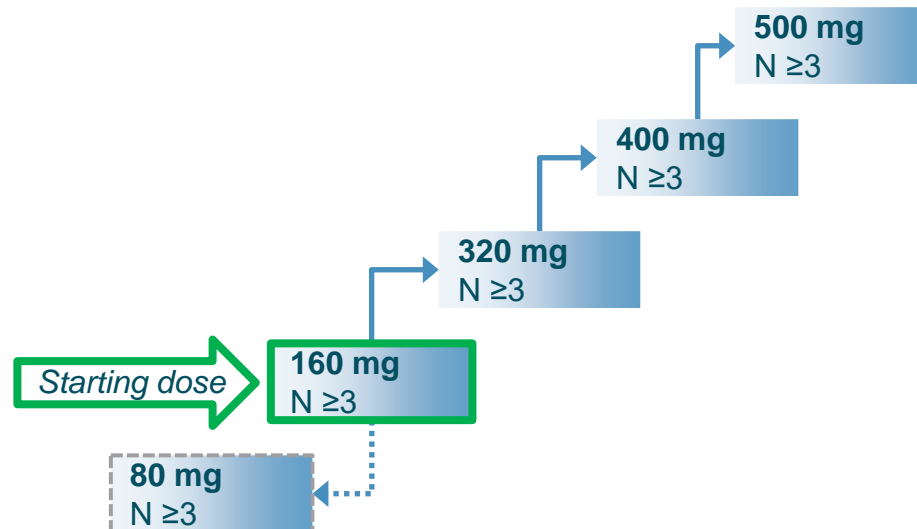
#### Endpoints For Part 1

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

## Part 1 Dose Escalation

### TERN-701 Once-daily Monotherapy (N~24-36)

BOIN design with optional backfill cohorts

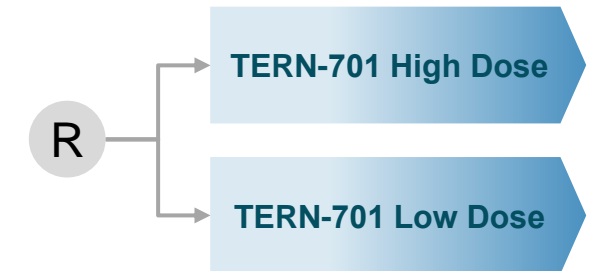


## Part 2 Dose Expansion

### TERN-701 Once-daily Monotherapy (N~40)

At least 2 dose levels will be selected

RDE Selection\*



#### Endpoints For Part 2

- Primary: Efficacy (hematologic, molecular responses)
- Secondary: Safety, tolerability, PK

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

Note: Terns starting dose represents 4X that of the 40mg starting dose in the China Phase 1 trial of TERN-701

† 2<sup>nd</sup> gen active-site TKI = dasatinib, nilotinib, or bosutinib

\*RDE = recommended doses for expansion; will be selected following a Part 1 interim analysis; CP: Chronic phase, BOIN: Bayesian optimal interval

# Next Steps for TERN-701 in CML

*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 frontline patients and second line:

**Phase 3 Monotherapy**  
*Frontline CML patients*

**Phase 3 Monotherapy**  
*2L+ CML 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

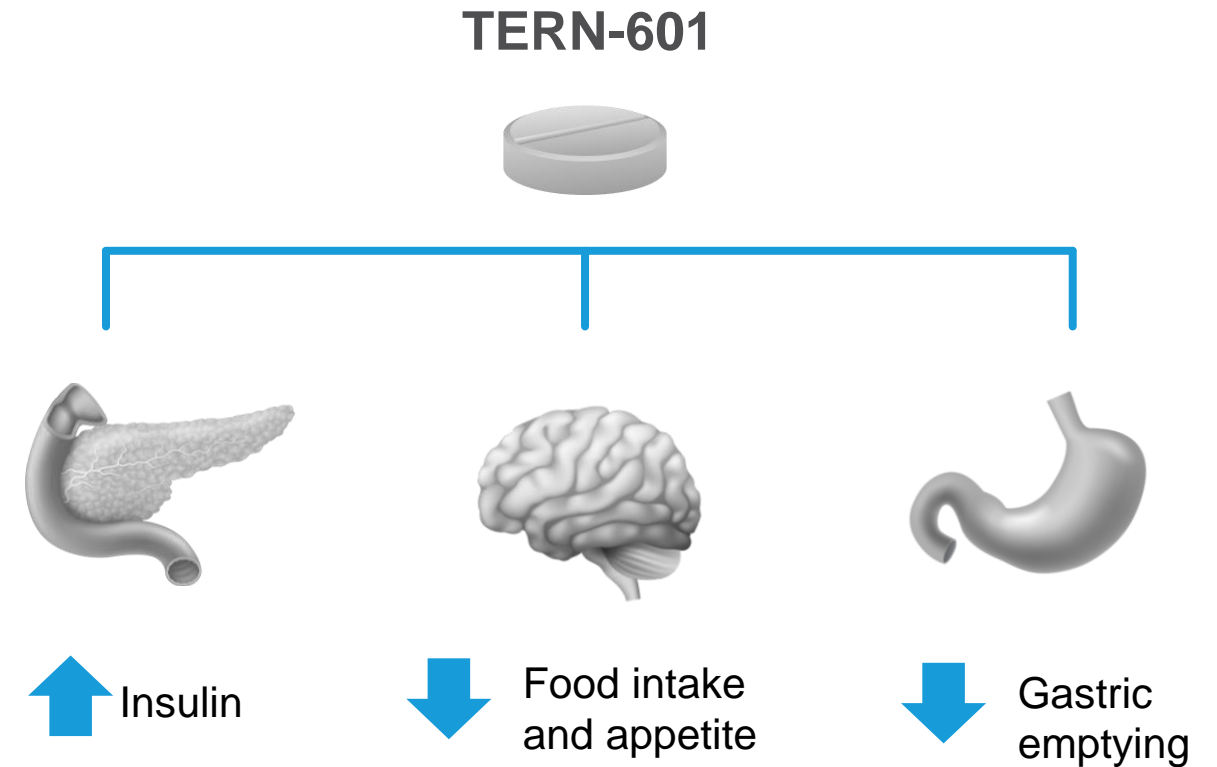
## Oral GLP-1 Agonist with Differentiated Profile for Obesity

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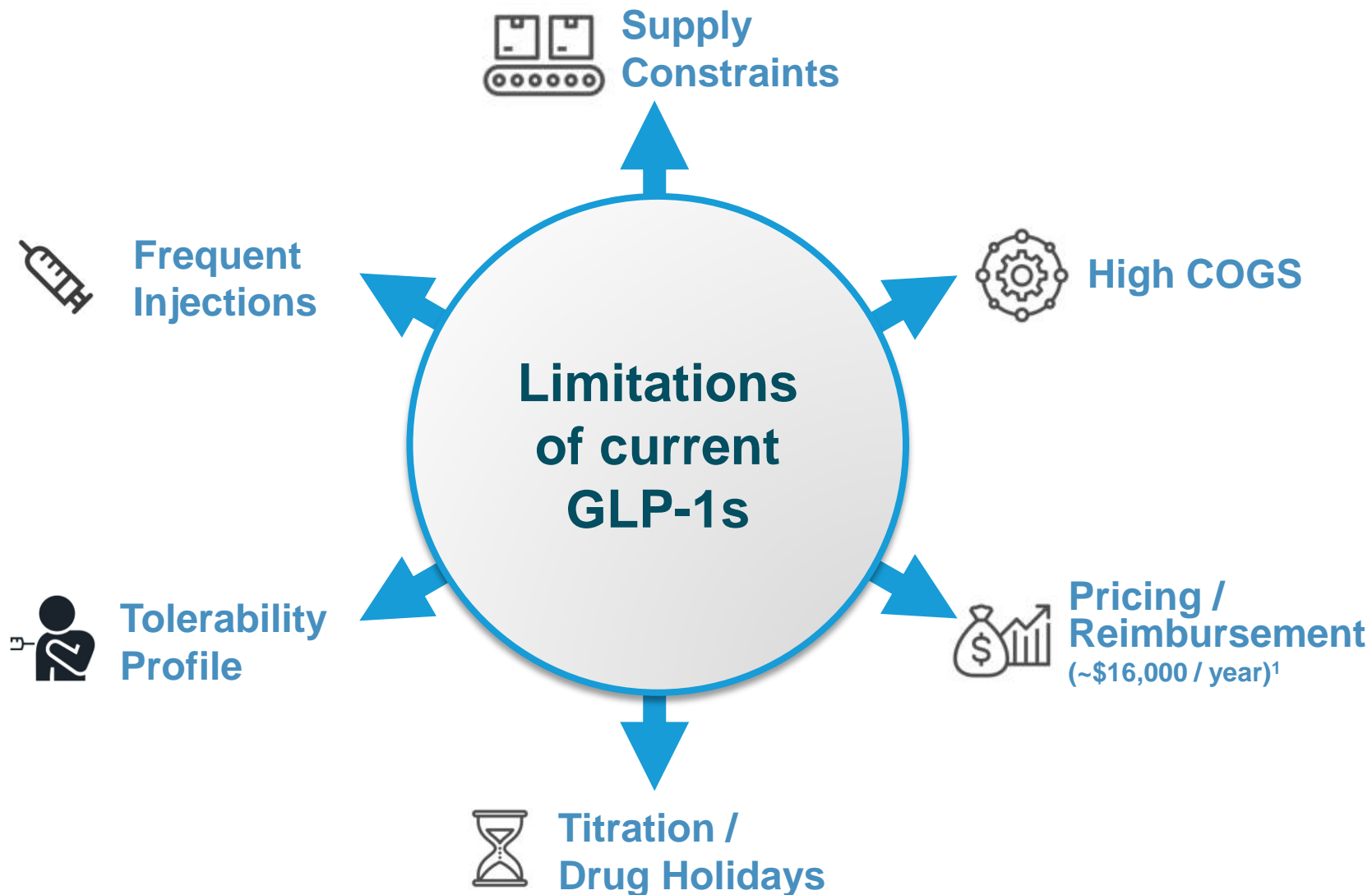
- Small molecule (non-peptide) with oral once-daily dosing
- Suitable for combination and co-formulation
- Ph 1 top-line data (28-day proof of concept) expected in 2H24

*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

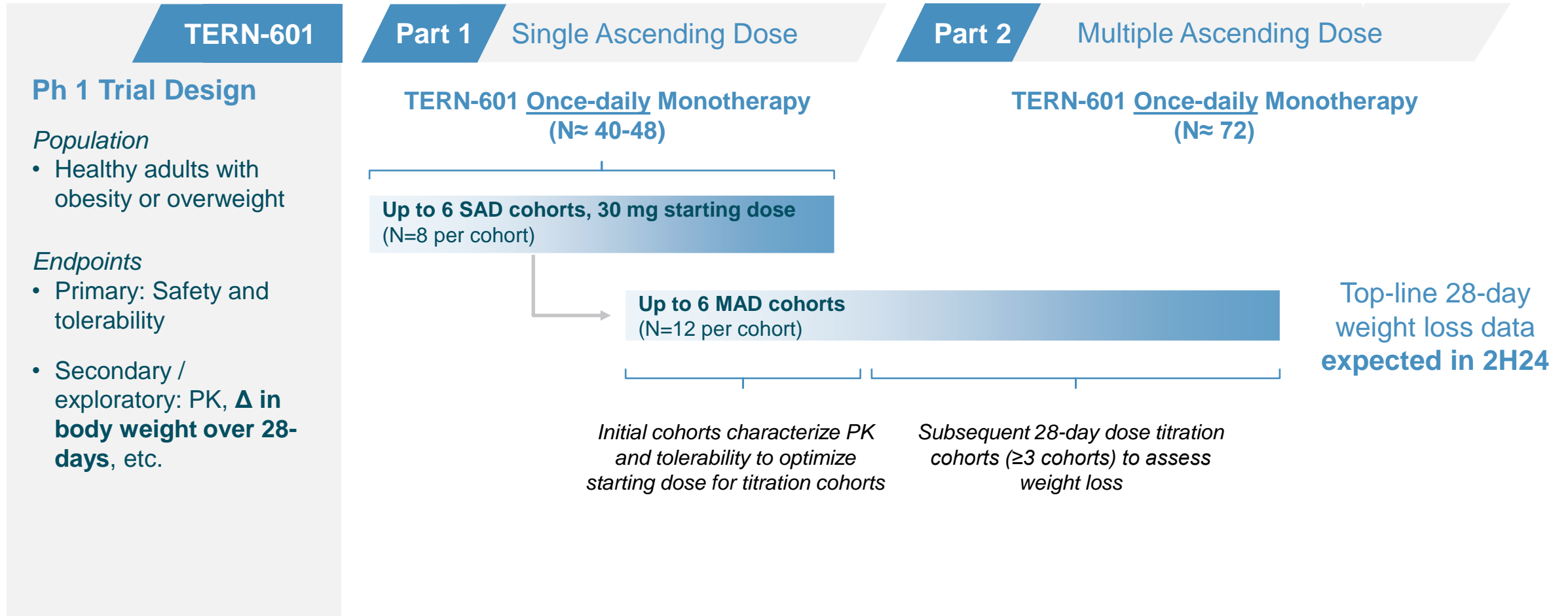


1. [Novocare](#): Wegovy has a list price of \$1,349 / package \* 12 pkgs/year

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

TERN-601

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

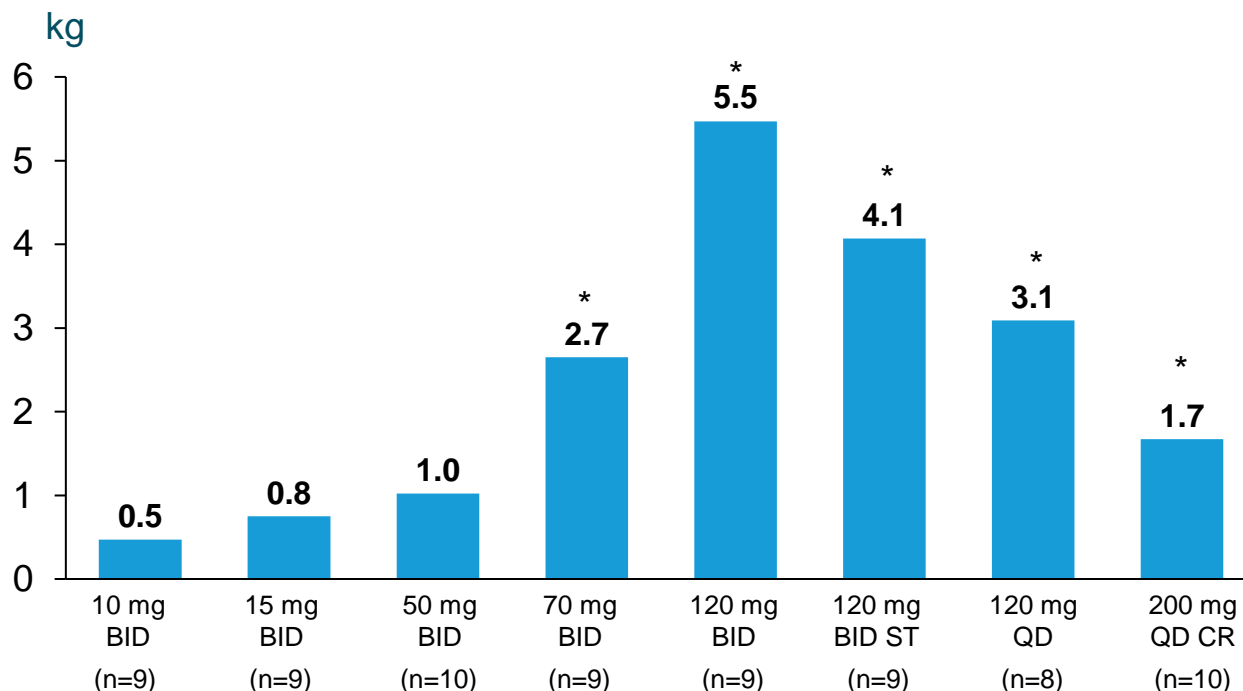


SAD participants with Body Mass Index (BMI) of  $\geq 25$  to  $< 40$  kg/m<sup>2</sup>; MAD participants with BMI of  $\geq 27$  to  $< 40$  kg/m<sup>2</sup>

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

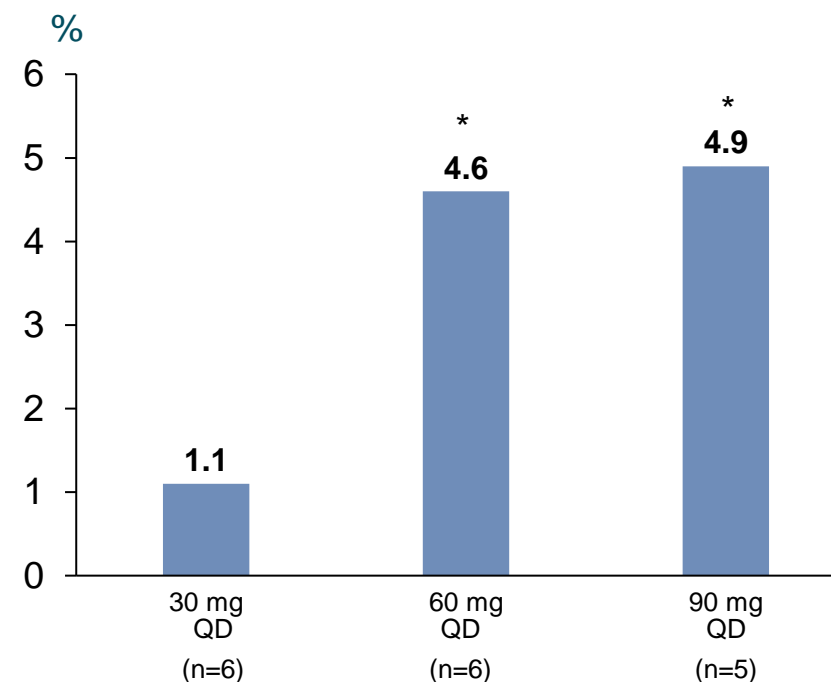
## danuglipron 28-day Phase 1 Results

Placebo-adjusted mean body weight loss (kg)



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

Placebo-adjusted mean body weight loss (%)



Source: [Nature](#) and Company press releases

QD, once daily; BID, twice daily; ST, slow titration; CR, controlled-release; HbA1c, glycated hemoglobin

\* Statistically significant vs placebo



## TERN-800 Series

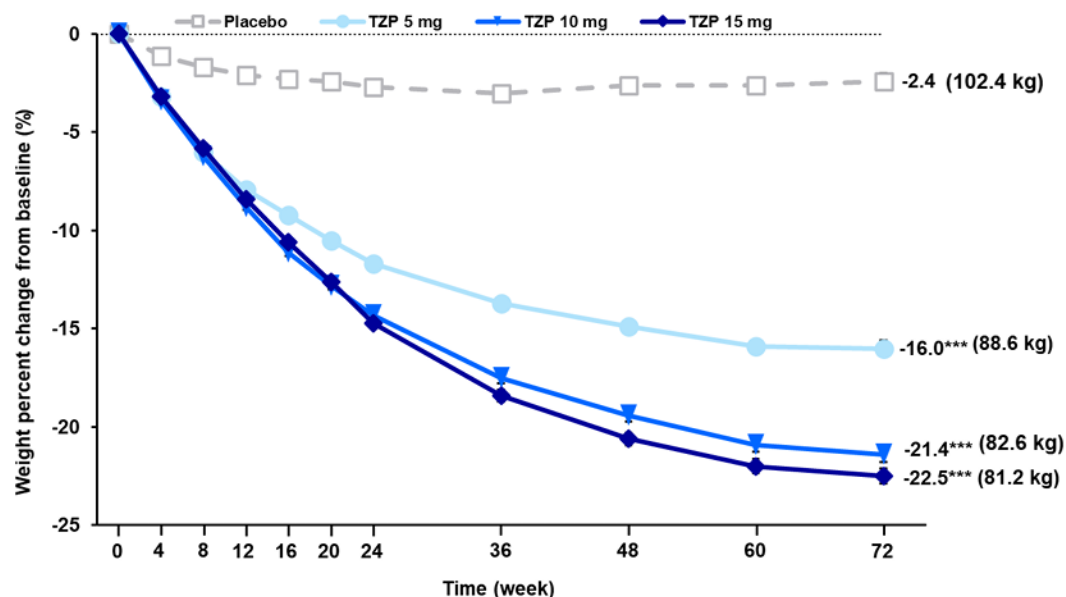
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- Exploring GIPR agonist and antagonist molecules that can be combined with GLP-1s
- Candidate nomination and IND-enabling activities ongoing
- Focused on potential first-in-class oral GIPR modulators

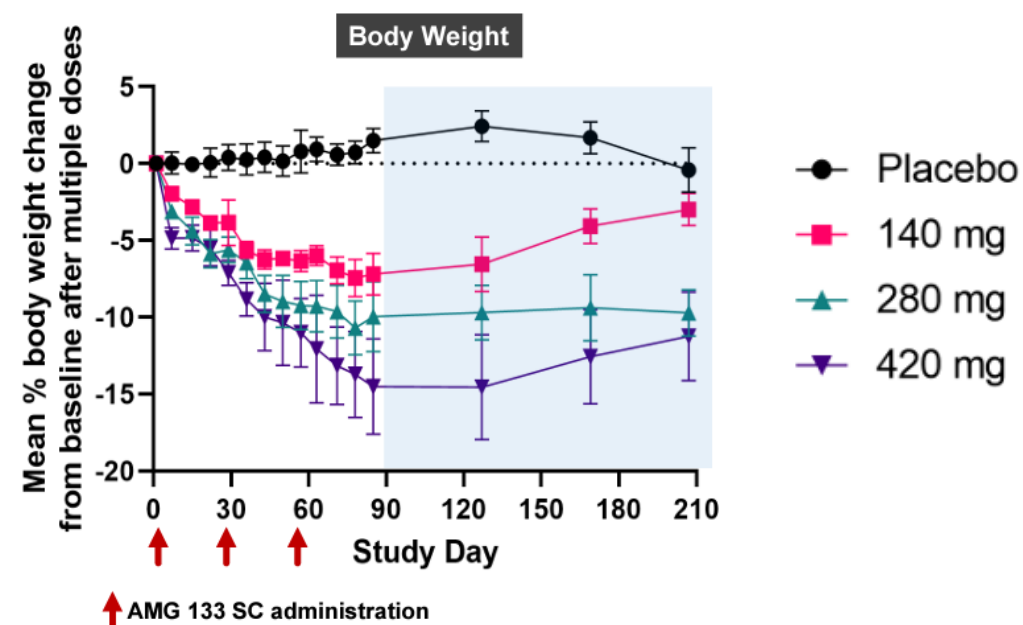
# GIPR Modulators Have Shown High Potential in Weight Loss (~15% - ~20%)

*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- $\beta$ Agonist

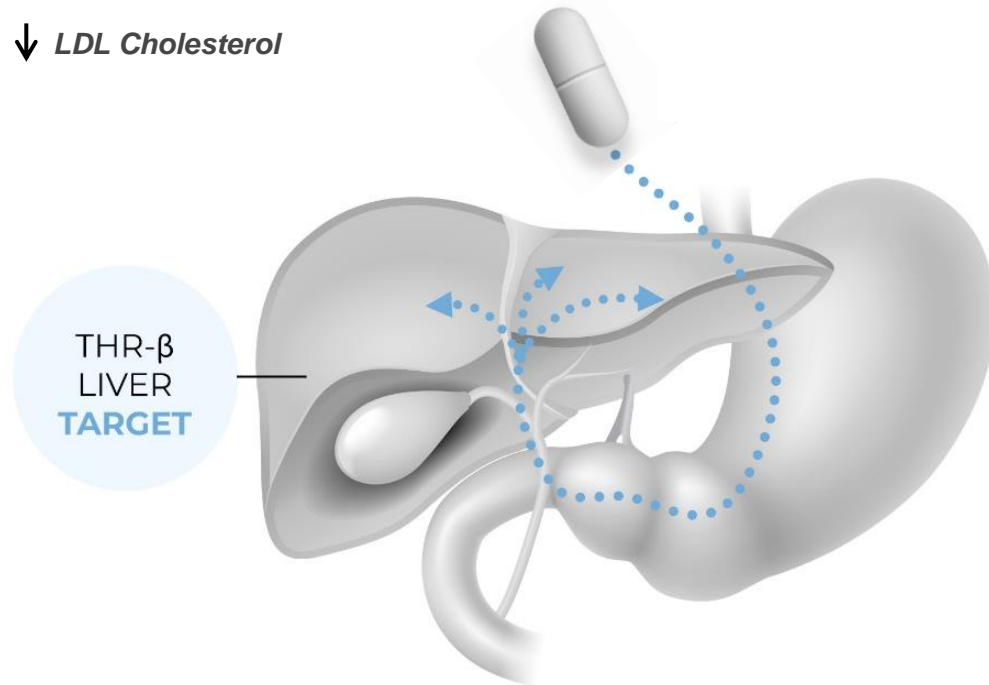
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- Potential best-in-class THR- $\beta$  agonist on efficacy and tolerability based on Phase 2 clinical data
- Emerging superior profile for combinations with GLP-1s to enhance weight loss and metabolic health
- Evaluating opportunities to further develop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

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

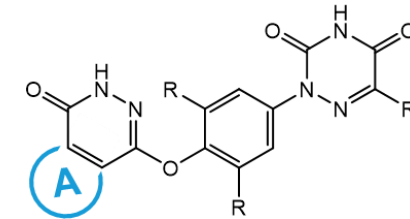
↑ Sex Hormone Binding Globulin

↓ LDL Cholesterol



Other THR- $\beta$  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**:



TERN-501

- High  $\beta/\alpha$  selectivity → 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

TERN-501

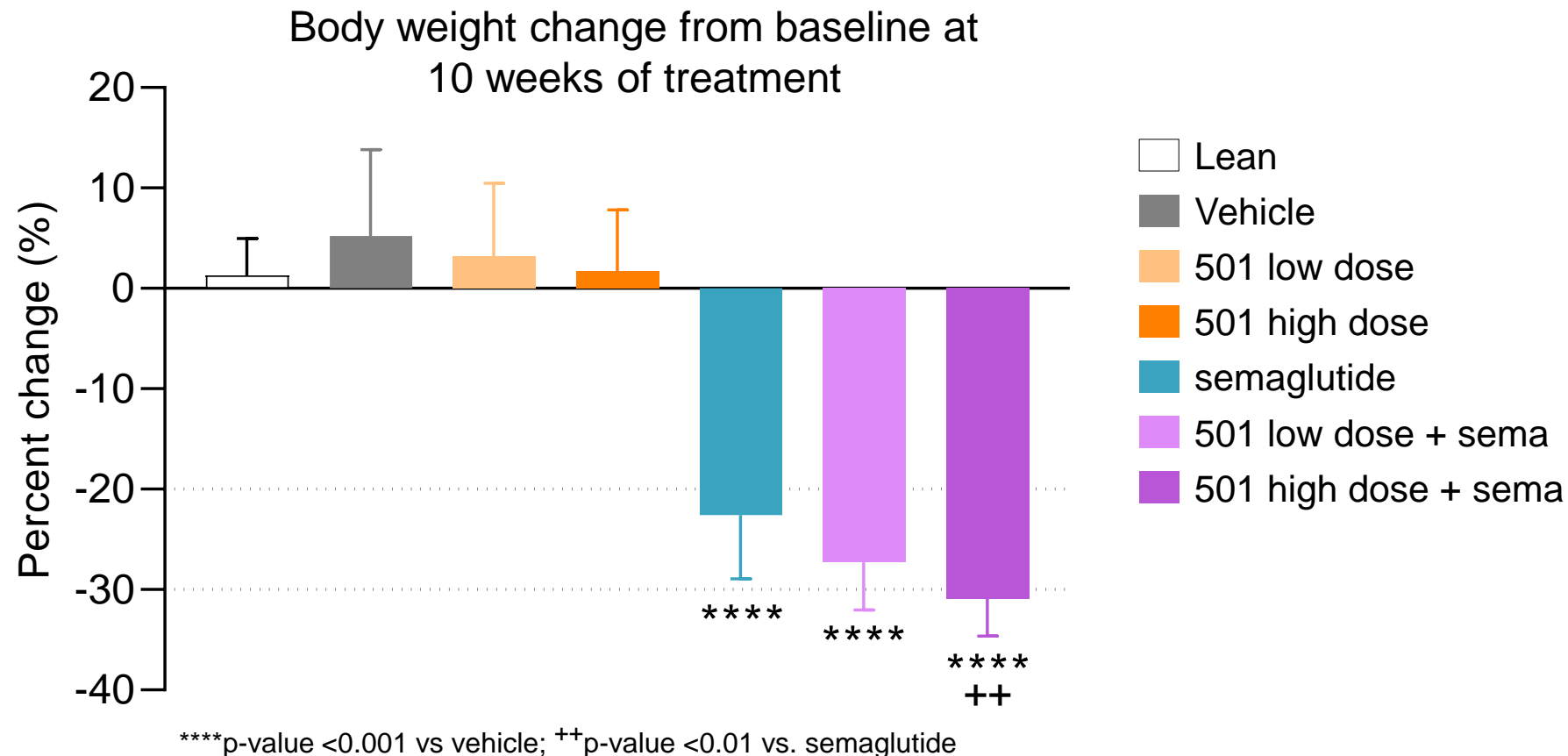
Comparison of THR-βs	TERN-501	Resmetirom	VK2089	ALG-055009	ASC41
Class Leading Liver Fat Reductions	✓	-	✓ -	?	-
Once-Daily Dosing	✓	✓	?	✓	✓
Safe/Efficacious @ Low Dose	✓	-	?	-	-
High THR-β / α Selectivity	✓	✓	-	✓	-
Combinability (Linear, Non-variable PK)	✓	-	-	✓	-
Not Metabolized by CyP	✓	-	-	✓	-
Lack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

Scoring based on publicly available data; comparisons were not done on a head-to-head basis and includes cross-trial and/or cross-phase comparisons; AEs refer to treatment-related AEs; references available upon request.

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

*Preliminary data in diet-induced obese (DIO) NASH mice<sup>1</sup>; study remains ongoing*

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



1. Body weight change after 10-weeks of treatment; mice on Gubra amylin high fat, cholesterol, and fructose diet for >35-weeks prior to study start  
 Note: TERN-501 dosed orally, once-daily; semaglutide dosed subcutaneously, once-daily. The same doses of TERN-501 and semaglutide monotherapy arms were used in combination arms

# Combination of GLP-1 and THR- $\beta$ 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- $\beta$  combination

## GLP-1R agonism

*Weight loss & CV benefits*



+ Weight loss



+ Improved glycemic control



+ Insulin sensitivity

++ Liver fat reduction

++ Potential additive / synergistic metabolic benefits

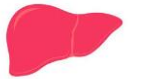
## THR- $\beta$ agonism

*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

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- Strong Balance Sheet
- Multiple upcoming milestones

# Strong Financial Position Supports Upcoming Milestones

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Cash\*  
**~\$263M**

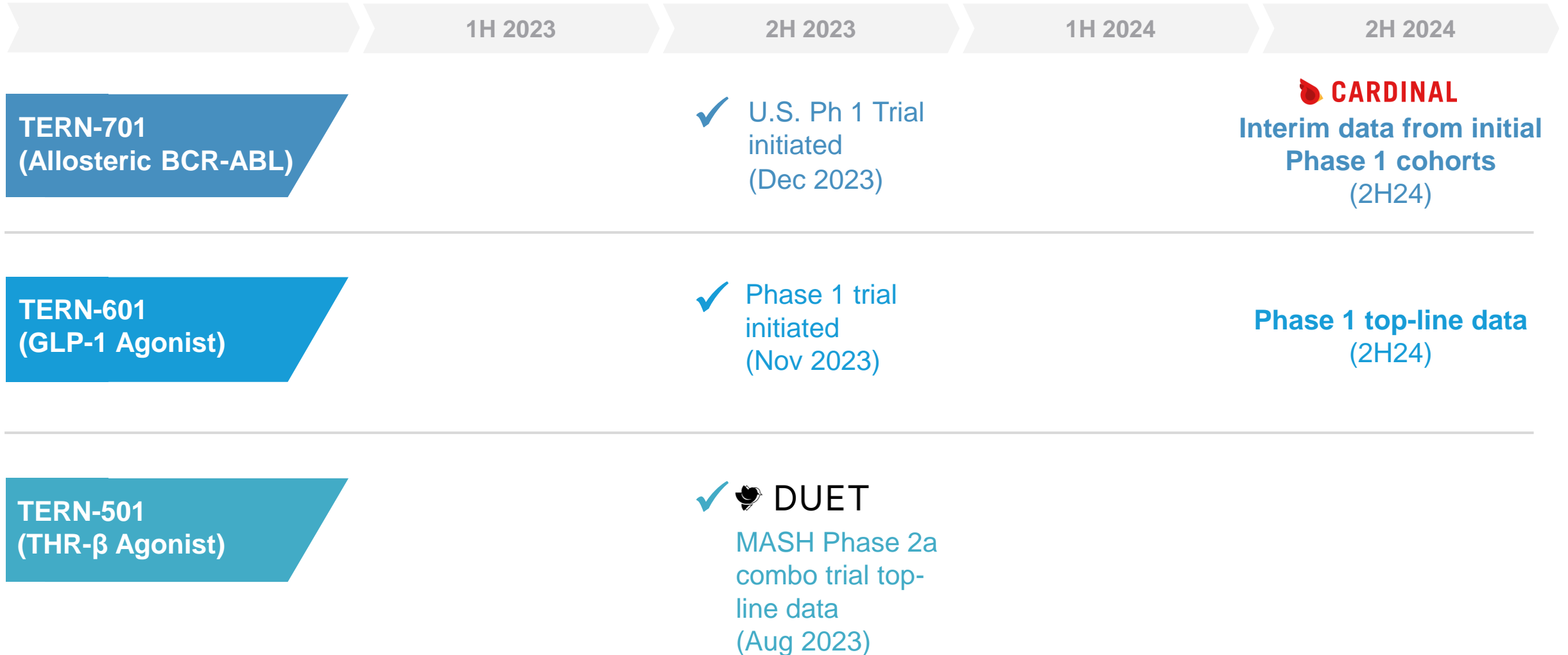
Runway into  
**2026**

Shares\*  
**~74M**

\* As of December 31, 2023; shares include common stock and prefunded warrants

# Key Completed and Upcoming Milestones

Multiple clinical milestones expected across Terns' pipeline

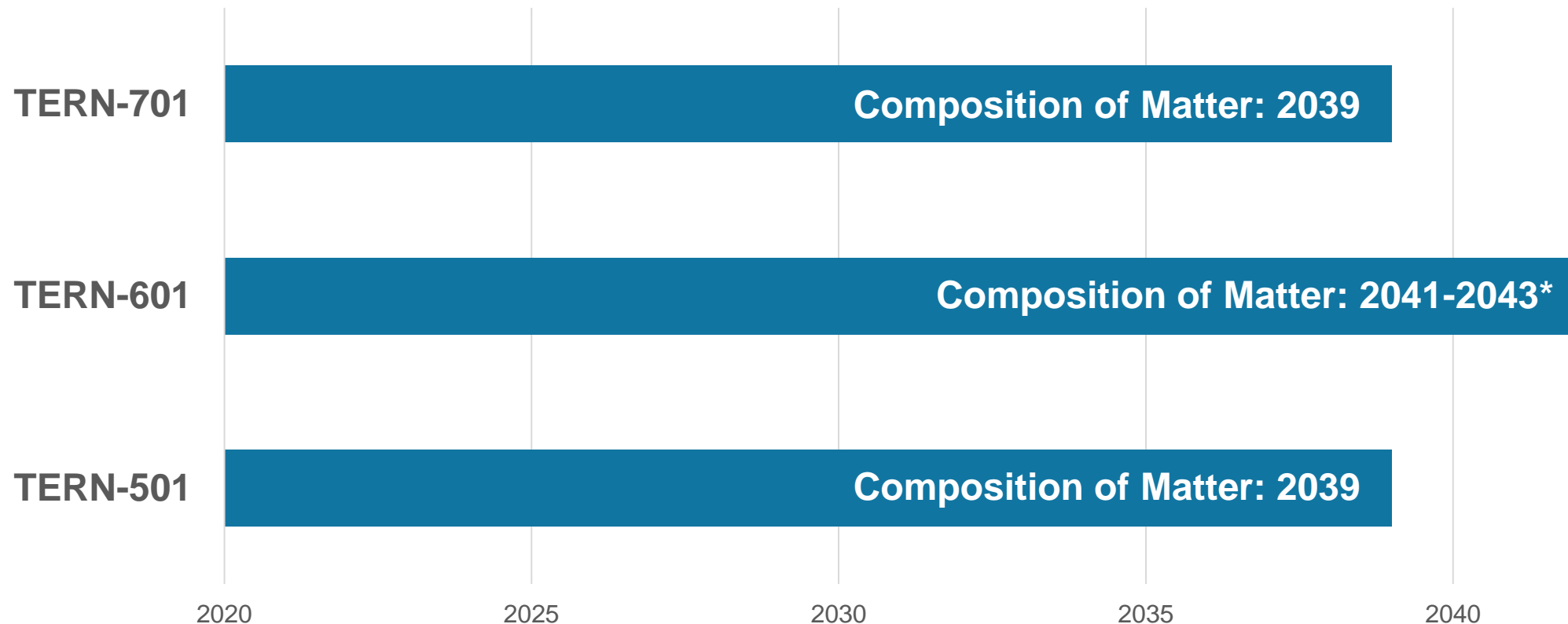


Note: Check mark (✓) denotes completed milestones, all other milestones are anticipated future milestones. Relative position of completed or expected milestones on illustration does not denote or imply chronological order



# 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



All figures above denote US timelines only, similar coverage periods assumed for other territories. \* We own multiple composition of matter patent application families directed to our GLP-1R agonist compounds, including TERN-601, for which claims have not yet been granted. Any patents that may issue from applications in these families are generally projected to expire in 2041-2043, not including any patent term adjustments and/or patent term extensions that may be available.

# Mission. Vision. Core Values.

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## 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



**TERNs**  
PHARMACEUTICALS

# Appendix

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

TERN-701

*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

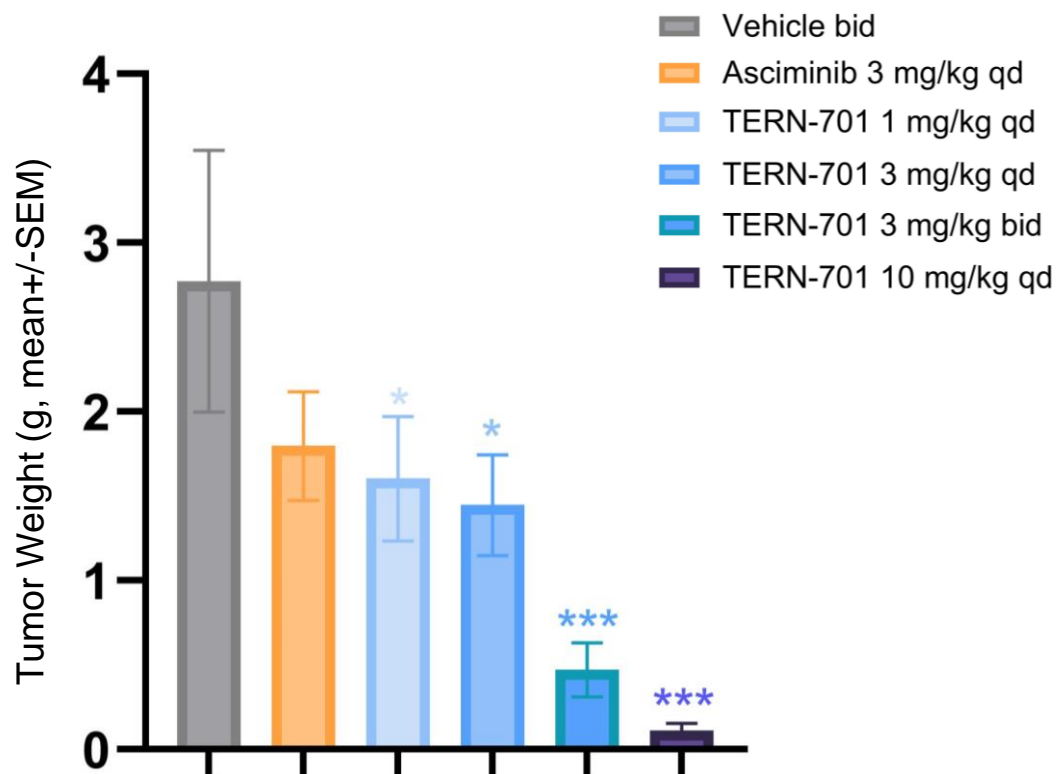
*Allosteric MoA excitement*

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

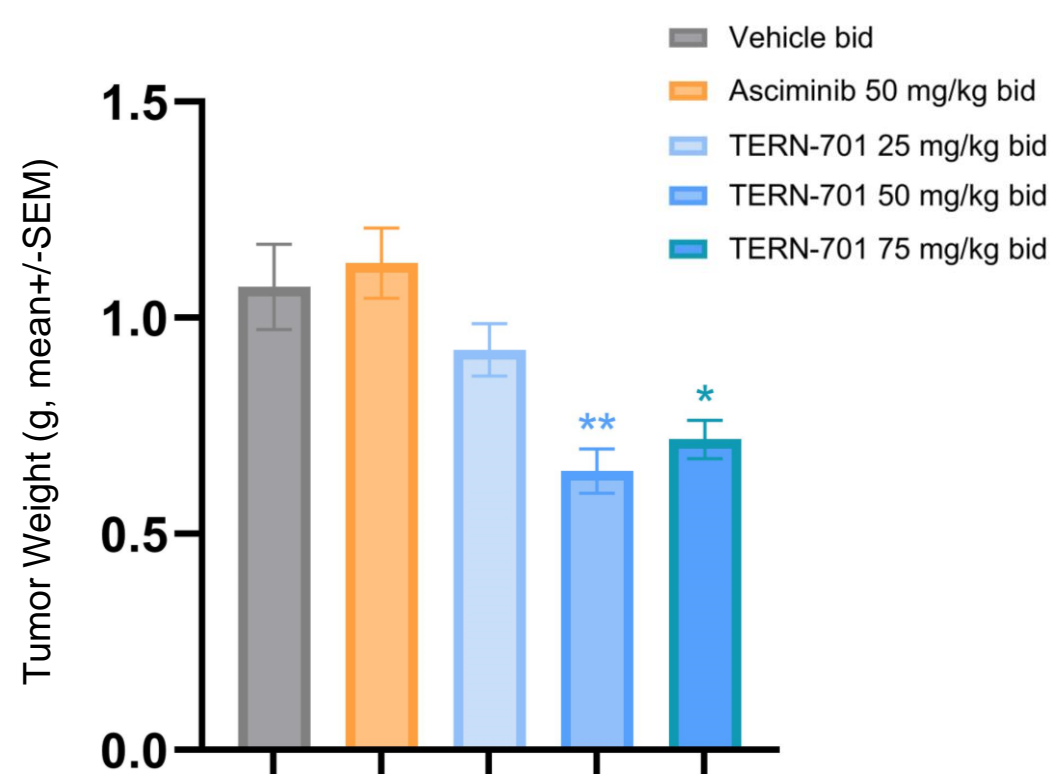
Opportunities for TERN-701 to be uniquely positioned →  
**Initial data expected in 2H24**

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

**K562 Xenograft**  
(Day 14)



**Ba/F3 BCR-ABL1-T315I Allograft**  
(Day 15)



Source: ASPET [TERN-701 poster](#)

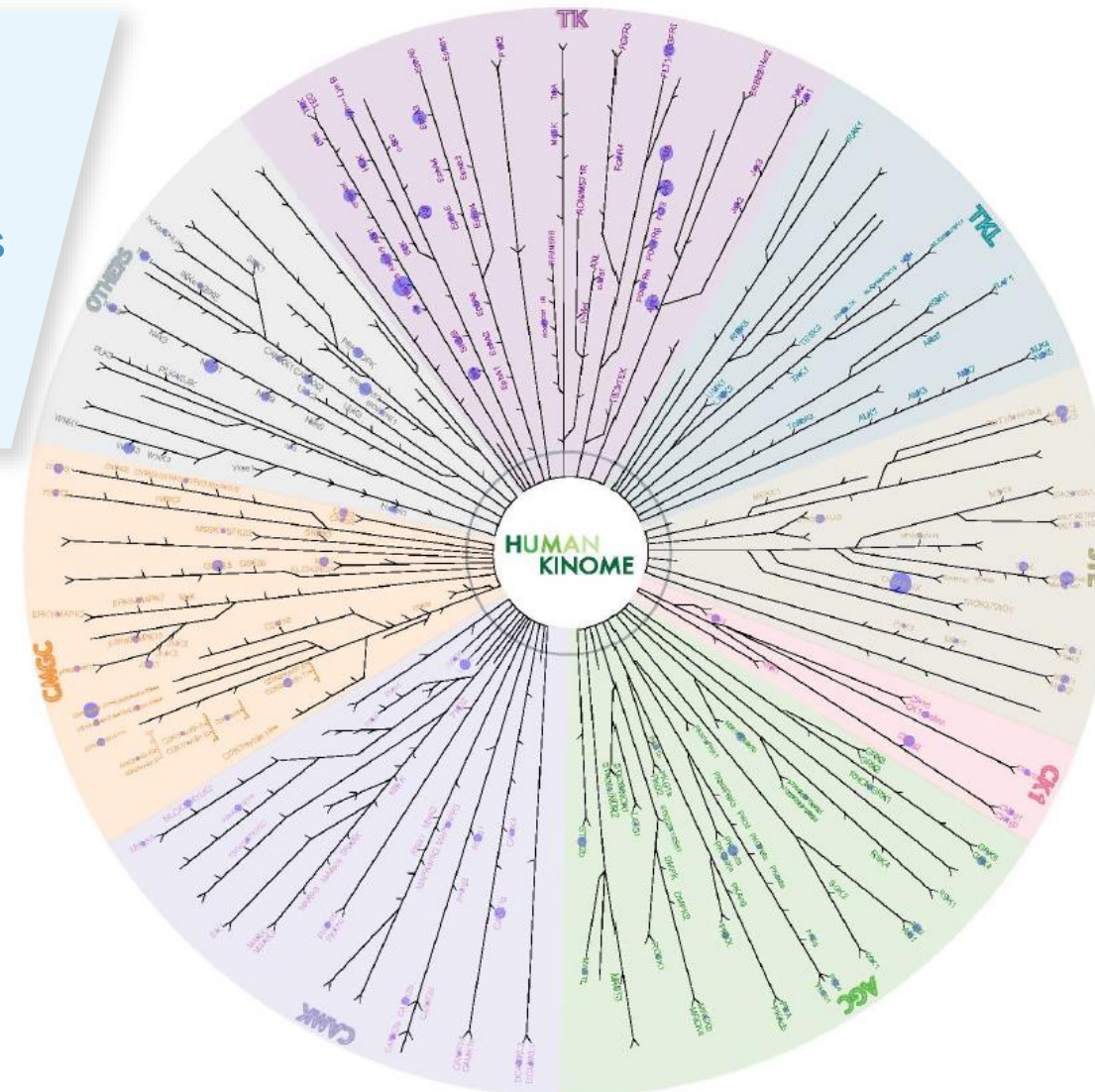
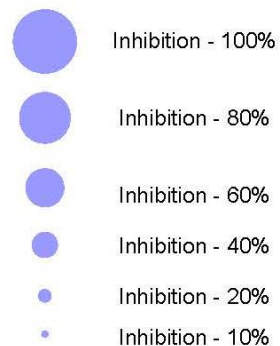
Note: NOD-SCID (K562) and BALB/c nude mice (Ba/F3T315I) were implanted with CML cells, randomized, and administered the indicated TKIs once tumor volumes reached a mean size of 110 mm. Mean tumor weights for each of the treatment groups at the conclusion of the study. All error bars represent the SEM. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001. asciminib was utilized as the free base. TERN-701 was formulated as an optimized salt form

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

TERN-701 was assessed at 1  $\mu$ M against a panel of 375 kinases

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

Dot Size by Percent Inhibition

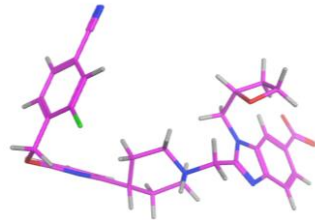


# Terns' Proprietary Model Predicts New GLP-1RA Molecular Activity with Greater Accuracy than Physics-based Evaluations

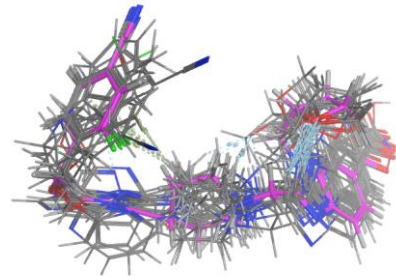
TERN-601

## Terns' Discovery Approach for GLP-1

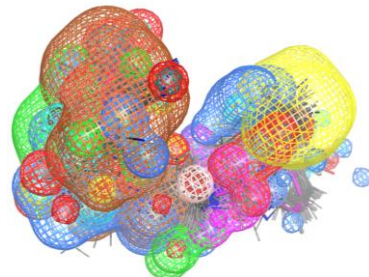
1 Begin with original reference molecule...



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



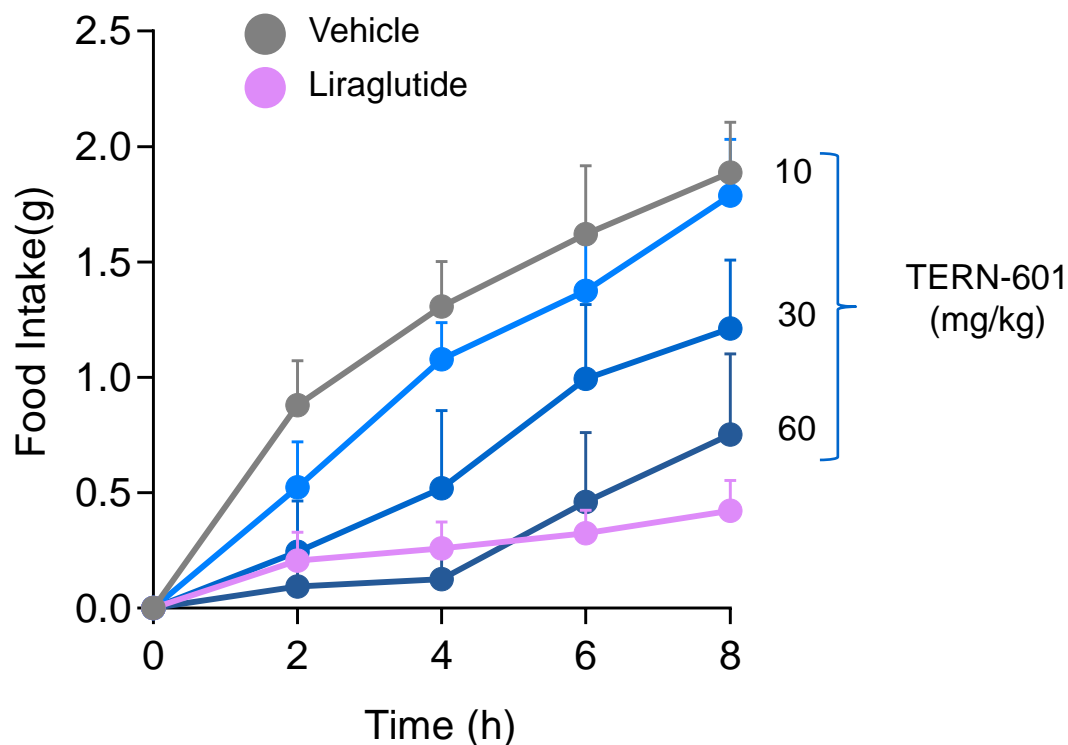
3 ... to build a 3D QSAR model (Terns' proprietary screening tool)



- 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  $\beta$ -arrestin
- Our lead molecule, TERN-601, is a potent GLP-1R agonist partially biased towards cAMP generation

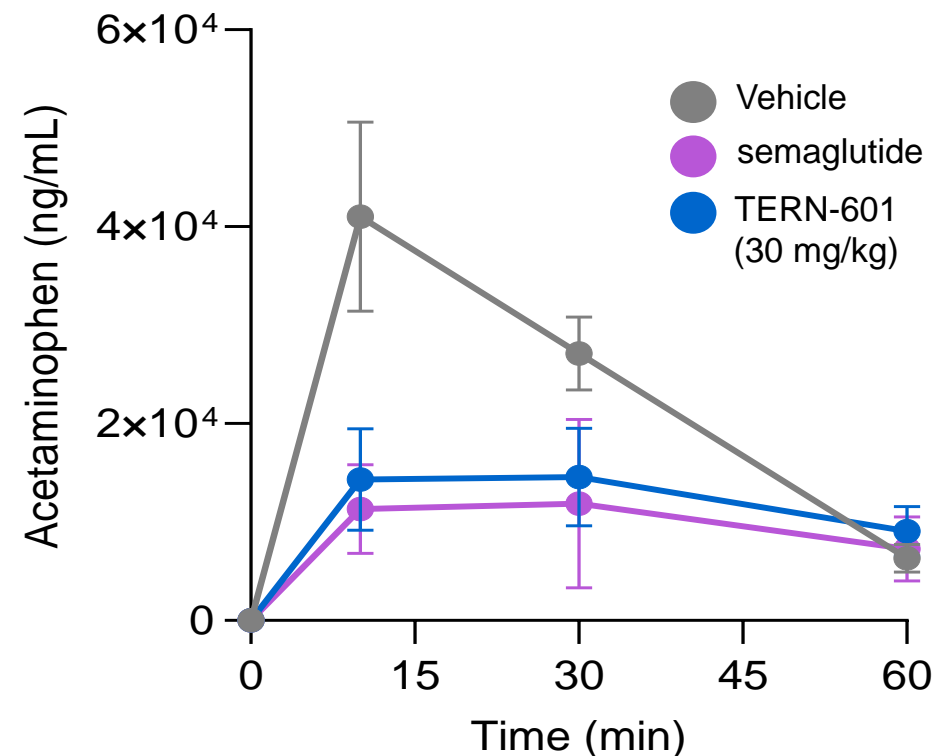
# TERN-601 Reduced Food-intake & Slowed Gastric Emptying in Humanized GLP-1R Mice

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

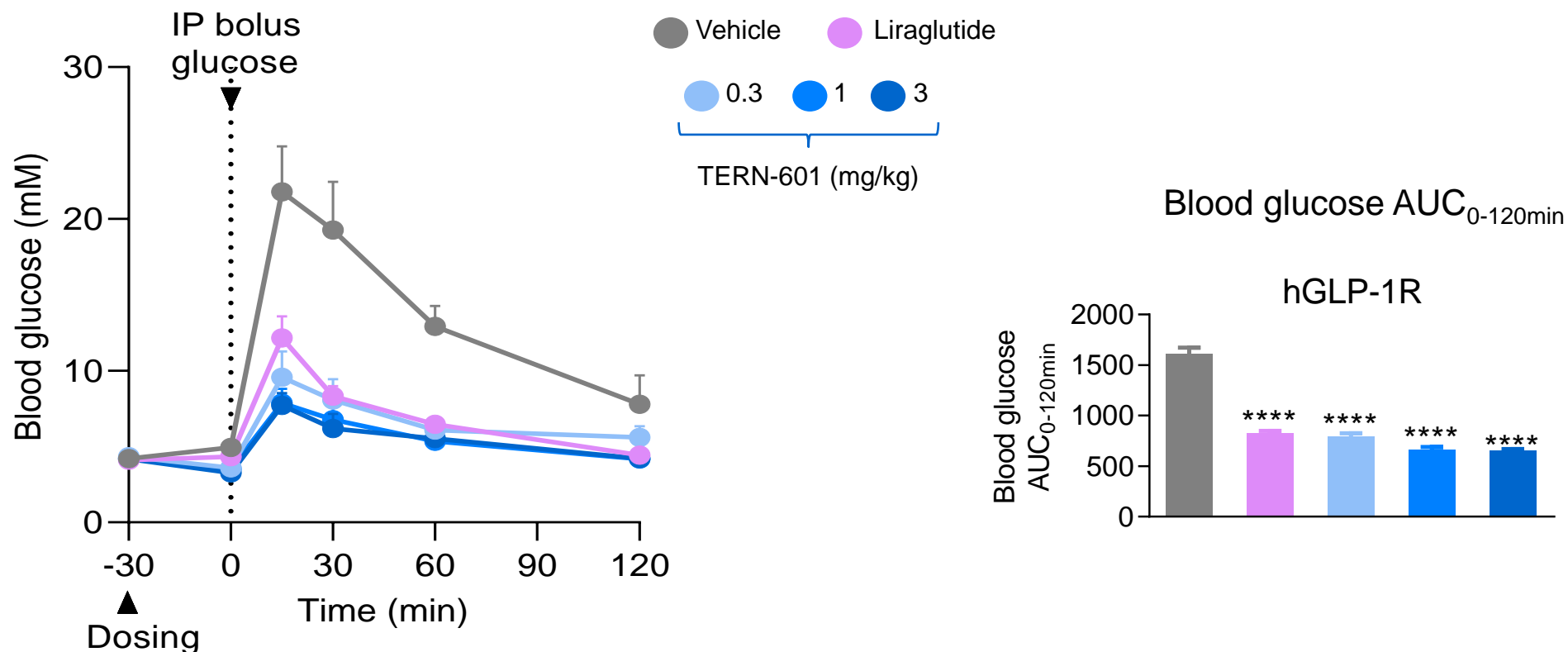


Gastric emptying was assessed using acetaminophen pharmacokinetics as a marker in fasted mice given TERN-601 (30 mg/kg, PO) or semaglutide (10 nmole/kg, SQ), followed by acetaminophen (APAP, 100 mg/kg) and glucose (2 g/kg). Acetaminophen levels in plasma were measured at various time points by LC-MS/MS. 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*



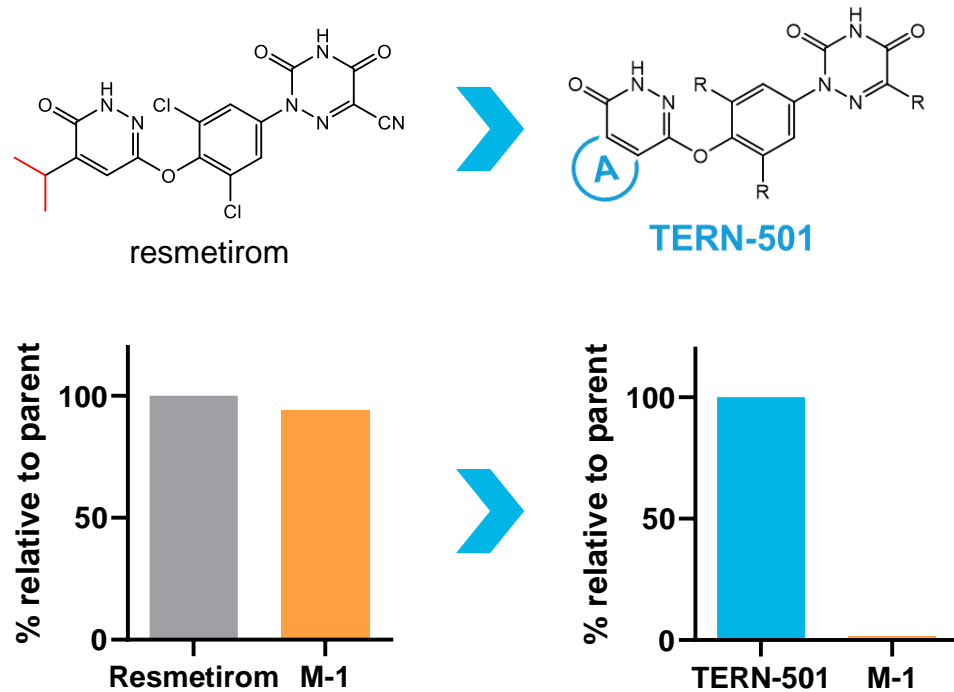
Fasted hGLP1R and WT mice received TERN-601 (0.3, 1, 3 mg/kg, PO) or liraglutide (0.3 mg/kg, SQ) before glucose challenge (2 g/kg IP) and blood glucose was monitored for 120 minutes. Data presented as mean ±SD (n = 5-7/group) ns= not significant; \*\*\*\*p<0.0001 vs. Vehicle.

# TERN-501 Improved PK & THR- $\beta$ Selectivity

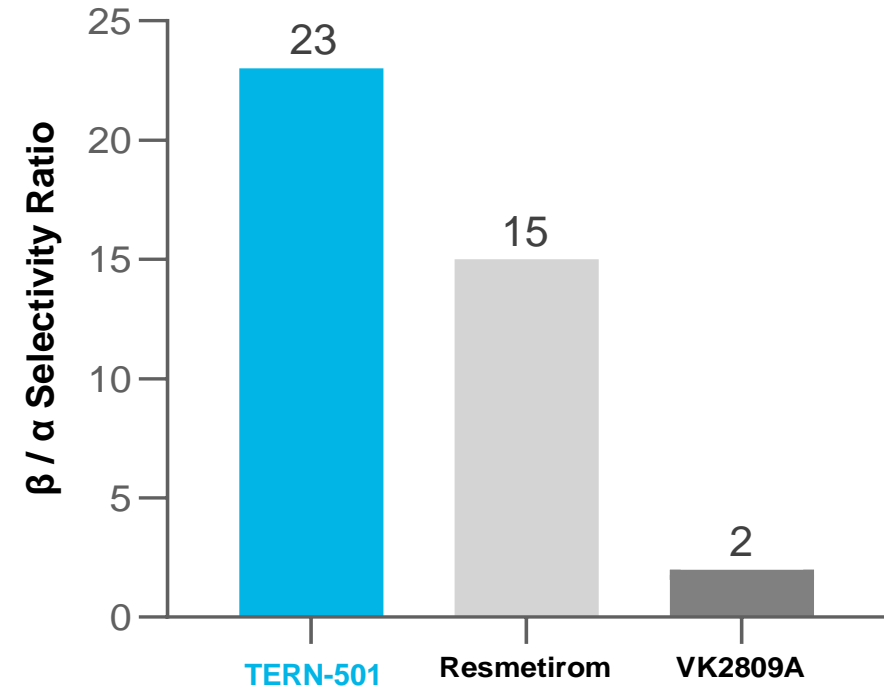
TERN-501

*Differentiated and excellent candidate for co-formulation*

## TERN-501: Improved Pharmacokinetics

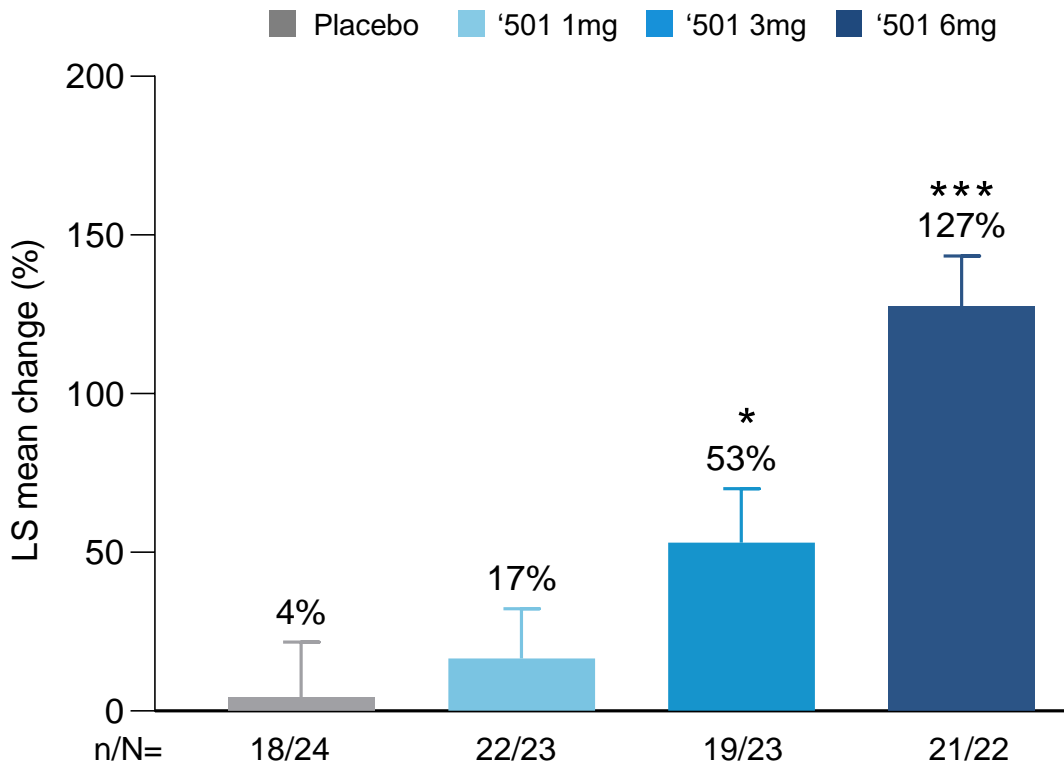


## TERN-501: Improved THR- $\beta$ ratio



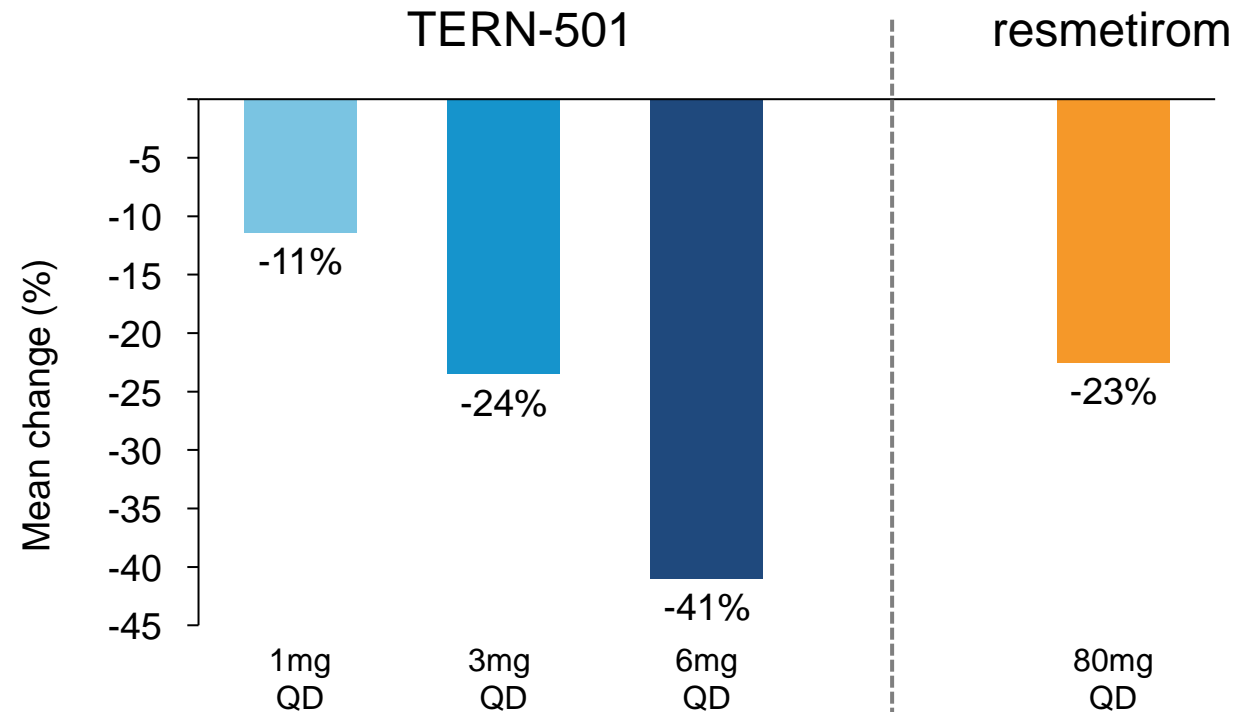
# TERN-501 Demonstrated Compelling SHBG Increases and Liver Fat Reduction with Convenient Once-Daily Dose

## TERN-501 Relative Change in SHBG (Week 12)



\*p-value <0.05; \*\*p-value <0.01; \*\*\*p-value <0.001 for monotherapy vs. placebo  
 n=number of patients with data available; N=number of patients in analysis set  
 SHBG: sex hormone binding globulin

## Placebo Adjusted Mean Relative Change in Liver Fat from Baseline (MRI-PDFP at Week 12)†



† The Phase 2 clinical trial evaluating resmetirom was conducted by another party in a similar patient population with different protocols at different sites and at different times from the DUET trial. Results do not reflect a head-to-head trial and are shown for illustrative purposes only.  
 Source: MDGL: [Harrison et al. Lancet \(2019\)](#), Table 2, placebo response -10.4%  
 Baseline liver fat % (n): TERN-501: 1mg QD 17% (n=23), 3mg QD 20% (n=23), 6mg QD 17% (n=22);  
 resmetirom: 80mg QD 20% (n=84)

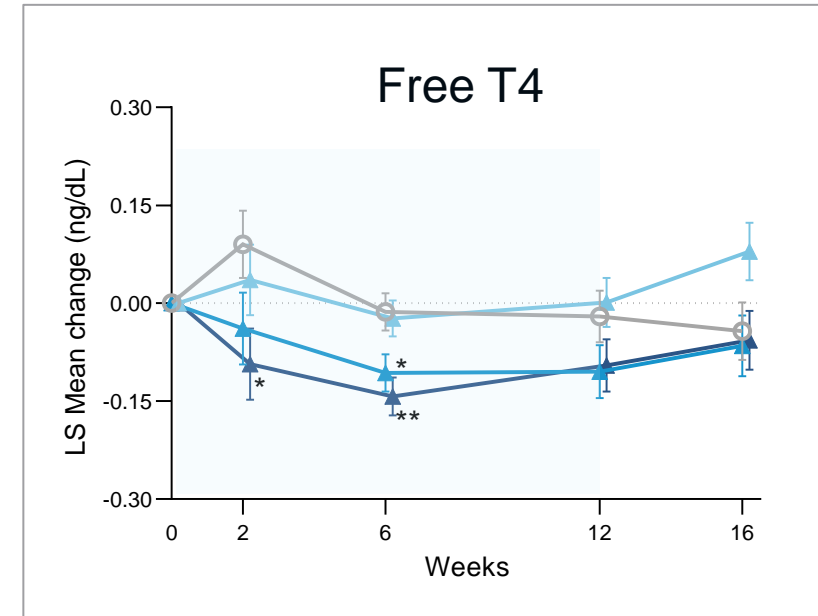
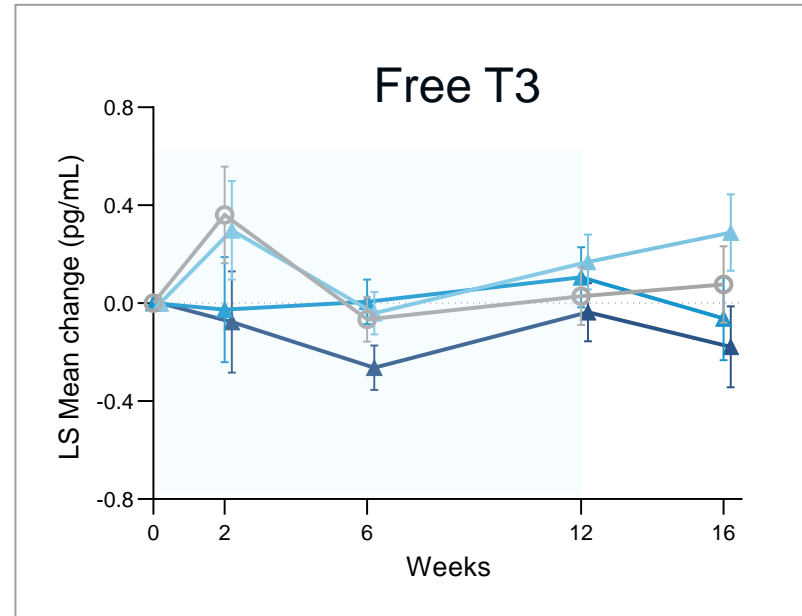
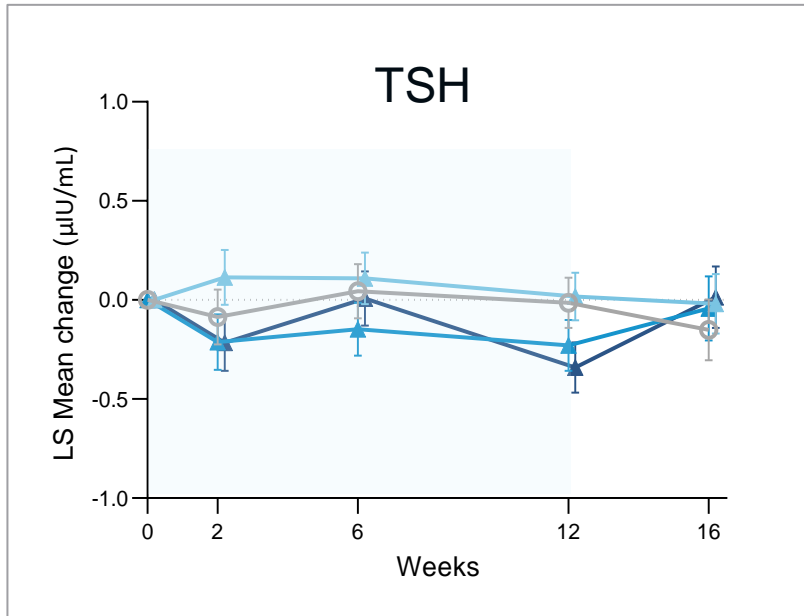
# Drug-related AEs of Interest for TERN-501 Were Balanced Among Treatment Arms

*No differences seen between TERN-501 and placebo; no drug-related CV events observed*

	Placebo (N=24)	TERN-501 1mg (N=23)	TERN-501 3mg (N=23)	TERN-501 6mg (N=22)
<i>Participants, n</i>				
<b>Gastrointestinal disorders</b>	<b>2</b>	<b>1</b>	<b>3</b>	<b>2</b>
<i>Diarrhea</i>	1	1	2	1
<i>Nausea</i>	0	0	1	0
<i>Abdominal distension</i>	0	0	0	0
<i>Abdominal pain (upper)</i>	0	0	0	0
<i>Constipation</i>	0	0	0	1
<i>Dyspepsia</i>	0	0	0	0
<i>Frequent bowel movements</i>	1	0	0	0
<i>Vomiting</i>	1	0	0	0
<b>Cardiac disorders</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>Pruritus</b>	<b>2</b>	<b>0</b>	<b>1</b>	<b>2</b>

# No Signs of Central Thyroid Axis Modulation Observed

○ Placebo ▲ 501 1 mg ▲ 501 3 mg ▲ 501 6 mg



- Mean changes in thyroid axis hormones (TSH, free T3, and free T4) at Week 12 were similar to placebo and remained within normal limits in all TERN-501 containing arms (monotherapy and combination [not shown])
  - No difference from placebo in TSH and free T3 at any time point
  - Initial transient decreases in free T4 up to Week 6 in TERN-501 3 mg and 6 mg arms, as observed with other THR- $\beta$  agonists; no difference from placebo at Week 12

\*p-value <0.05; \*\*p-value <0.01 for monotherapy vs. placebo  
The blue shaded area indicates treatment period

T3, triiodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone

Taub et al. *Atherosclerosis*. 2013 Oct;230(2):373-80. Harrison et al. *Lancet*. 2019 Nov 30;394(10213):2012-2024. Lian et al. *Meeting of the American College of Cardiology*. 2016. Charfi et al. *Hepatology* 2022 Oct; 76:S638