



STRUCTURE
THERAPEUTICS

Corporate Presentation

August 2023



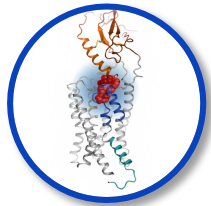
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Our mission is to replace injectable biologics and peptides with oral small molecule medicines accessible to all



Advanced computational and structure-based technology **platform** for drug discovery in chronic diseases



Global strategy with experienced **team** and **\$185M IPO** completed in 2023 to deliver on multiple catalysts through 2025



Two molecules in the **clinic** demonstrate the potential for platform success to efficiently generate oral small molecule drug candidates

Our mission is to replace blockbuster biologics and peptides with smaller and improved medicines



2022 Biologics Market
> \$300B USD Annual Global Sales

Peptide or Biologic Challenges

- Generally not orally available
- Higher total costs
- Limited stability, cold supply chain
- Broad signaling profile

Oral Small Molecule Opportunities

- Orally available, better patient compliance
- Lower costs
- Stable, no cold-chain requirements
- Dialed out arrestin signaling

 **HUMIRA**
adalimumab

 **Stelara**
(ustekinumab)

ONCE-WEEKLY
 **OZEMPIC**
semaglutide injection 0.5mg, 1mg, 2mg

 **Skyrizi**
risankizumab-rzaa

 **Enbrel**
etanercept

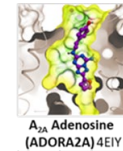
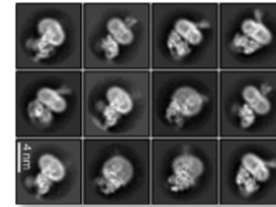
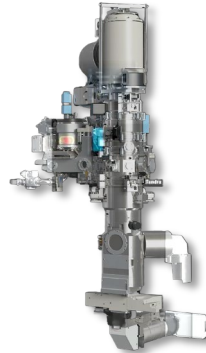
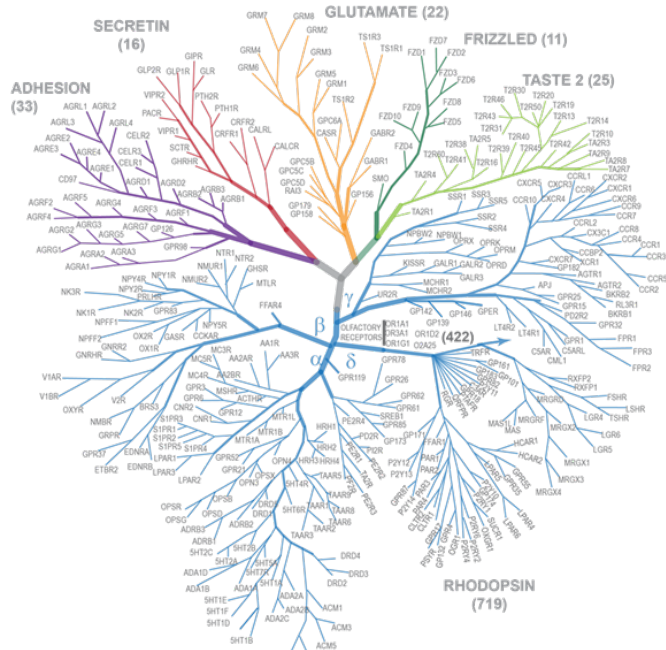
 **trulicity**
(dulaglutide)

Top Biologics and Peptide Drugs

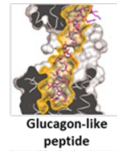
Initial GPCR focus represents broad potential to address global healthcare needs

GPCRome (~800 GPCRs)
Largest and most drug targeted
human protein family

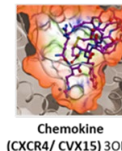
Cryo-Electron Microscopy
Multi-Conformations



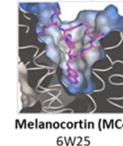
A_{2A} Adenosine (ADORA2A) 4EIY



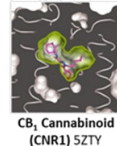
Glucagon-like peptide



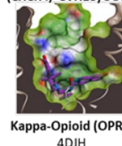
Chemokine (CXCR4/CVX15) 3OE0



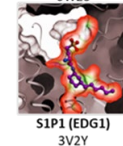
Melanocortin (MC4R) 6W25



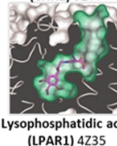
CB, Cannabinoid (CNR1) 5ZTY



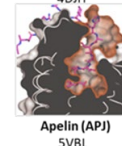
Kappa-Opioid (OPRK1) 4DJH



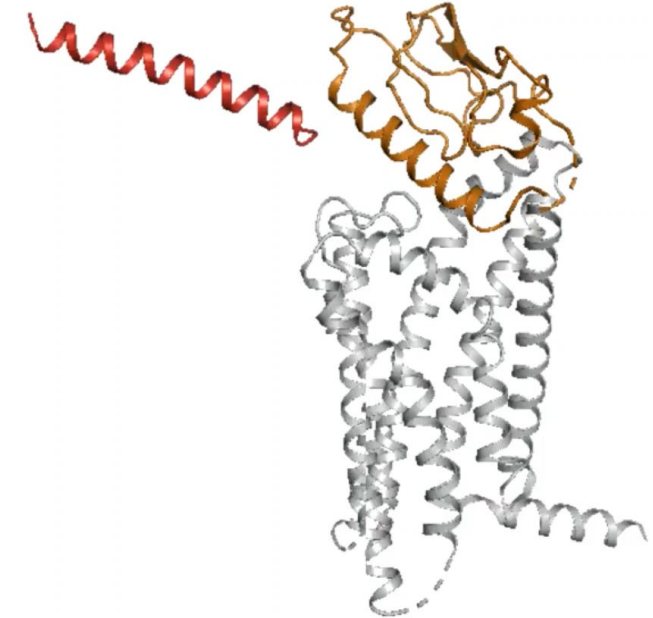
S1P1 (EDG1) 3V2Y



Lysophosphatidic acid (LTPAR1) 4Z35



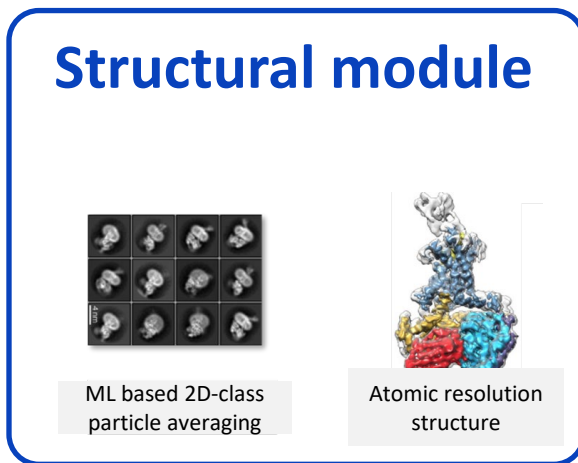
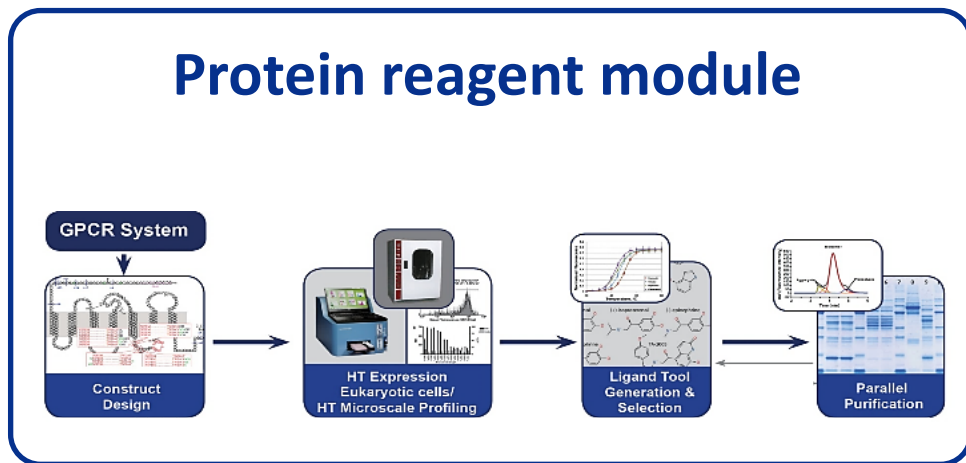
Apelin (APJ) 5VBL



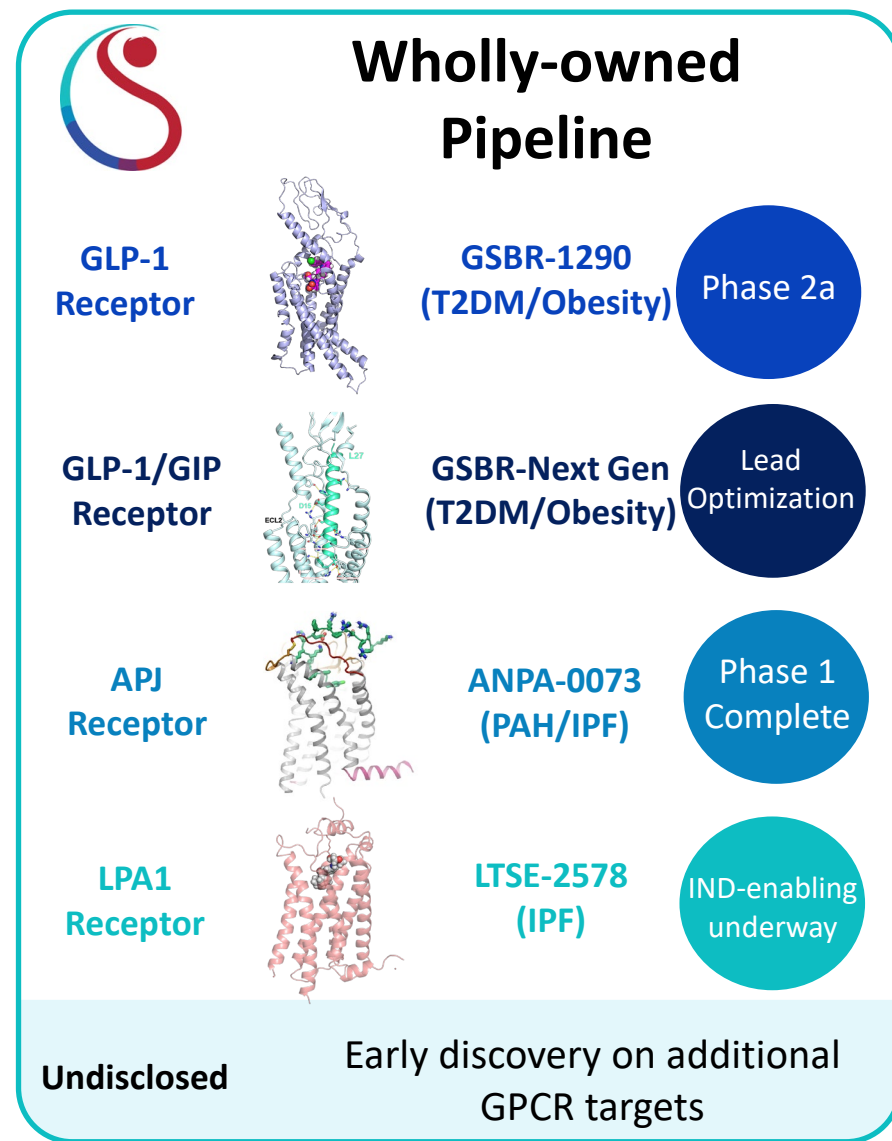
Only ~ **16%** have approved drugs

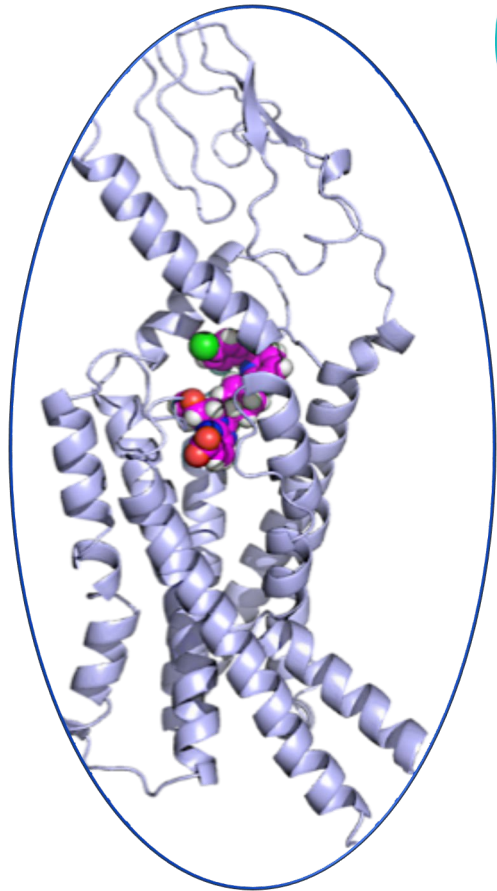
Replacing Peptide with Oral Small Molecule

Platform-enabled internal R&D engine to generate GPCR pipeline



Computational and chemistry module





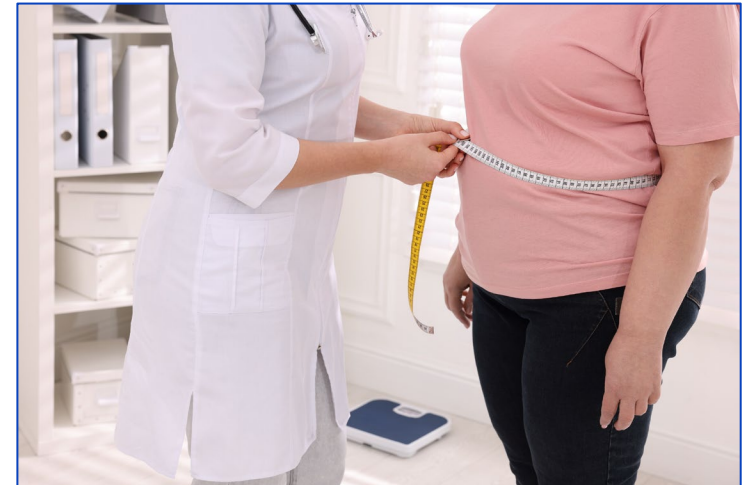
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Oral Incretin Franchise

Highly selective GLP-1R agonists
GLP-1R+ Combo



GLP-1R agonist therapies for diabetes – today and the future

Oral small molecule GLP-1R agonist has the potential to be the future

Improved cost, dosing convenience, flexibility in titration and combination, patient preference

	Today		Future
Compound	Injectable Peptide	Oral Peptide	Oral Small Molecule
Administration	s.c. injection, once a week	p.o. once a day	p.o. once a day
Patient Consideration			
	Long term use of injectables	At least 30 min food and beverage restriction, low bioavailability	Ease of use, accessibility

Disrupting the GLP-1R peptide-dominated market with oral small molecules

Significant Opportunity to Increase Accessibility and Treat More People with Type 2 Diabetes & Obesity

537M+ People with T2D
764M+ Adults with Obesity

>\$50B TAM¹



“Early days of GLP-1 research”

Peptide GLP-1R Agonists
\$22B+

OZEMPIC
semaglutide injection

VICTOZA
liraglutide injection

RYBELSUS
semaglutide tablets 3mg/4mg

wegovy
semaglutide injection

Byetta
(exenatide) injection

Saxenda
liraglutide injection 3mg

trulicity
dulaglutide injection

2005 - 2021

Peptide Dual GLP-1/GIPR Agonists

now APPROVED
mounjaro
(tirzepatide) injection

2022

“Early Innings”

Oral Small Molecules
GLP-1R Agonists

Oral Small Molecules
GLP-1R+ Combo

FDA Approval

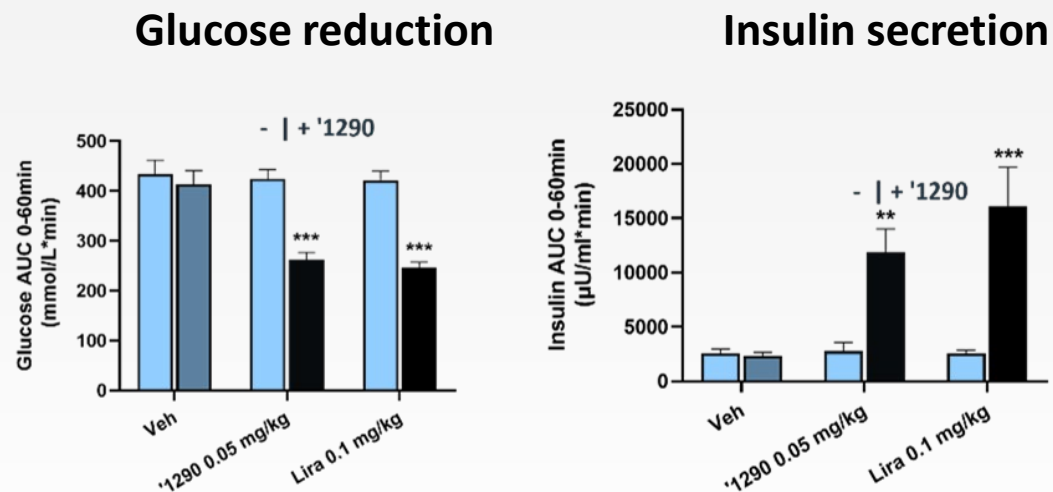
2028+

1. EvaluatePharma 2028 forecast for T2D and Obesity

TAM: Total Addressable Market

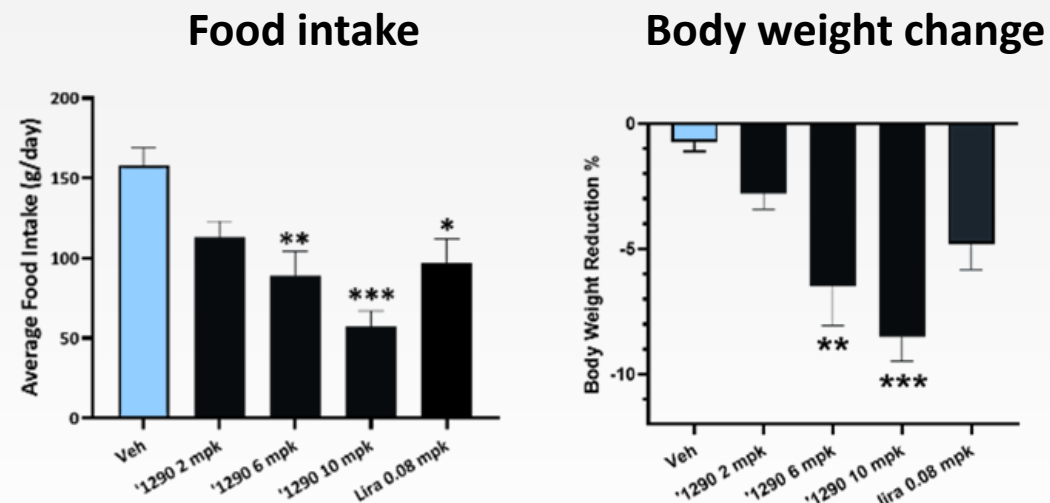
GSBR-1290: Robust glycemic and weight loss activity observed in non-human primate studies

Acute NHP ivGTT with *i.v.* dosing of GSBR-1290



- Robust glucose clearance and insulin induction activity in NHP study 1h post *i.v.* dosing

7-day NHP *p.o.* repeating dosing of GSBR-1290



- Robust food intake and body weight reduction
 - Maximum insulin induction at 2 mpk (C_{average} 6.8 nM)
 - Clear dose response for food intake and **body weight reduction with 8% reduction at top dose**

Mean \pm Sem; One-way or Two-way ANOVA followed by Dunnett's multiple comparisons test or Šídák's multiple comparisons test. * $P < 0.05$, ** $P < 0.01$, *** $p < 0.001$ vs vehicle or baseline

GSBR-1290 preclinical results support development for diabetes and obesity¹

✓ Poster presentation at 2023 American Diabetes Association (ADA) Conference in June 2023

“Discovery of GSBR-1290, a Highly Potent, Orally Available, Novel Small Molecule GLP-1 Receptor Agonist”



83RD SCIENTIFIC SESSIONS

Clinical Stage		Phase 2a
In vitro activity	K _i	<10 nM
	cAMP Signaling	Fully Biased ²
In vivo activity	*NHP ivGTT C _{efficacious}	<10 nM
Preclinical Safety	Rat toxicity NOAEL	1000 mkd (3 mo GLP-tox)
	GSH Reactivity	Negative
Clinical Dose	#Dose & Frequency	30mg/QD (For Glycemic Control)



GSBR-1290 showed balanced preclinical profile with a **potentially greater safety window** to allow maximum dose flexibility



Danuglipron
Phase 2

(First generation)
Dose: 120 – 200mg BID



Orforglipron
Phase 3

Dose: 9 – 45mg/QD

Oral small molecule GLP-1R agonists

¹ No head-to-head study has been conducted evaluating the GSBR-1290 against other product candidates included herein. Differences exist between study designs and subject characteristics, and caution should be exercised when comparing data across studies.

² GSBR-1290 analog

* Drug exposure to reach significant or maximal insulin induction.

** Drug exposure shown as AUC₀₋₂₄ to achieve similar body weight loss to Semaglutide

Dose reported or predicted

GSBR-1290 Phase 1 SAD study completed

- ✓ **Poster presentation at the 2023 American Diabetes Association (ADA) Conference in June 2023**
“A First-in-Human Single Ascending Dose Study of GSBR-1290, a Novel Small Molecule GLP-1 Receptor Agonist, in Healthy Volunteers”



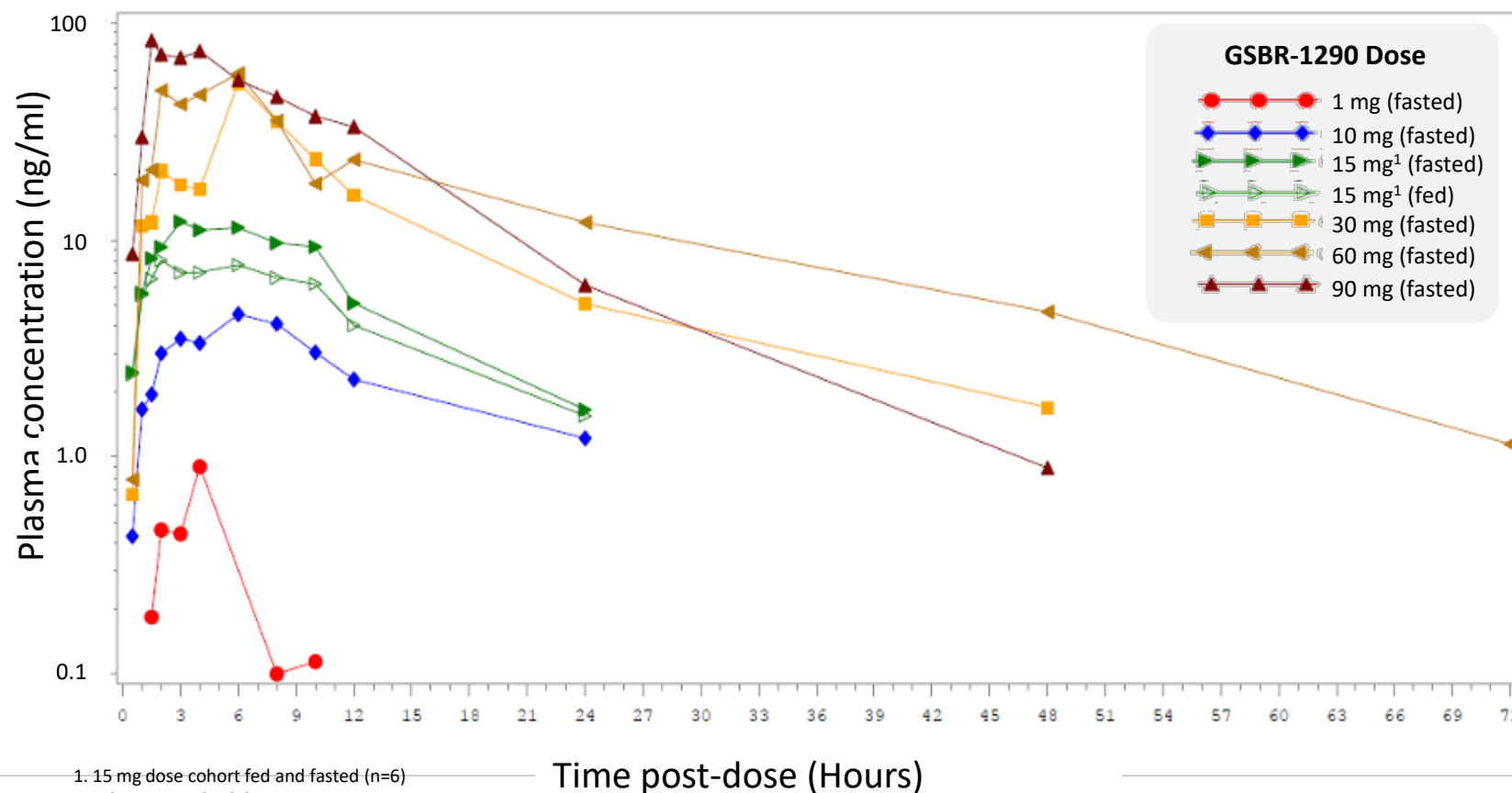
83RD SCIENTIFIC SESSIONS

Study design: Healthy volunteers (n=48, 8/cohort, 3:1 drug:placebo)

Key takeaways:

- ✓ No Serious Adverse Events (SAEs)
- ✓ Well-tolerated and AE profile consistent with GLP-1R class
- ✓ GLP-1R target engagement confirmed with expected dose-related on target GI effects
- ✓ A daily dose of 30 mg achieved a plasma level estimated to be sufficient for glycemic control

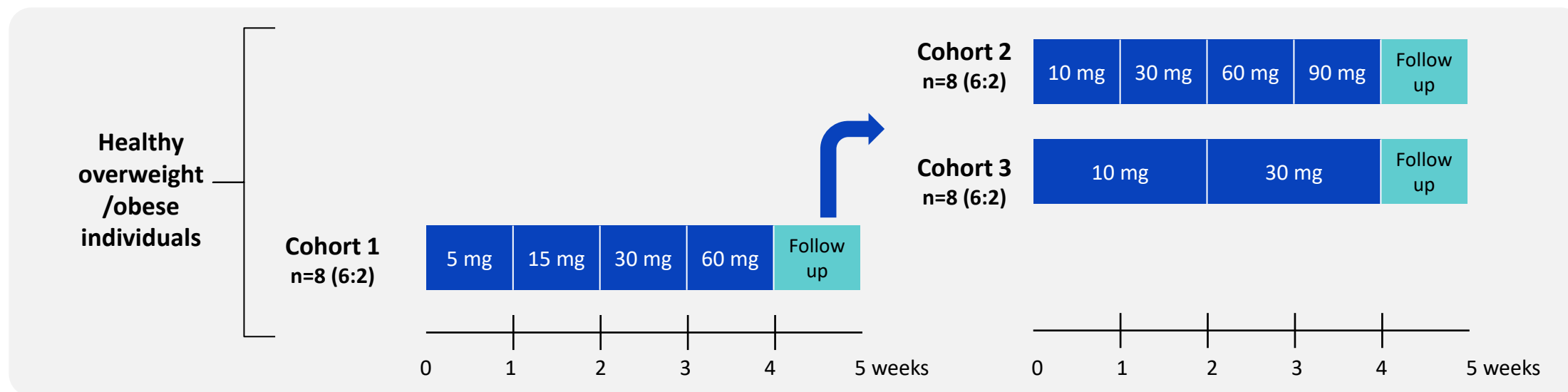
Single Dose Pharmacokinetics (PK)



GSBR-1290 Phase 1b MAD study completed dosing

✓ Enrollment Completed

☐ Phase 1b MAD study results to be announced with Phase 2a results in latter half Q4 2023



Primary objective:

- Multiple dose study focused on **safety, PK and tolerability**

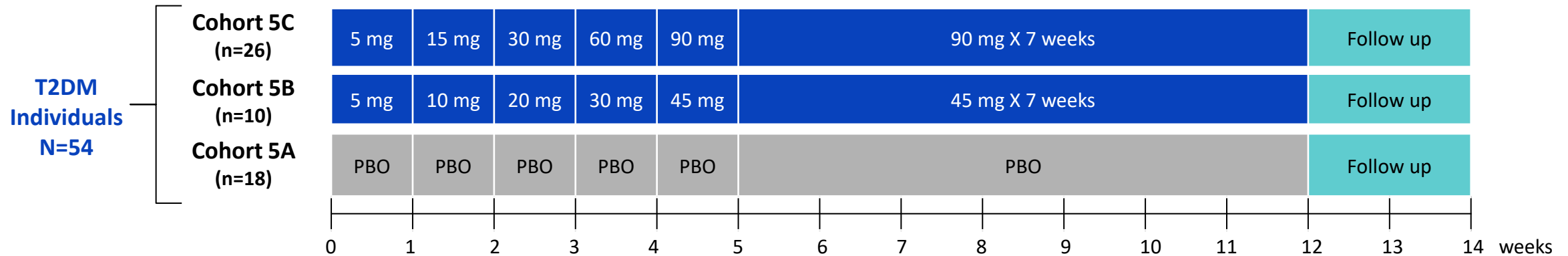
Secondary objectives:

- Pharmacokinetics
- Determine the starting dose for titration and help define the titration scheme

GSBR-1290 Phase 2a study in T2DM and overweight/obese over 12 weeks

✓ Enrollment Completed

☐ Top-line 12-week study results anticipated in latter half Q4 2023



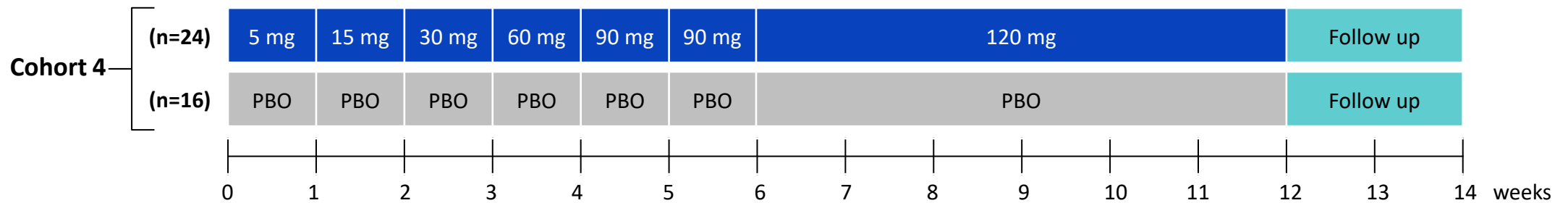
Primary endpoint: Safety and tolerability

Secondary endpoints:** Demonstrate **decrease in HbA1c**

Demonstrate **decrease in weight**

Demonstrate **dose response in decrease in HbA1c** and **weight**

Healthy overweight /obese Individuals N=40



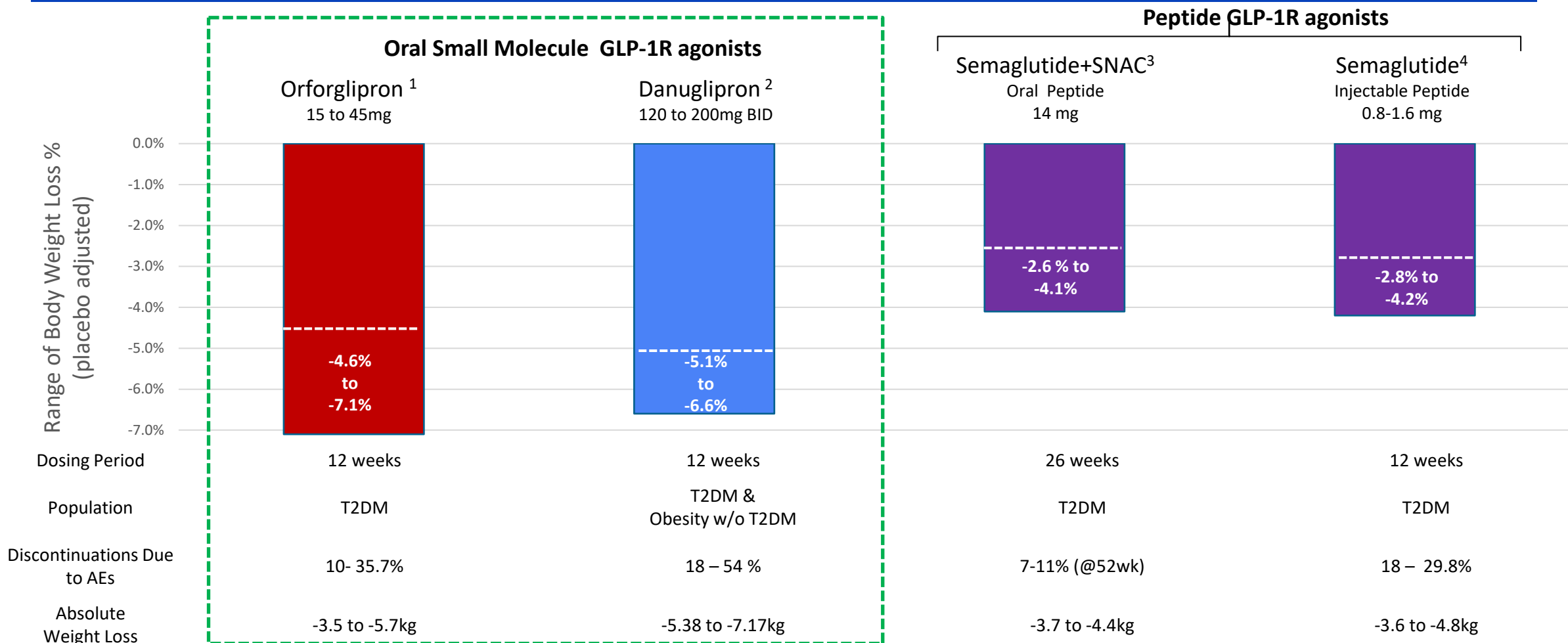
Primary endpoint: Safety and tolerability

Secondary endpoint:** Demonstrate **decrease in weight**

**Relative to placebo

GSBR-1290 Opportunity to demonstrate competitive efficacy profile in Phase 2a

Highly Selective GLP-1R Competitive Landscape



¹ Diabes Obes Metab.2023;1-8; ² EASD 2022: OP#588. Efficacy, safety and tolerability of danuglipron (Pf-06882961) over 12 weeks in adults with type 2 diabetes. ³ Adapted from Drugs (2021) 81:1003–1030; ⁴Diabetes Care 2016;39:231–241

GSBR-1290 – Highly selective GLP-1RA oral small molecule



Potential Best-in-Class

- ✓ Highly selective oral small molecule GLP-1R agonist
- ✓ Potentially greater safety window to allow maximum dose flexibility
- ✓ Positive Phase 1 SAD data (n=48):
 - ✓ Well tolerated w/ expected dose-related on target GI AEs
 - ✓ No SAEs
- ✓ Phase 1 MAD (4 wk) dosing completed (n=24)
- ✓ Phase 2a (12wk) in T2DM and obesity dosing completed (n= 90 including 40 obese/overweight, 54 T2DM)
- ✓ JP PK bridging study (4wk) dosing completed (n=18)
- ☐ Top line data anticipated 2nd half of 4Q 2023

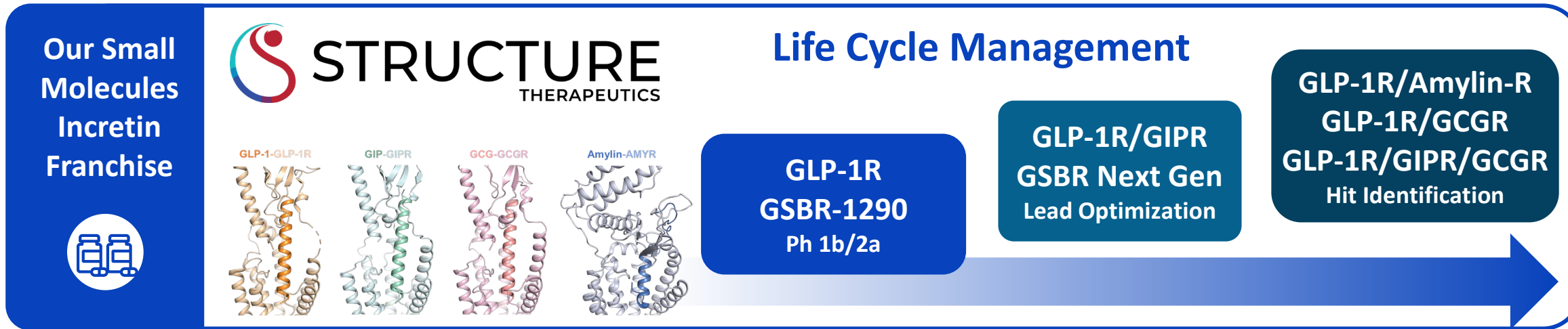
Large Addressable Market

- 537M+ People with T2D
- 764M+ Adults with Obesity
- High unmet need for well tolerated, safe and effective oral agents in GLP-1R market dominated by injectable peptides
- \$22B+ GLP-1 worldwide sales in 2022 and TAM projected to be >\$50B by 2028¹

Our oral incretin franchise approach – to replace marketed peptides with small molecules

Peptide Drugs on the Market	 (exenatide) injection	 liraglutide injection 3mg	GLP-1R		GLP-1R/GIPR	
	 liraglutide injection	 dulaglutide injection	 semaglutide injection	 semaglutide tablets 7mg/14mg	 semaglutide injection	 NOW APPROVED once weekly (tirzepatide) injection
Approval:	2005/2010	2014	2017	2019	2021	2022

Incretin drugs evolution – Improving convenience & clinical efficacy for patients

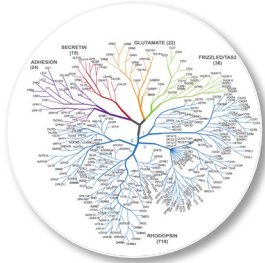


**Our powerful platform enables
a franchise approach to potentially replace the marketed peptides**

Platform to wholly-owned pipeline in high impact disease areas



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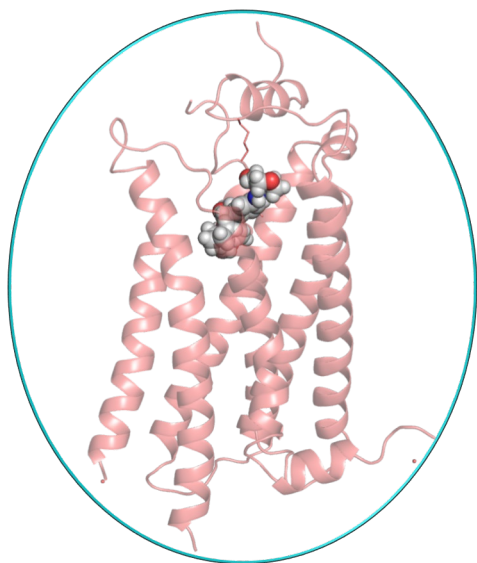


Program	Indications	Preclinical		Clinical			Anticipated Milestones	Global Rights	
		Discovery	IND-enabling	Phase 1	Phase 2	Phase 3			
Oral Incretin Franchise	Type 2 Diabetes/ Obesity	GSBR-1290 GLP-1R	[Progress bar: Phase 1, Phase 2, Phase 3]					<ul style="list-style-type: none"> Phase 1b/2a data latter half of Q4 2023 Nominate development candidate 2024 	
		GLP-1R+Combo Dual GLP-1R/GIPR	[Progress bar: Discovery, IND-enabling]						
Oral APJR	Cardio-pulmonary	ANPA-0073 APJR	[Progress bar: Phase 1, Phase 2]					<ul style="list-style-type: none"> Phase 2 ready 2024 	
Oral LPA1R	IPF	LTSE-2578 LPA1R	[Progress bar: Discovery, IND-enabling]					<ul style="list-style-type: none"> Phase 1 initiation 2024 	



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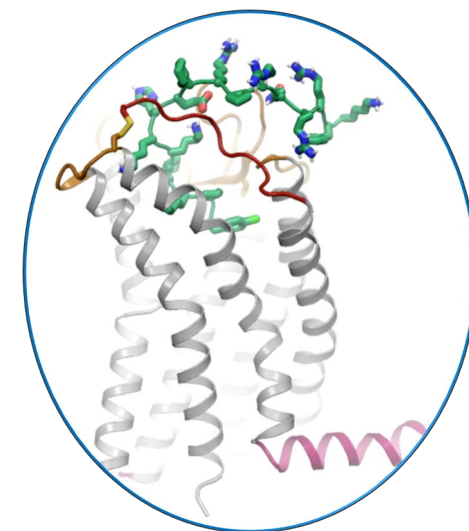
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LTSE-2578



ANPA-0073

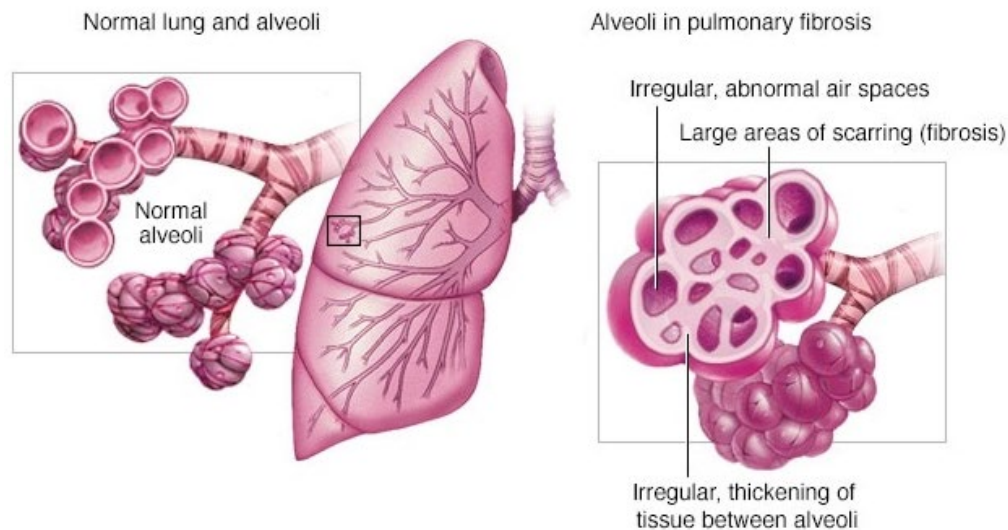


LPA1R Antagonists & APJR Receptor Agonists
Cardiopulmonary Diseases

Pipeline activities focusing on cardiopulmonary disease with unmet need

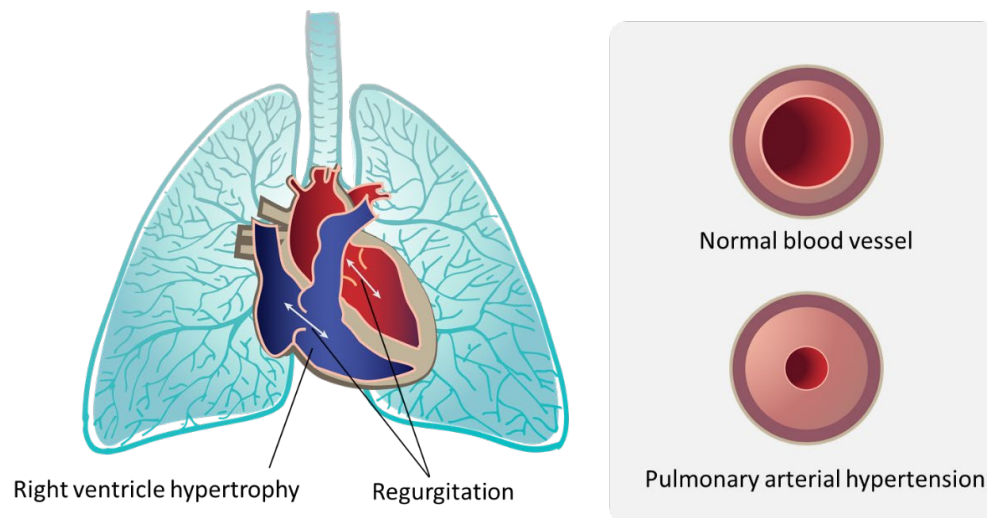
Idiopathic Pulmonary Fibrosis (IPF)

- **Progressive lung disease** affects ~5 million people worldwide with 30,000 to 40,000 new cases per year
- **Poor prognosis:** median survival time from diagnosis is 3-5 years
- **Unmet need:** SOCs limited efficacy & poor tolerability
- **Large market:** ~\$4.1B worldwide sales in 2021



Pulmonary Arterial Hypertension (PAH)

- **Rare, orphan disease** affects 40,000 to 100,000 people worldwide
- **Poor prognosis:** 5-year survival rate of 60-65% with right ventricular failure as leading cause of death
- **Unmet need:** SOCs primarily act as vasodilators
- **Large market:** ~\$5.4B worldwide sales in 2020

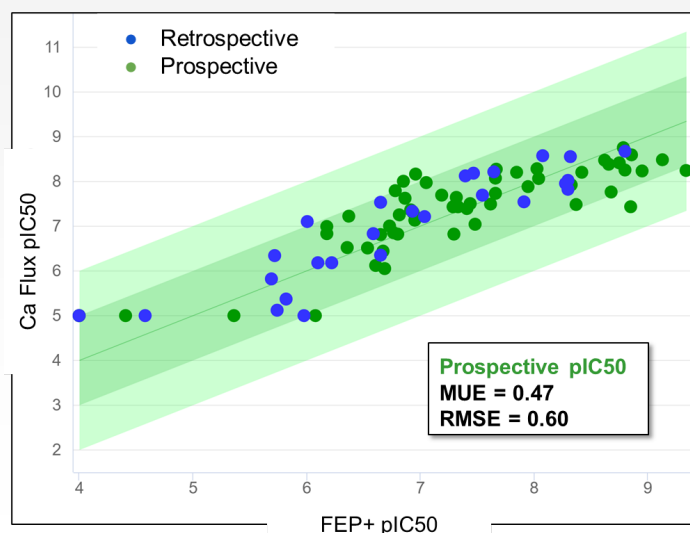


Partnering with Schrödinger to rapidly identify and optimize LPA1R antagonist

- ✓ LTSE-2578 Development Candidate (DC) in IND-enabling studies with Phase 1 study planned in 1H 2024
- ✓ Poster presentation held at American Thoracic Society Conference (ATS) in May 2023

“Structure Based Discovery and Anti-fibrotic Activity of Novel Antagonists of Lysophosphatidic Acid Receptor 1 (LPA1R)” 

Structure-based drug discovery



Leveraging LPA1R structure with cutting edge computational techniques to rapidly identify **LPA1R antagonist lead molecule** (<400 compounds and 12 months)

Potentially differentiated profile¹



		BMS-986020	BMS-986278	LTSE-2578
Status		Phase 2 discontinued	Phase 2	Preclinical
Activity	In vitro IC ₅₀	21 nM	251 nM	<10 nM
	PK/PD IC ₈₀	45 ng/mL	200 ng/mL	<10 ng/mL
Safety	BSEP IC ₅₀	3.4 μM	>100 μM	>50 μM
Clinical dose (BID)		600 mg [#] (Phase 2 POC)	60/30 mg ^{##} (Phase 2 POC)	<30 mg (projected)



HZN-825 (SAR100842)
Phase 2b, SSc-ILD and IPF

¹ No head-to-head study has been conducted evaluating the LTSE Lead product candidate against the other product candidates included herein. Differences exist between study designs and conditions, and caution should be excised when comparing data across studies.
NCT01766817, CHEST 2018
##NCT04308681, BMJ Open Resp Res 2021, potential hypotension limited

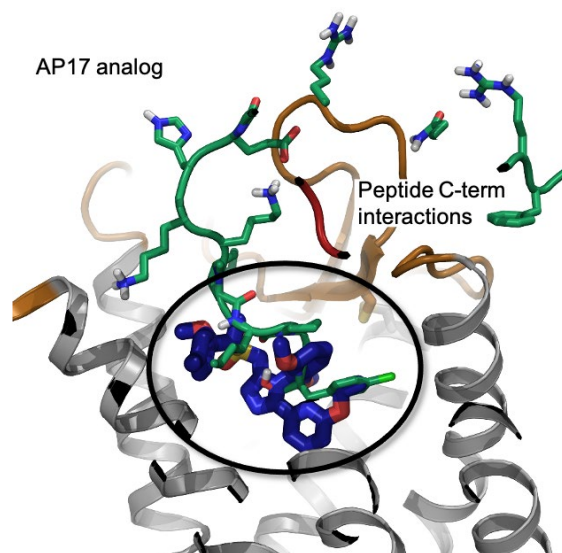
Rapid identification of clinical candidate APJR agonist for IPF and PAH

- ✓ Poster presentation held at American Thoracic Society Conference (ATS) in May 2023

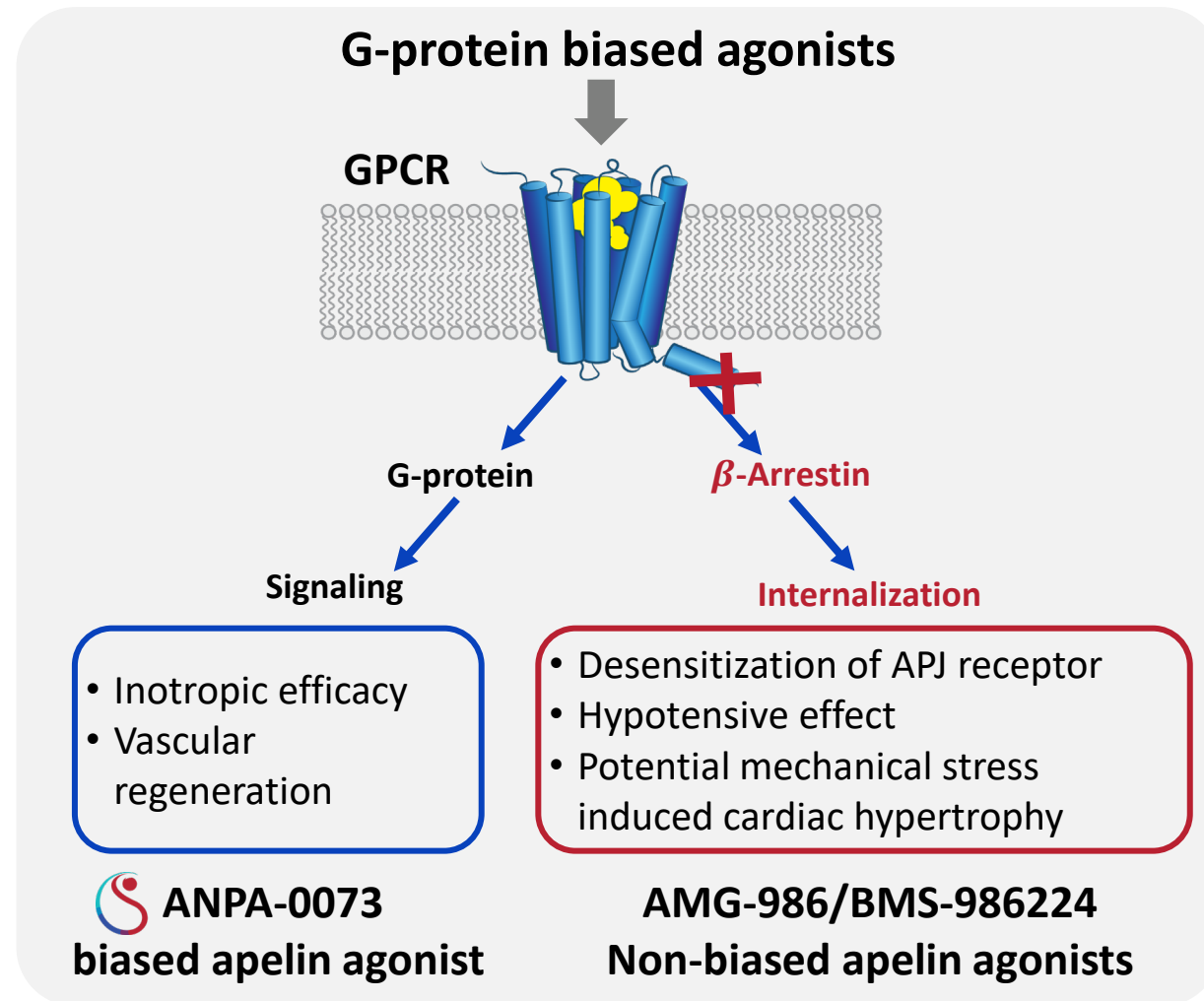
“Discovery of G-protein Biased APJ Agonist Small Molecule for Pulmonary Diseases”



Structure-based drug discovery



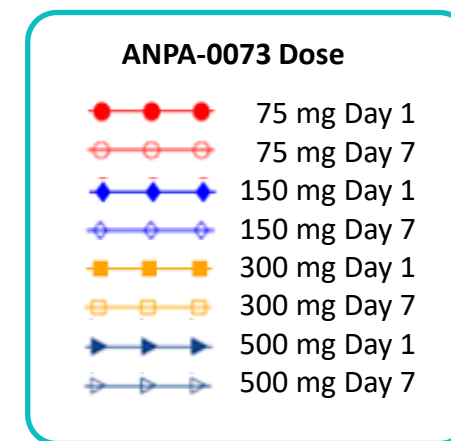
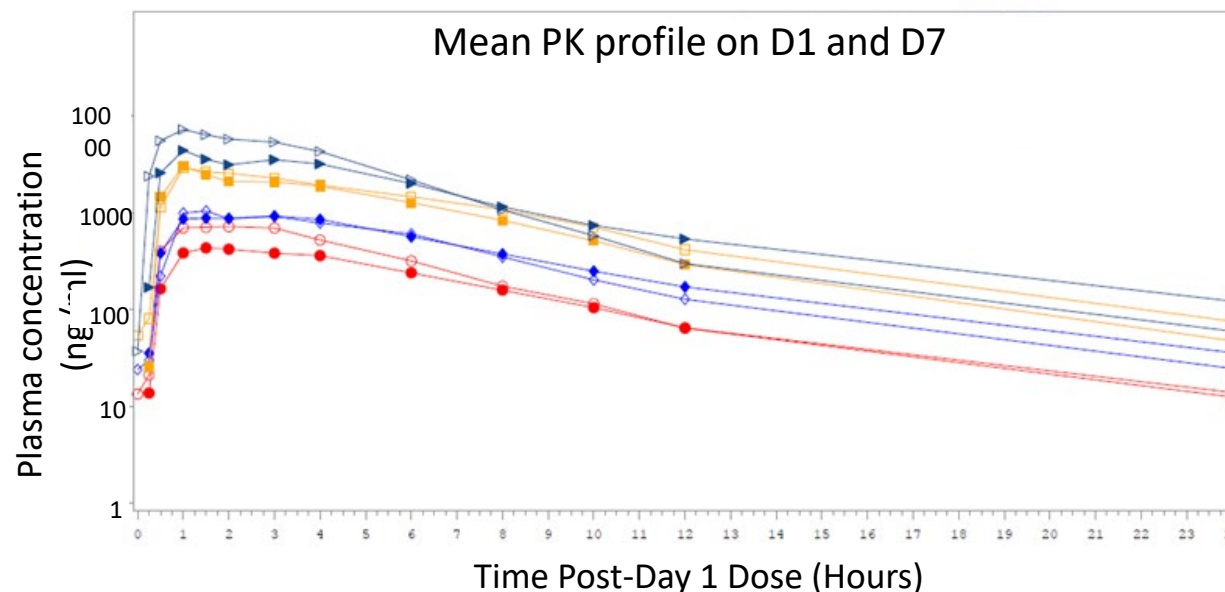
- **Rapid identification of ANPA-0073** by combining in-house data and FEP computational technology in partnership with Schrödinger
 - **310 compounds/9 months**



ANPA-0073 successfully completed Phase 1 studies

- ✓ Poster presentation held at American Thoracic Society Conference (ATS) in May 2023

“A First-in-Human Single/Multiple Ascending Dose Study of ANPA-0073, a Novel Small Molecule G-protein Biased Apelin Receptor Agonist, in Healthy Volunteers”



ANPA-0073 well-tolerated in single and multiple ascending doses in healthy volunteers (n=96)

- Evaluated up to single dose of 600 mg and multiple doses of 500 mg
- Dose proportional PK from 75 mg to 500 mg on Day 1 and Day 7
- No SAEs and no adverse changes in laboratory tests were observed

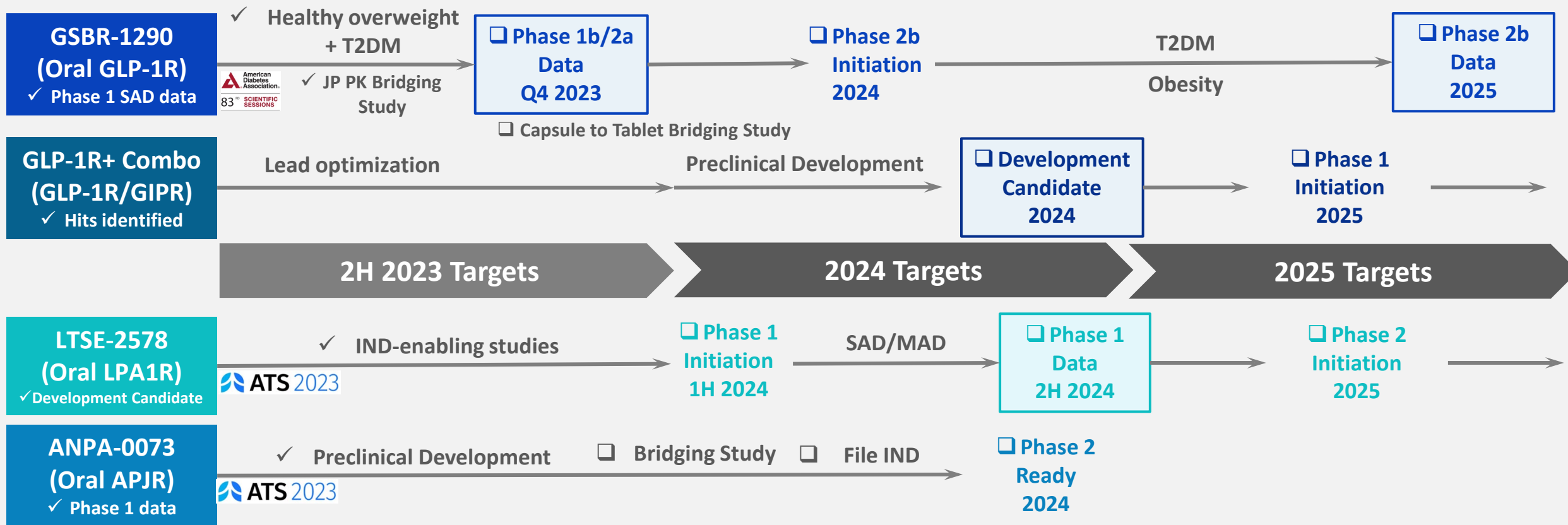
Anticipated next milestones

- Complete additional preclinical studies in IPF and PAH including bridging study
- Phase 2 ready in 2024

Strong momentum and execution to continue into 2023 – 2025 with multiple anticipated catalysts

\$224.6M Cash Balance as of June 30, 2023 to fund operations through the end of 2025

Anticipated Milestones



Clear strategy and runway to execute on value creating programs



- ✓ **Focused on replacing injectable biologics and peptides with oral small molecules**
Highly selective GLP-1R agonist GSK-1290 in Phase 2a with GLP-1R Combo life cycle management



- ✓ **Large diabetes and obesity TAM worth >\$50B by 2028 and growing¹**
Targeting GLP-1R and incretins dominated by injectables and peptides with high demand for oral agents



- ✓ **Initial GPCR focus represents broad potential to address global healthcare needs**
100% owned internal R&D engine to discover and develop small molecule pipeline



- ✓ **Advanced computational and structure-based technology platform**
25+ years GPCR experience and know-how combined with Schrödinger partnership



- ✓ **\$185M IPO completed in Feb 2023 and strong momentum to execute with multiple catalysts**
\$224.6M Cash Balance as of June 30, 2023 to fund operations through the end of 2025



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Thank you!

CONTACT US FOR ADDITIONAL INFORMATION:

Email: ir@structuretx.com

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