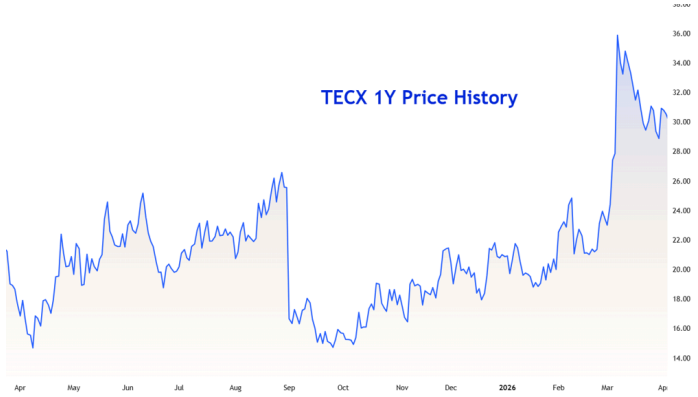
Benjamin Shar

Long Tectonic Therapeutic (NASDAQ: TECX)

April 23rd, 2026

Cap Table (USD MMs)	
Share Price	27.5
Shares Outstanding	19
Market Capitalization	**516**
Cash and Equivalents	254
Debt	0
Enterprise Value	263



Investment Overview

Tectonic Therapeutic (NASDAQ: TECX) is a clinical stage biotech working on a GPCR (G-Protein Coupled Receptor) platform aimed at a wide range of pulmonary diseases. TECX's price is currently derived around their flagship Phase 2 TX45 PH-HFpEF program, which targets the relaxin hormone. The stock traded down on the back of Eli Lilly and AstraZeneca program failures in adjacent relaxin analogs, which in my view mispriced TX45 as guilty by association. The recently published Phase 1a/b results show pharmacokinetics and pharmacodynamics that meaningfully differentiate TX45 from both prior failures. Dosing sits in a window that is high enough to produce the efficacy signal missing from AZD3427, but well below the supratherapeutic levels that drove the congestion signal in volenrelaxin. Patient enrichment for CpcPH mirrors the design of the successful CADENCE sotatercept trial, the only positive Phase 2 ever run in PH-HFpEF/CpcPH. A cash runway into Q4 2028 limits downside around a failed readout, and a thin float with roughly 22.7% short interest sets up favorable squeeze dynamics on a positive APEX print. My work implies a ~30% PoS against a market-implied ~12% PoS, and I recommend a long position in TECX.

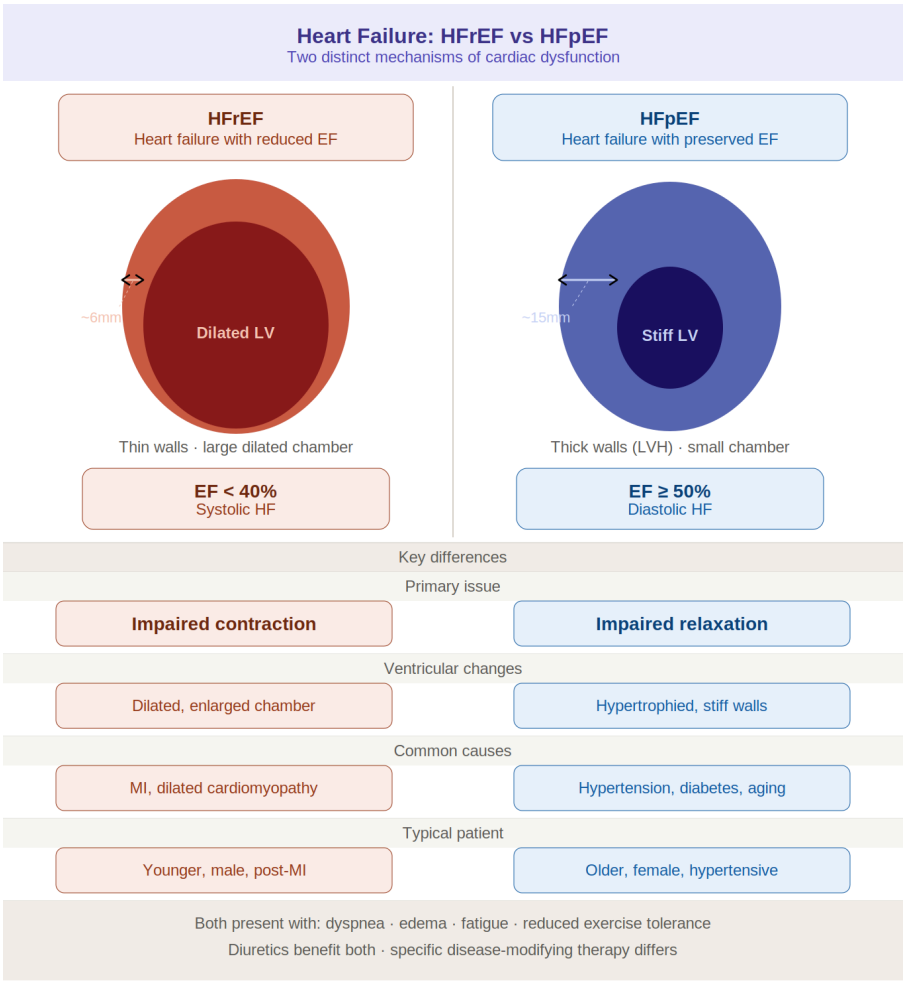
Business Overview

Tectonic Therapeutic is a clinical-stage biotech founded in 2019 that went public through a reverse merger with AVROBIO, a gene therapy company, in June of 2024. Tectonic focuses on developing proteins to modulate the activity of GPCRs, a transmembrane receptor family that remains the target for nearly 50% of modern FDA-approved drugs. Tectonic's lead asset, TX45, uses an engineered relaxin to target the RXFP1 receptor, which is associated

with vasodilation and anti-fibrotic effects. Though relaxin is naturally at its highest concentration in the body during pregnancy, Tectonic and other companies have engineered biologic forms of relaxin intended to redirect those effects toward Pulmonary Hypertension, a lung disease that can ultimately lead to heart failure. AstraZeneca and Eli Lilly both advanced engineered relaxin analogs into the clinic, only to discontinue their programs; AZD3427 for insufficient efficacy and volenrelaxin for safety concerns. Tectonic is specifically targeting Group 2 PH-HFpEF, with enrichment for CpcPH, which I explain below.

Background on Pulmonary Hypertension, PH-HFpEF, Relaxin, RXFP1, and TX45

Pulmonary Hypertension (PH) represents a state of high blood pressure in the lung arteries, which ultimately makes the right side of the heart work harder than it normally has to. Blood has to travel from the right ventricle into the lung circulation and then into the left side of the heart. When the pressure inside that path is higher, less blood gets through, and other organs have to work harder to get the necessary amount of oxygenated blood across the body. PH is categorized into multiple groups based on cause. In Group 2 PH, the left ventricle is either unable to eject blood efficiently or is unable to relax and fill adequately. This raises left ventricular end-diastolic pressure, which over time backs up into the left atrium and ultimately the pulmonary veins and capillaries, causing the lung vessels to constrict as well. Within Group 2 PH, there are two subsets called Heart Failure with Reduced Ejection Fraction (HFrEF) and Heart Failure with Preserved Ejection Fraction (HFpEF). The two categories are determined by Ejection Fraction (EF), with EF < 40% for HFrEF and EF > 50% for HFpEF. Ejection Fraction is defined as how much blood the left ventricle pumps out with each beat. HFrEF patients have a weaker ventricle that cannot eject blood well, while HFpEF patients have fibrotic issues with stiffening of the ventricle or nearby arteries. Tectonic is specifically focused on Group 2 PH-HFpEF.



There is currently no approved therapy specifically for Group 2 PH-HFpEF. True "treatment" today is limited to controlling blood pressure and general decongestion, commonly SGLT2 inhibitors. A TX45 approval would therefore be a first mover.

Going deeper into the biology of HFpEF, comorbidities such as obesity create a state of chronic inflammation that injures the endothelium. This causes the endothelium to make less nitric oxide, which makes the arteries and arterioles stiffer and less able to dilate. The arteries also get stiff in a second way. Fibroblasts, the cells responsible for repairing inflammation with collagen, are designed to patch an inflamed area and then stop depositing collagen. Under chronic inflammation, fibroblasts turn into myofibroblasts and continuously

deposit excess collagen to inflamed areas, making blood vessels stiffer over time. Endothelial dysfunction and excess matrix deposition together increase vascular stiffness, worsen microvascular function, and contribute to the elevated filling pressures and exercise intolerance seen in HFpEF.

This is where **relaxin** comes in. Relaxin is a hormone usually secreted in pregnancy to facilitate the physical changes necessary for delivering a baby. It is associated with vasodilation, increased renal blood flow, and anti-fibrotic tendencies, all of which theoretically address core parts of HFpEF biology. This was the thesis when scientists first developed an engineered form of relaxin called serelaxin. Serelaxin was created through recombinant DNA and therefore closely resembled native relaxin. That resemblance left it with a very short half-life and a high isoelectric point. The short half-life of only a few hours drove a fast decline in concentrations and lower receptor occupancy. The high isoelectric point gave serelaxin a strong net positive charge, which caused it to stick to negatively charged glycosaminoglycans on many cell surfaces. This is a likely reason it was difficult to sustain clinical benefit within the large Phase 3 RELAX-AHF-2 trial.

Since then, scientists have been experimenting with a different form of treatment called Fc-fusion proteins. An antibody has two parts: Fab, which binds to a target, and Fc, the tail region. The Fc region does not usually recognize an antigen, but it gives the antibody important physical characteristics. One of the most important is recycling through FcRn. The Fc region can bind to FcRn, which protects the antibody from lysosomal degradation and recycles it back into circulation, dramatically increasing half-life. AstraZeneca's AZD3427 bound relaxin to an antibody Fc tail, while Eli Lilly's volenrelaxin bound to serum albumin. TX45 is also an Fc-fusion protein. TX45 binds to the RXFP1 receptor, which activates signaling pathways that increase nitric oxide, stimulate matrix metalloproteinases that degrade collagen, and increase renal blood flow in the kidneys. Some of these features, such as the anti-fibrotic effects, have no proof of concept in human trials thus far.

Since all past trials failed to indicate efficacy in humans, the main proof of concept in the current investor debate is the Phase 1 data for TX45. Before walking through those results, some definitions:

PCWP: Pulmonary Capillary Wedge Pressure - An indirect estimate of left atrial pressure and often a proxy for left-sided filling pressure.
mPAP: mean Pulmonary Arterial Pressure - The average pressure in the pulmonary arteries.
CO: Cardiac Output - The amount of blood the heart pumps per minute. CO = Heart Rate x Stroke Volume

PVR: Pulmonary Vascular Resistance - The resistance the right side of the heart has to pump against through the pulmonary circulation. PVR = (mPAP – PCWP)/CO

Investment Thesis: Phase 1 Results Contain More Negatives Than Positives, Lack Reliable Proof of Efficacy, and Rest on a Weak Surrogate Endpoint

The market currently prices TX45 at roughly a 12% chance of approval, based on patient enrichment and the Phase 1 pharmacokinetic and pharmacodynamic results. The bear case discounts those Phase 1 results as not differentiated from AZD3427 or volenrelaxin, and assigns TX45 to the same failure bucket. I will be disputing that bear case. The Phase 1 data, combined with where TX45 sits on the relaxin dose-response curve relative to failed competitors, and a trial design that mirrors the only positive Phase 2 ever run in this indication, together support a meaningfully higher PoS than what the market implies.

In January of 2025, TECX released interim Phase 1b PH-HFpEF results for TX45, and the full results in May of 2025. The hemodynamic profile over an 8-hour window was strong. The interim readout reported a 17.9% average decrease in PCWP across the overall group, which moved to 19.0% in the full dataset. PVR fell 32% in patients with PVR > 2 WU (IpcPH enrichment) and 35% in patients with PVR > 3 WU (CpcPH enrichment). CO moved 17.4% from baseline in the interim data and 18.5% in the full dataset.

Secondary Endpoints	Absolute CFB, Mean [95% CI]	Average % CFB, [95% CI]
Hemodynamics (Key 2º) (N = 16)		
Mean Δ PCWP in all participants	- 2.9 [-1.7 to -4.2] mm Hg	**-17.9% [-9.8% to -26.1%]**
Mean Δ PVR in CpcPH (PVR ≥ 2 WU) (n= 9)	- 1.06 [-0.78 to -1.34] Woods Units	**-32.0% [-28.1% to -35.9%]**
Mean Δ PVR in CpcPH (PVR ≥ 3 WU) (n= 5)	- 1.35 [-1.15 to -1.55] Woods Units	**-35.5% [-32.5% to -38.6%]**
Other Hemodynamic Effects		
Mean Δ Cardiac Output in all participants	+0.65 [0.34 to 0.96] L/min	**+17.4% [8.9% to 25.9%]**
Mean Δ Stroke Volume in all participants	+7 [2 to 12] mL	**+13.8% [5.3% to 22.3%]**
Mean Δ TPR in all participants	-1.79 [-1.24 to -2.34] Woods Units	**-26.3% [-20.1% to -32.5%]**
Mean Δ mPAP in all participants	-4.33 [-3.02 to -5.65] mmHg	**-15.9% [-11.2% to -20.6%]**

At face value these results are very impressive. In heart failure, the body detects a heart that cannot pump adequately and responds by constricting blood vessels, retaining fluid, and raising heart rate, which drives up PVR and PCWP. In TX45's Phase 1 data, the right

ventricle appears to be facing far less resistance, blood is flowing more easily, and PVR, PCWP, and mPAP all fall.

The question the bears raise is whether the CO increase is the right kind of CO increase. Since CO = HR x SV, it matters whether CO rose via stroke volume or via heart rate. This distinction matters because of how RAAS (the Renin-Angiotensin-Aldosterone System) behaves, which is the pathway responsible for congestion and blood backup in the pulmonary area. Renin is an alarm signal the kidneys use to raise blood pressure when they sense something is wrong. Once renin is in circulation, it cleaves angiotensinogen into angiotensin 1, a relatively inactive decapeptide, which then passes through the lungs and encounters angiotensin-converting enzyme, which chops off two amino acids to produce angiotensin 2. Angiotensin 2 directly constricts blood vessels, forces the kidneys to retain salt and water, and raises blood pressure. This compensatory response can counteract the drug over time, and is likely what happened in the volenrelaxin trial. The response is driven by two sensors: the arterial baroreceptors, which respond to mean arterial pressure and pulse pressure, and the renal afferent arterioles, which respond to perfusion pressure and trigger renin. If CO rises via stroke volume, the ventricle is filling well, cardiopulmonary receptors sense good stretch, and both the sympathetic nervous system and RAAS get suppressed. A larger SV also widens pulse pressure, which fires more baroreceptors and further inhibits SNS. If instead CO rises via heart rate, tachycardia already activates the SNS, and shorter diastolic filling may actually pull SV down, reducing baroreceptor stretch.

If we do the math based on phase 1 data, baseline HR = $\frac{3740mL/min}{50.7\ mL} = 73.8\ bpm$,
If our new CO is 3.74 + 0.65 = 4390 mL/min, and new SV = 57.7 mL (50.7 baseline + 7 change), then $\frac{4390}{57.7} = 76.1\ bpm$, 76.1 - 73.8 = 2.3, or a 3.1% change in bpm. Given that stroke volume increased by 13%, and that this is in the first 8 hours, this is actually a good sign when compared with the fact that the heart rate increase is likely caused by baroreflexes, but is still concerning once we compare it to AZD3427. Tectonic also reported their own 29-day echo data to rebut the acute data concern, and Tectonic actually did not report any HR data for days 2, 15, and 29 of their echo analysis, which is a small red flag (For the record, this data is from the HFrEF phase 1, not HFpEF).

In February 2026, AstraZeneca discontinued AZD3427 following its Re-PHIRE Phase 2 readout, citing insufficient efficacy. This is the single most important recent data point for assessing TX45. AZD3427 was a long-acting Fc-relaxin fusion, architecturally nearly identical to TX45, and tested the exact hypothesis on which the TX45 bull case rests: that extending relaxin's half-life rescues its clinical efficacy. That hypothesis has now failed its first controlled Phase 2 test, and the scoreboard for long-acting relaxin biologics in cardiovascular

disease sits at 0-for-3: serelaxin (short half-life), AZD3427 (long half-life Fc-fusion), and volenrelaxin (long half-life, supratherapeutic dosing). This is where I diverge from consensus. Comparing TX45 Phase 1 data to AZD3427 Phase 1 data, AZD3427 showed no change in heart rate with trends toward increased stroke volume. The most likely explanation for the difference in heart rate is dosing: AZD3427 was mostly subcutaneous, while TX45 was dosed IV, which hits the system more quickly. TX45 was also being dosed to higher pharmacologically equivalent concentrations than AZD3427. Lilly, by contrast, gave volenrelaxin at levels pharmacologically equivalent to thousands of times peak pregnancy relaxin, and the resulting supratherapeutic dosing plausibly explains the congestion signal that emerged. The cleanest way to evaluate where TX45 sits is to calculate the relaxin concentrations used in each program relative to natural pregnancy levels. The more TX45 differentiates from AZD3427, the higher the chance of congestion appearing in the APEX Phase 2 trial, and the more it differentiates from volenrelaxin, the better.

> The average concentration at steady state (Css,ave) at the three dose levels are predicted to range from sublevels to supra levels of corresponding relaxin levels in pregnancy: 0.5-fold, 2.5-fold, and 15-fold of relaxin pregnancy levels, respectively. This correlation between levels of AZD3427 and relaxin accounts for the difference in *in vitro* potency between serelaxin and AZD3427 (approximately 40-fold) based on cAMP production in CHO cells expressing the recombinant human RXFP1 receptor and the difference in molecular weight between serelaxin and AZD3427 (AZD3427 being 10-fold greater) and assumes a relaxin concentration of 0.2 ng/mL in pregnancy (in-house data). In addition, using concentration-response relationships for ejection fraction, stroke volume, and systemic vascular resistance from the NHP HFrEF model and PK data from the SAD/MAD study (study D8330C00001), it is predicted that the dose range selected in the Ph2b study will enable characterization of the dose-response for these parameters (FIG. 10, FIGs. 11A-11C).

(Page 61, https://patentimages.storage.googleapis.com/97/c9/66/7ce89fd83a1e9e/WO2024121362A1.pdf)

Attached is an excerpt from the application for AZD3427's patent, describing the dosage that was used in the RE-PHIRE Phase 2 trial for AstraZeneca. We note that the relaxin levels were 0.5x, 2.5x, and 15x the levels of natural relaxin in pregnancy. Now we have to analyze this for TX45 and volenrelaxin.

To estimate the (xPREGNANCY) numbers for TX45, we can estimate using AstraZeneca's data as a reference. We will use AZ's 0.2 ng/mL reference to calculate for the Q2W and Q4W dosing, using 110x less potency as a number for TX45 (cited here: https://www.jhltonline.org/article/S1053-2498(25)00927-1/fulltext), and using an 11-fold adjustment for molecular weight:

$$Q4W: \frac{2000ng/mL}{\sim 110*11} = 1.65\ ng/mL\ native, \frac{1.65}{0.2} = 8.25x\ pregnancy$$

$$Q2W: \frac{8000ng/mL}{\sim 110*11} = 6.61\ ng/mL\ native, \frac{6.61}{0.2} = 33x\ pregnancy$$

Q2W numbers imply 33x pregnancy at 0.2 ng/mL reference.

My total comparison comes out to:

AZD3427: 0.5x, 2.5x, 15x pregnancy levels
TX45: 8.25x, 33x pregnancy levels
Volenrelaxin: ~1500x pregnancy levels, using 8.7x less potency and around 3.7-fold molecular weight.

Given AstraZeneca's own comments about finding the balance between efficacy and congestion, AZD3427 was likely dosed too low relative to natural pregnancy, especially because commonly cited native relaxin concentration in pregnancy is closer to 1 ng/mL. On that reference, TX45's true multiples are closer to roughly 2x and 7x natural pregnancy, which is the target zone. TX45 is also orders of magnitude below the concentrations used in volenrelaxin, where safety was the main concern. TECX also has by far the most granular description of dose selection. AZD cited basic PK/PD analysis, while TECX used an Emax model built on over 200 RPF measurements per subject, producing a maximum effect of 33% (SE 3.3%, $p<0.0001$). That is unusual specificity, and it points to a dose level with the highest likelihood of clinical success.

One fair bear counter is that the AZD3427 patent application also reports that at doses above 45 mg QW, hematocrit and hemoglobin fell below the acceptable safety profile,

implying a threshold for congestion was being approached in the AZ trial. There are two issues with extrapolating that straight across to TX45. First, that data was not recorded at steady state. Running the math, fraction of steady state reached after n doses with a 14-day half-life:

$$1 - e^{(-n\times 0.693\times 7/14)} = 1 - e^{(-0.347n)} = 1 - e^{(-1.73)}(after\ 5\ doses) = 2830\ ng/mL$$

2830/80 (80 = 0.2 x 40 x 10) = 35.3x steady state

So the highest TX45 dose, at 33x natural pregnancy, actually sits below the threshold cited for renin activation in the AZ patent. Second, the N supporting the monotonic dose response on hematocrit and hemoglobin in the patent is low double digits to high single digits, which makes statistically meaningful conclusions difficult. TX45's dosing is far below volenrelaxin's congestion zone, and sits comfortably under the AZD3427-implied threshold, while being high enough to drive the efficacy signal AZ likely missed. This is the best-positioned shot relaxin has had at combining safety with efficacy.

Given the dose positioning, safety should not be the primary concern. On efficacy, the Phase 1a trial showed Renal Plasma Flow increases of up to 42%. In the Phase 1b Part A, PCWP decreased by 19%, CO increased by 17.4%, stroke volume increased by 13.8%, mPAP decreased by 15.9%, and TPR decreased by 26.3%. For comparison, volenrelaxin actually saw PCWP increase (E/e' +1.7). As a side note, this shows also that nothing in TX45's 8-hour Phase 1b data is consistent with congestion. PVR fell 32% in the PVR > 2 WU subgroup (IpcPH) and 35% in the PVR > 3 WU subgroup (CpcPH), which is a clean signal that the enriched population responds. Favorable signals also showed up in both the EF < 40% and EF > 41% subgroups, while in AZD3427, the EF > 41% group showed no effect on stroke volume, cardiac output, or eGFR. This both weakens the congestion concern and strengthens the efficacy case.

On the concern that acute benefits could reverse, TECX reported echocardiographic data on days 2, 15, and 29 in the HFrEF trial that showed LVEF up 19.4%, RVFAC up 20.3%, and TAPSE/SPAP up 36.3%, which implies PVR fell, since TAPSE/SPAP moves inverse to PVR.

The other major leg of my thesis is trial design. TECX is enriching for roughly 70% of the APEX population to have CpcPH, with the primary endpoint defined in the enriched subgroup. AZD3427's Re-PHIRE had no enrichment and likely skewed IpcPH. The

CADENCE Phase 2 trial for Merck's WINREVAIR (sotatercept), whose MoA focuses on inhibiting signals that drive abnormal pulmonary vessel wall cell growth, was enriched for CpcPH. In that trial, PVR decreased by a statistically significant 1.02 WU over 24 weeks, PCWP improved, LVEF stayed stable, and functional capacity improved. That was the first positive Phase 2 ever run in PH-HFpEF/CpcPH. Sotatercept at 0.3 mg/kg also outperformed 0.7 mg/kg, with the difference tied to safety-driven interruptions, which is evidence that dose response in CpcPH can be non-monotonic. Trial design comparison is also favorable: APEX enriches for PVR WU > 3, CADENCE enriched for PVR WU > 4 (both CpcPH signals), patient populations are broadly similar, the mean age in CADENCE was 75, and APEX allows enrollment up to 80 so APEX will likely skew older. Overall, APEX looks structurally like the trial that has actually worked in this indication, which is a major point for Tectonic.

Back on AZD3427, relative relaxin concentrations were 0.5x, 2.5x, and 15x natural pregnancy. AZD3427 was discontinued in February 2026, and other than a comment about efficacy, nothing has been published since. Sharon Barr, executive vice president of biopharmaceuticals R&D at AstraZeneca, commented:

"You really have to find that perfect space between efficacy and congestion, and we think we've put in the hard yards to really understand the posology there, and we\'re moving forward with our existing program."

AstraZeneca also has a small molecule relaxin, AZD5462, which should theoretically be easier to advance given what they have learned through AZD3427, and which runs on a 3-6 hour half-life with BID dosing. I think there is a very high chance that the two lowest AZD3427 doses produced no efficacy but the 15x native dose did, and that poor enrichment prevented that signal from reaching statistical significance. AstraZeneca can either rerun an expensive Phase 2 that enriches for CpcPH and compete head-to-head with TECX, or pivot to a cleaner MoA (AZD5462) while holding back full AZD3427 data. In their shoes, I take the second path. That means there may have been an efficacy signal in AZD3427 we will not see, which further supports the case that a 12% market-implied PoS on TX45 is too low.

A further point on upside sizing: because of the unusual hemodynamic profile of this drug, strong Phase 2 results are likely to be priced in at a higher PoS than the standard ~50% Phase 3 to approval assumption typically used in cardiovascular trials, which means the stock re-rate on a positive APEX print should exceed the modeled implied upside. On top of that, TECX already sits with ~22.7% short interest of float on a thin float of roughly 10-12

million shares after stripping out insider holdings, which layers meaningful short squeeze risk on top of the fundamental re-rate.

Finally, TECX has an anticipated cash runway into Q4 2028. A poor APEX Phase 2 readout would not immediately force the stock to trade to cash, which softens the downside of the residual failure risk. Combining the dose positioning, CpcPH enrichment, Phase 1 hemodynamics, short interest, and cash runway, I recommend a long position in TECX.

Valuation: At the current $27.50, with a risked NPV of $154 at PoS=100% and $13.52 at PoS=0%, the market is pricing approximately 12% PoS. My analysis implies 30%, an approximately 18pp gap to consensus. To value TECX, I used TD Securities assumptions for the revenue build and DCF through 2035, then projected based on analyst estimates out to 2042. Since my differentiation is on PoS, I did not differentiate on the revenue build. Applying a risk-adjusted analysis to the UFCFs gives a base case of 103.31% upside, a bear case of 30.56% upside, and a bull case of 226.44% upside.

Valuation (USD MMs)	
WACC	11.39%
GGM Terminal Value	**1,897**
PV of Terminal Value	303
PV of Cash Flows	493
Enterprise Value	**796**
Debt	0
Cash	254
Market Cap	**1,050**
Implied Price	**55.91**
Implied Upside / (Downside)	**86.00%**

Risks & Catalysts:

Risks

- APEX Phase 2 Trial is either delayed or completely cancelled due to concerns of congestion, or lack of efficacy. Similar result to volenrelaxin / AZD3427.

- AZD3427 results are fully posted and reveal more info that can connect similar biology to congestion, therefore decreasing the probability of TX45 succeeding substantially.

Catalysts

- APEX Phase 2 Trial data is released and shows tangible efficacy without safety risks. It is shown that the cardiac output increase is actually helping the heart produce more blood in accordance with its healthy capacity, and the congestion risk thesis is proved to be wrong. NT-proBNP levels show no statistically significant increase.
- Acquisition chance, if a big pharma wants RXFP1 exposure after key competitors (Eli Lilly, AZD3427 subcutaneous injection) have been eliminated, TX45 shows strong hemodynamics in Phase 1 trials.