Trinity Delta

Arecor Therapeutics

Update

EASD 2024: Positive Phase I for AT278 in Type II diabetes

17 September 2024

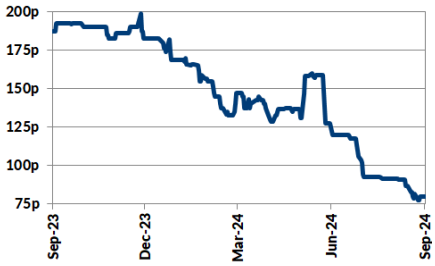
Detailed data from the Phase I study in Type II diabetes (T2D) of Arecor's lead asset AT278, a unique ultra-rapid and ultra-concentrated insulin, were presented at the European Association for the Study of Diabetes (EASD) 2024 meeting. These data confirm its attractive profile, with faster onset and stronger early glucose-lowering effect in comparison to gold standard fast-acting insulin NovoRapid/NovoLog (NovoNordisk). Clinical data to date suggest a pertinent and highly differentiated profile that is suited for T2D patients with high insulin needs, and which could also enable miniaturised 'next generation' insulin delivery systems with longer-wear times. Given the data and unmet patient need, an optimal strategy for continued AT278 development is under evaluation by Arecor. This includes plans for a small pump study, alongside consideration of strategic co-development. Following the recent fundraise and trading statement, our reinstated valuation is £157m, or 415p/share.

Year-end: December 31	2022	2023	2024E	2025E
Revenues (£m)	2.4	4.6	6.2	10.4
EBITDA (£m)	(10.2)	(8.7)	(7.7)	(5.2)
Adj. PBT (£m)	(12.0)	(10.7)	(8.7)	(6.2)
Net Income (£m)	(9.3)	(8.6)	(7.7)	(5.2)
EPS (p)	(0.3)	(0.3)	(0.2)	(0.1)
Cash (£m)	12.8	6.8	3.9	1.1

Source: Trinity Delta Note: Adjusted numbers exclude share-based payments and exceptionals.

- **A consistently differentiated clinical profile…** AT278 is an ultra-high concentration (U500) insulin aspart formulation that also has ultra-fast absorption. Full data at EASD from the Phase I study in high BMI T2D patients, who are typically more difficult to treat, show AT278's superiority to the gold-standard rapid insulin NovoRapid U100 (mirroring findings from the Phase I trial in otherwise healthy Type I diabetics), with topline results indicating superiority vs Humulin-R U500.
- **…which could help address emerging diabetes market needs** The prevalence of diabetes patients with high insulin needs is rising, but this demographic remains poorly served by existing insulins and pen/pump devices. An ultra-rapid and ultra-concentrated insulin such as AT278 could enable next-generation insulin pump delivery systems (or AIDs) allowing both miniaturisation and longer wear time, which should drive their uptake, including by T2D patients where adoption is low.
- **Diabetes franchise remains the key value driver** Positive clinical data, the unmet need, and shifting diabetes landscape, support continued AT278 development. An ability to administer high doses of a mealtime (fast-acting) insulin in smaller volumes should be highly attractive to potential partners. Arecor plans to conduct a small pump study, subject to additional funding, to demonstrate AT278's potential and provide validation in this key market segment.
- **Valuation of £157m, or 415p per share** We reinstate our valuation and forecasts following the recent £6.4m (gross) fundraise and trading update, slightly decreasing our revenue forecasts on lower near-term Tetris Pharma product sales due to timing of the equity raise and subsequent Ogluo inventory investment. Our Arecor rNPV valuation is now £157m, equivalent to 415p/share.

Price	80.0p
Market Cap	£30.2m
Enterprise Value	£23.9m
Shares in issue	37.8m
12-month range	75.0p-199.0p
Free float	36.4%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	AREC
Corporate client	Yes



Company description

Arecor Therapeutics is a clinical stage drug developer, with a well-balanced portfolio of in-house and partnered assets, and an internal focus on diabetes. Its proprietary Arestat formulation platform results in enhanced products with lower development risks and less onerous regulatory approvals.

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Arecor: EASD data confirm AT278's profile

The emerging diabetes franchise underpins our investment case

Arecor's diabetes franchise is central to its investment case, with ultra-rapid and ultra-concentrated insulin AT278 making a significant contribution. AT278, a novel and unique U500 formulation of insulin aspart (IAsp), is Arecor's key in-house clinical-stage programme. Its clinical profile opens the promise of miniaturised "next generation" automated insulin delivery (AID) pump systems with longer-wear times, and increased convenience and suitability for a wider range of patients, such as those with high insulin requirements (eg some Type II diabetes, T2D patients), irrespective of delivery device (pen or pump).

AT278 appears ideally placed to enable the next generation of integrated insulin pumps

AT278 has the potential to be a disruptive insulin that is ultra-concentrated yet also ultra-rapid acting, unlike currently available U500 and U200 concentrated insulins, allowing high doses of a mealtime (fast-acting) insulin to be administered in smaller injection volumes, supporting better blood-glucose control.

Latest data confirm attractive absorption profile and its relevance to patients

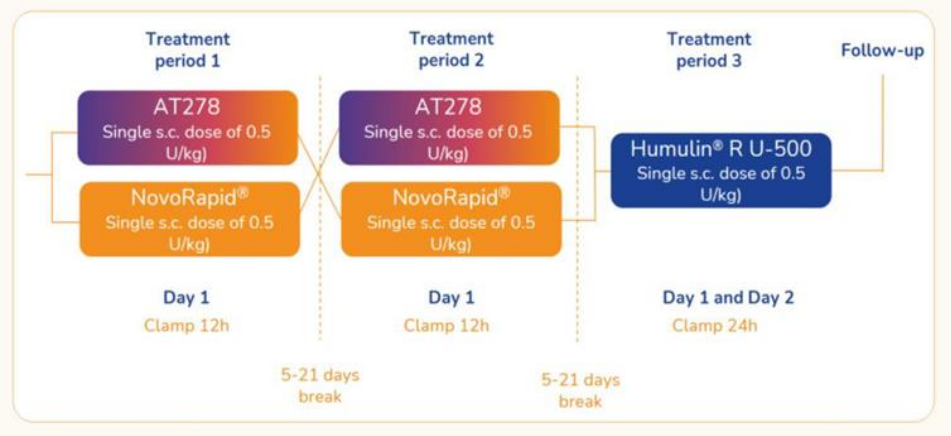
Clinical data from Phase I studies confirm a superior pharmacokinetic and pharmacodynamic (PK/PD) profile to gold-standard rapid insulin NovoRapid U100 in both overweight/obese T2D patients (May 2024 Update) and in otherwise healthy Type I diabetics (May 2022 Update, September 2021 Lighthouse), suggesting a highly differentiated fast-acting profile irrespective of diabetes type and BMI. In the T2D trial, AT278 also showed superiority to a concentrated comparator, Humulin-R U500. Detailed data, summarised below, from the T2D study were recently presented at the European Association for the Study of Diabetes (EASD) 2024 meeting in a late-breaking oral session ('Pharmacokinetic and pharmacodynamic properties of highly concentrated insulin aspart AT278 U500 in overweight and obese people with Type II diabetes').

Phase I data in T2D patients presented at EASD 2024

Results from Type II patients study presented at EASD 2024

Data were presented at EASD 2024 from the randomised, double-blind, two-way crossover Phase I ARE-278-104 trial (Exhibit 1) evaluating 41 overweight/obese patients with Type II diabetes. Type II diabetes patients often have highly variable outcomes given the frequent incidence of high BMI (body mass index) in the overweight (BMI of 25 to <30 kg/m^2) and obese (BMI of ≥30 kg/m^2) ranges.

Exhibit 1: Phase I study in overweight/obese Type II diabetics



Source: Arecor

AT278 compared to NovoRapid in representative overweight and obese patients…

Patients enrolled in the study had a median BMI of 29.7 kg/m^2, median HbA1c (a measure of blood glucose) of 58 mmol/mol (48 mmol/mol is the level for diagnosing diabetes), and a median diabetes duration of 18 years. Patients were allocated to receive a single subcutaneous 0.5 U/kg dose of AT278 U500 and Novo Nordisk's U100 insulin aspart NovoRapid (NovoLog in the US), followed by a 12-hour euglycaemic clamp.

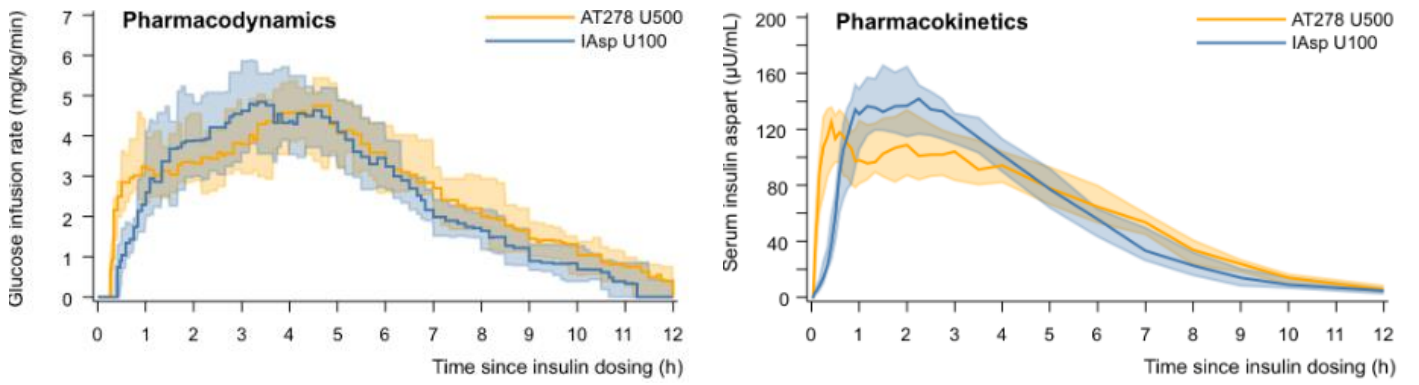
…and also compared to high dose Humulin R 500

The study also had an added comparator of a high concentration insulin, Eli Lilly's Humulin-R U500. While top-line results indicated that AT278 had superior absorption to both NovoRapid U100 and Humulin-R U500, data presented at EASD 2024 focused on the PK/PD profiles of AT278 and NovoRapid U100.

Detailed data confirm the benefits seen are relevant and clinically attractive

The data presented showed significantly accelerated early PK/PD profiles with AT278 U500 in comparison with IAsp U100 in high BMI T2D patients (Exhibit 2). The primary endpoint of non-inferiority for glucose-lowering effect ($AUC_{GIR,\ 0\text{-}60min}$ or area under the curve for the glucose infusion rate from time zero to 60 minutes) was met; in fact, AT278 demonstrated a 1.7-fold (95% CI: 1.32 – 2.96) higher glucose-lowering effect within the first 60 minutes and statistical superiority to NovoRapid (p<0.0001). A pre-specified subgroup analysis based on BMI showed that the difference in the primary endpoint ($AUC_{GIR,0\text{-}60min}$) remained. The onset of glucose-lowering effect was more rapid with AT278 vs NovoRapid, with a five-minute earlier onset of action and 25-minute earlier time to half-peak metabolic activity ($t_{Early50\%GIRmax}$). In addition, the glucose-lowering effect was higher with AT278 up to two hours post-dose.

Exhibit 2: PK/PD profiles of AT278 and IAsp in overweight and obese people with Type II diabetes



Source: Arecor, EASD 2024 Note: PK/PD of AT278 U500 (orange line) and IAsp U100 (blue line) after subcutaneous administration of 0.5 units/kg in overweight and obese people with Type II diabetes. Lines show the median; variability bands the 95% confidence interval

Absorption profiles demonstrate the ultra-rapid onset

With respect to onset of insulin exposure, a faster onset was seen with AT278 compared with NovoRapid, with a five-minute faster insulin appearance and 24-minute faster time to half-peak serum concentration ($t_{Early50\%Cmax}$). Within the first 60 minutes, insulin exposure with AT278 was 1.5-fold (95% CI: 1.28 – 1.71) higher than with NovoRapid.

Glucose lowering effect was as expected, with a clean side-effect profile

Both AT278 and NovoRapid have comparable offset and overall insulin exposure and glucose-lowering effect: treatment difference (95% CI)] $t_{Late50\%Cmax}$ 30 min (-5; 64) and $t_{Late50\%GIRmax}$ 26 min (-0.6; 53); treatment ratio $AUC_{Insulin,0\text{-}12h}$ 0.97 (0.93; 1.00) and $AUC_{GIR,0\text{-}12h}$ 1.06 (0.97; 1.16). From a safety perspective, both insulins were well tolerated with adverse events being mostly mild to moderate and unrelated to the study drugs.

Evaluating next steps for AT278

Such positive Phase I studies support move to Phase II trials

Positive comparative Phase I results for AT278 in both Type I and II diabetics vs current benchmark rapid or concentrated insulins support further clinical development. If these results could be replicated in Phase II trials, AT278 has the potential to become the first disruptor insulin in several decades and is ideally placed to address various emerging needs from the evolving diabetes landscape and market from both a patient and device perspective (May 2024 Update).

Key questions centre on how management will choose to progress AT278…

Understandably, investors are focused on the likely format, and cost, of the next steps for AT278's clinical programme, the regulatory pathway, and on possible partnering options and their timing. As the next generation of insulin delivery devices, including miniaturised and longer wear pumps, will only be able to be achieved with an insulin like AT278, we believe that strong relationships with device manufacturers will be critical. Hence, we view positively Arecor's existing, albeit unrelated, collaboration with Medtronic (May 2024 Lighthouse) to formulate and develop a high concentration, thermostable insulin for use with a next-generation implantable pump.

…meanwhile a pump study will help to validate AT278's potential

On the theme of insulin pumps, Arecor has stated its intention that, subject to funding (which may include co-development options), it will conduct a small pump study to demonstrate AT278's potential and provide important validation in this significant market segment. Data from this study could be a precursor to potentially high value strategic partnering for future development and ultimately commercialisation.

Valuation and Financials

New funds and new investors

Our valuation has been reinstated following the recent £6.4m (gross) fundraise, with 7.13m new shares issued at 90p. Arecor has confirmed investment by two new strategic healthcare funds. Estimated net proceeds of c £5.8m will be invested to deliver significant value inflection points with: (1) £2.7m for continued R&D investment focused on an oral peptide delivery platform (including GLP-1) and enhanced injectables to drive significant future upside from licensing; and (2) £2.7m investment in Tetris Pharma to increase Ogluo sales, including building up inventory plus education and marketing, with an aim for Tetris Pharma to be cashflow positive in 2026. The remainder will provide general working capital.

Small tweak to near-term Tetris Pharma forecasts

An insight into current trading was provided during the fundraise, with unaudited H124 revenues of £1.9m. This excludes Q224 royalties on AT220, hence they relate to a mix of Arecor formulation business revenues and Tetris Pharma product sales, with Ogluo impacted by supply constraints. While the fundraise will ease this situation, we take our usual conservative approach and now forecast slightly lower £4.0m product sales in FY24 (from £4.4m), and £6.9m in FY25 (from £7.6m). Our updated FY24e and FY25e revenue forecasts are £6.2m (from £6.8m) and £10.4m (from £11.2m), respectively (Exhibit 4).

Updated rNPV of £157m, or 415p per share; key value driver remains the diabetes franchise

We value Arecor using a rNPV (risk-adjusted net present value) model, including the diabetes franchise, partnered assets, and the in-house Specialty Hospital research portfolio. This now reflects the £6.4m (gross) fundraise (including an estimate of current net cash) and reflects our near-term Tetris forecasts, whilst keeping the peak sales potential intact. Together with slightly later launches for AT292 (SAR-447537) and AT307, this results in a valuation of £157m, with this diluted to 415p per share based on the share count post the fundraise. An overview of our valuation, together with key assumptions, is provided in Exhibit 3.

Exhibit 3: Arecor rNPV valuation

Programme	NPV (£m)	NPV ($m)	Success probability	Royalty	rNPV (£m)	rNPV ($m)	rNPV/ share (p)	Notes
Diabetes franchise (AT278, AT247)	153.3	184.0	60%	High single to double-digit	92.0	110.4	243.7	Peak sales: c $875m; Launch year: 2028
Research (Specialty Hospital)	64.7	77.7	Various	High single to double-digit	21.3	25.6	56.4	Various with peak sales of $20-80m; Launch year: 2026+
AT220 (undisclosed biosimilar - partnered)	14.8	17.8	100%	Low single digit	14.8	17.8	39.2	Peak sales: $500m; Launched
Tetris Pharma/Ogluo	9.0	10.8	100%	N/A	9.0	10.8	23.9	Peak sales: $10m; Launched
AT292/SAR-447537 (AATD - Sanofi)	17.9	21.5	50%	Low single digit	9.0	10.8	23.7	Peak sales: $515m; Launch year: 2027
AT307 (Specialty Hospital - Hikma)	11.3	13.6	60%	High single to double-digit	6.8	8.1	17.9	Peak sales: $65m; Launch year: 2027
Operating costs	(2.6)	(3.1)			(2.6)	(3.1)	(6.9)	
Net cash	6.3	7.6			6.3	7.6	16.7	
Total	**274.8**	**329.8**			**156.6**	**187.9**	**414.7**	

Source: Trinity Delta based on a 12.5% discount factor and £/$ FX rate of 1.20. Note: AATD = Alpha-1 antitrypsin deficiency.

Exhibit 4: Summary of financials

Year-end: Dec 31	£'000s	2021	2022	2023	2024E	2025E
INCOME STATEMENT						
Revenues		**1,158**	**2,403**	**4,573**	**6,223**	**10,395**
Cost of goods sold		0	0	0	0	0
Gross Profit		**1,158**	**2,403**	**4,573**	**6,223**	**10,395**
R&D expenses		(5,386)	(8,613)	(5,977)	(4,543)	(3,861)
SG&A expenses		(2,389)	(5,381)	(8,913)	(9,804)	(12,067)
o/w Share-based payments		(484)	(503)	(638)	(657)	(670)
Exceptionals		(462)	(171)	0	0	0
Other revenue/expenses		640	1,250	1,142	0	0
Operating Profit		**(6,439)**	**(10,512)**	**(9,175)**	**(8,123)**	**(5,533)**
EBITDA		**(6,268)**	**(10,171)**	**(8,679)**	**(7,657)**	**(5,166)**
Financing costs/income		(21)	88	274	34	20
Profit Before Taxes		**(6,945)**	**(10,424)**	**(8,901)**	**(8,089)**	**(5,514)**
Adj. PBT		**(7,122)**	**(12,006)**	**(10,681)**	**(8,747)**	**(6,184)**
Current tax income		776	1,164	347	409	309
Net Income		**(6,169)**	**(9,260)**	**(8,554)**	**(7,681)**	**(5,205)**
EPS (p)		**(0.3)**	**(0.3)**	**(0.3)**	**(0.2)**	**(0.1)**
Adj. EPS		**(0.3)**	**(0.4)**	**(0.3)**	**(0.2)**	**(0.2)**
Average no. of shares (m)		23.0	28.9	30.6	34.2	37.9
BALANCE SHEET						
Current assets		**20,515**	**17,477**	**11,170**	**10,263**	**5,921**
Cash and cash equivalents		18,316	4,765	5,093	3,926	1,076
Short-term investments		0	8,041	1,659	0	0
Accounts receivable		1,423	2,215	3,189	3,508	3,275
Inventories		0	1,131	771	1,856	1,122
Other current assets		776	1,325	458	973	448
Non-current assets		**406**	**4,288**	**4,207**	**3,907**	**3,714**
Property, plant & equipment		328	838	834	625	518
Intangible assets		30	3,402	3,296	3,205	3,119
Other non-current assets		48	48	77	77	77
Current liabilities		**(2,267)**	**(3,728)**	**(5,150)**	**(5,150)**	**(5,150)**
Short-term debt		0	0	0	0	0
Accounts payable		(2,141)	(3,526)	(4,903)	(4,903)	(4,903)
Other current liabilities		(126)	(202)	(247)	(247)	(247)
Non-current liabilities		**(105)**	**(582)**	**(700)**	**(700)**	**(700)**
Long-term debt		0	0	0	0	0
Other non-current liabilities		(105)	(582)	(700)	(700)	(700)
Equity		**18,549**	**17,455**	**9,527**	**8,320**	**3,786**
CASH FLOW STATEMENTS						
Operating cash flow		**(5,450)**	**(10,780)**	**(5,841)**	**(8,477)**	**(2,675)**
Profit before tax		(6,945)	(10,424)	(8,901)	(8,089)	(5,514)
Non-cash adjustments		1,156	569	884	1,089	1,018
Change in working capital		(419)	(1,659)	891	(1,904)	1,467
Interest paid		0	0	0	34	20
Taxes paid		758	734	1,285	393	334
Investing cash flow		**(68)**	**(7,993)**	**6,520**	**1,493**	**(174)**
CAPEX		(69)	(345)	(151)	(166)	(174)
Acquisitions/disposals		0	284	0	0	0
Other investing cash flows		1	(7,932)	6,671	1,659	0
Financing cash flow		**20,931**	**5,160**	**(180)**	**5,817**	**0**
Proceeds from equity		18,565	5,648	0	5,817	0
Increase in loans		2,500	0	38	0	0
Other financing cash flow		(134)	(488)	(218)	0	0
Net increase in cash		**15,413**	**(13,613)**	**499**	**(1,167)**	**(2,849)**
Cash at start of year		2,898	18,316	4,765	5,093	3,926
Cash at end of year		**18,316**	**4,765**	**5,093**	**3,926**	**1,076**
Net cash at end of year		**18,316**	**12,806**	**6,752**	**3,926**	**1,076**

Source: Company, Trinity Delta. Note: R&D forecasts are largely illustrative pending development plans

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