Trinity Delta

Arecor Therapeutics

Update

AT278 hits the sweet spot

31 May 2022

The detailed data from the successful Phase I study of AT278, Arecor's ultra-concentrated ultra-rapid insulin, clearly showed improvement and superiority over current fast-acting insulins. This, coupled with highly supportive commentary from a Key Opinion Leader (KOL) event, gives us rising confidence that Arecor's diabetes franchise is well positioned to capture a meaningful share of the evolving diabetes care market. In-house programmes, AT278 and AT247 (ultra-rapid insulin), can address the needs of both higher dose requirements as the global obesity epidemic drives daily insulin doses upwards and emerging pump applications (artificial pancreas). Revising our rNPV model to reflect this improved confidence sees our valuation increase to £159.8m, or 574p per share (from £140.9m and 506p). We reiterate that Arecor's development is materially de-risked and significant upside remains, both from the diabetes programmes and from specialty hospital products.

Year-end: December 31	2020	2021	2022E	2023E
Revenues (£m)	1.7	1.2	1.4	1.6
Adj. PBT (£m)	(4.3)	(7.2)	(13.0)	(9.4)
Net Income (£m)	(2.8)	(6.2)	(9.8)	(7.2)
EPS (p)	(0.2)	(0.3)	(0.4)	(0.3)
Cash (£m)	2.9	18.3	9.0	2.4
EBITDA (£m)	(3.3)	(6.3)	(11.0)	(8.0)

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

- **AT278 Phase I data confirm profile** Publication of full results of AT278's Phase I study highlight the quality of the Arestat formulation. The ultra-concentrated 500 units/ml (U500) dose is five-fold more concentrated than current fast-acting insulins, yet it demonstrated an absorption profile superior to the comparator, NovoRapid 100 units/ml (U100). There are no other ultra-rapid ultra-concentrated insulins in development with this desirable profile despite a clear need as diabetes care changes to reflect demographic shifts (obesity) driving daily insulin requirement upwards and technological advances bring pump applications to the fore.
- **KOL commentary supports clinical benefit** The Key Opinion Leader (KOL) event featured world leading clinical specialists who articulated the shifts in diabetes care and the clinical issues they are increasingly facing. Their view, individually and collectively, is that both AT247 (ultra-rapid insulin) and AT278 appear to have highly promising and well differentiated profiles. Notably, these are particularly suited to the emerging pump applications (artificial pancreas) and the growing number of patients (both Type 1 and 2) who have high daily insulin requirements.
- **Valuation increased to £159.8m, or 574p** We value Arecor using an rNPV model to capture the various programmes' commercial potential. Our increased valuation is £159.8m, or 574p per share (from £140.9m and 506p) based largely on a higher AT278 contribution following detailed trial data and positive KOL commentary. This remains based on conservative assumptions. Continued clinical progress, especially in diabetes, greater visibility on partnered products, and further licensing deals, would result in material upside revisions to our model.

Price	380p
Market Cap	£105.77m
Enterprise Value	£87.5m
Shares in issue	27.8m
12-month range	222p-472p
Free float	34.2%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	AREC
Corporate client	Yes

Company description

Arecor Therapeutics is a revenue-generating clinical stage drug developer, with a well-balanced portfolio of in-house and partnered programmes. Its proprietary Arestat formulation platforms result in enhanced products with lower development risks and less onerous regulatory approvals.

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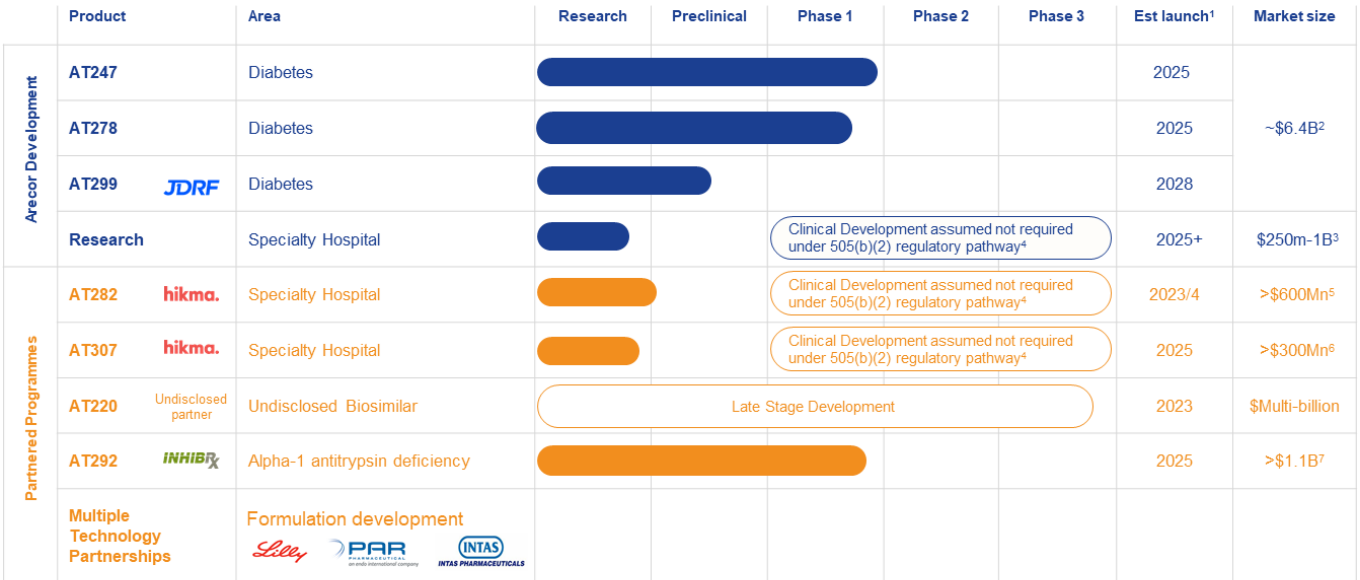
Arecor: well-positioned for diabetes innovations

Arecor's investment case centres on its proven Arestat formulation platform and the ability to create a portfolio of proprietary and partnered clinical assets. Whilst the specialty hospital programmes (both through collaboration and in-house development) should provide an attractive blend of near- and longer-term revenue streams, it is the diabetes programmes, AT247 (ultra-rapid insulin) and AT278 (ultra-rapid ultra-concentrated insulin), that have the near-term potential to add further significant value. Results from the first of a series of Phase I studies suggest they offer competitive and differentiated profiles that may be ideally suited for use in integrated insulin delivery systems ("artificial pancreas") and address the emerging needs of high dose insulin users. The recent KOL event, coupled with AT278 data publication, underpin our view that the clinical benefits and commercial potential of these assets are yet to be fully appreciated. Updating our Arecor rNPV model to reflect increased AT278 potential sees our valuation raised to £159.8m (574p per share) from £140.9m (506p per share).

A proven formulation platform that creates desirable products

Arecor's diabetes assets were developed using its proprietary Arestat platform. Arestat is a suite of technologies which can be employed to develop novel formulations of existing products. These are specifically created to offer improved attributes, ranging from better shelf life and stability, easier patient administration, and superior therapeutic profiles through tailored absorption characteristics.

Exhibit 1: A broad portfolio of de-risked and innovative assets



1. Management estimates; 2. Prandial insulin market 2019, estimate based on 2019 sales figures of Eli Lilly, Novo Nordisk and Sanofi Aventis reported in Company Annual Reports, exchange rates as at 15 February 2021; 3. Range of currently marketed products, source: company annual reports and IQVIA; 4. Management assumption that new formulation will not require clinical data for approval under 505(b)(2) guidelines, to be validated for each product with US Food & Drug Administration; 5. Product towards upper end of hospital RTU/RTA market sales; 6. Company annual report; 7 2018 global AATD augmentation therapy, projected to reach $1.9B by the end 2026, Inhibrx Corporate presentation, Jan 2021

Source: Arecor Therapeutics

Inherently lower development risks with faster timelines

Arecor's strategy aims to diversify risk through combining partnered projects with selected in-house development (Exhibit 1). Technology partnerships bring in near-term revenues, and licensing deals involve better success-based economics, including clinical and commercial milestones and net sales royalties or equivalent. The in-house portfolio is focussed on diabetes and specialty hospital products, with this note detailing the results of the AT278 Phase I study and the diabetes KOL (Key Opinion Leader) event.

Key takeaways from the Key Opinion Leader event

Diabetes specialists highlight the increasing treatment challenges

Arecor hosted a Key Opinion Leader (KOL) event where a panel of diabetes experts discussed the limitations of current treatment options and the need for new ultra-concentrated, rapid-acting insulins. The discussion focussed on the treatment challenges and covered various aspects of the clinical and patient need for improved glucose control, particularly for high insulin users, as well as providing a detailed overview of the recent Phase I AT278 clinical data.

Renowned experts in their fields

The session was moderated by Jay Skyler, Professor of Medicine, Pediatrics and Psychology, Division of Endocrinology, Diabetes and Metabolism, University of Miami, USA. Professor Skyler was joined by three experts in diabetes care:

- Wendy Lane, Clinical Endocrinologist, Director of Clinical Research, Mountain Diabetes and Endocrine Center, Asheville, USA: discussed the rising need for rapid-acting concentrated insulin products in treatment of Type 2 diabetes from a clinical perspective;
- Davida Kruger, Certified Diabetes Nurse Practitioner, Henry Ford Health System, Division of Endocrinology, Detroit, USA: provided a patient and caregiver viewpoint, reviewing several case studies demonstrating real world challenges and the benefits of concentrated insulin; and
- Thomas Pieber, Head of the Division of Endocrinology and Metabolism at the Medical University of Graz, Austria: presented results from Arecor's Phase I trial of AT278, its ultra-rapid, ultra-concentrated insulin.

Several important themes emerged from the discussion. Firstly, that an increase in the numbers of both Type 1 and Type 2 diabetic patients is being driven by the obesity crisis, which is also leading to increasing insulin requirements and the amount of insulin use on average per patient. Secondly, currently available insulins do not meet the needs of patients with high daily insulin requirements. The only available concentrated insulin (Eli Lilly's Humulin R U-500) does not act rapidly enough, and the next most concentrated insulins (Humalog U200 and Lyumjev) are often used off-label in pumps as clinicians seek "creative" approaches to help control glucose levels in their high insulin using patients. All session participants emphasised a desire to be able to provide better care for patients and the demand for a rapidly acting highly concentrated insulin, which could provide more optimal glucose control and would allow small volumes of high dose insulin to be used, ideally in a specifically designed prefilled pump.

A clear need for novel ultra-rapid formulations, particularly an ultra-concentrated one

Availability of an ultra-rapid ultra-concentrated insulin would bring several advantages, extending from clinical (improved blood glucose control and clinical outcomes), to comfort and convenience (reduction in pen or pump injection volumes and development of miniaturised pumps), to cost (via fewer cartridge changes, more insulin per co-pay). Importantly, AT278 was seen as potentially fulfilling both basal and bolus insulin needs in the same device, which could also simplify co-pay issues; these were described as "huge" given patients are often on multiple medications to treat their diabetes and comorbidities. The panel discussion concluded that patients and caregivers have been waiting for decades for the sort of formulations Arecor is developing, which offer the prospect of absorption profiles that closely match emerging clinical needs.

Clinically relevant and commercially attractive

Tailored absorption profiles address emerging clinical needs

Diabetes care is evolving rapidly, reflecting changing patient demographics and technological advances. The causes and drivers, as well as the opportunities and prospects, for Arecor's diabetes franchise were covered in our September 2021 Initiation report, with greater detail given in our January 2022 Update note. It is clear that diabetes is a growing problem, with rising patient numbers, while advances in delivery devices create a need for specifically formulated insulins. Such trends underpin the commercial attractiveness of the two ultra-rapid insulins in clinical development: AT247 and AT278 (an ultra-concentrated formulation).

Diabetes incidence, especially Type 2, is rising worldwide

The latest International Diabetes Federation (IDF) Diabetes Atlas fact sheets show there are currently 537m people with diabetes globally, and this is expected to grow by 19.7% to 643m in 2030 and 46.0% to 784m in 2045. Type 2 diabetes accounts for around 90% of diagnosed diabetes globally, although the accuracy of incidence (the rate of new cases, usually annually) and prevalence (the number of cases per defined population) statistics are limited due to the difficulty in, and hence differing rates of, accurate diagnoses across geographies. Type 1 diabetes affects c 9.5% of the global population, with 15 such diabetics per 100,000 people and growing by 2% to 5% per annum.

All Type 1 diabetics need insulin injections daily

Type 1 diabetes is an autoimmune process that results in the body's immune system attacking the insulin producing beta-cells of the pancreas so that very little or no insulin is produced. This means Type 1 diabetics need daily insulin injections to keep their blood glucose level within an appropriate range and a lack of insulin would result in death. Although it was originally known as juvenile diabetes, over half of patients are between 19 and 40 years at diagnosis and will need daily insulin for the remainder of their lives.

Most Type 2 diabetics are currently controlled with oral medications…

Type 2 diabetes is associated with older populations, with a strong link to obesity. Here the pancreas continues to produce insulin, but the body's cells begin to respond less well (insulin resistance) and, over time, fail to maintain blood glucose levels in the normal range. Most Type 2 diabetics can control their disease adequately through a combination of improved diet, more exercise, and the appropriate use of oral hypoglycaemics.

…yet Type 2 population is large and already accounts for most insulin usage

However, as beta cell production wanes, an increasing number of patients (currently 7% to 8%) need to add in injected insulin. It is estimated that better diagnosis and greater access would see this rise to over 15% of Type 2 diabetics. The size of this population means there are three to four times as many Type 2 diabetics using insulin than there are Type 1 insulin dependent diabetics and, importantly, they tend to require larger doses of insulin than the equivalent Type 1 diabetic.

Striving to achieve the physiological insulin profile

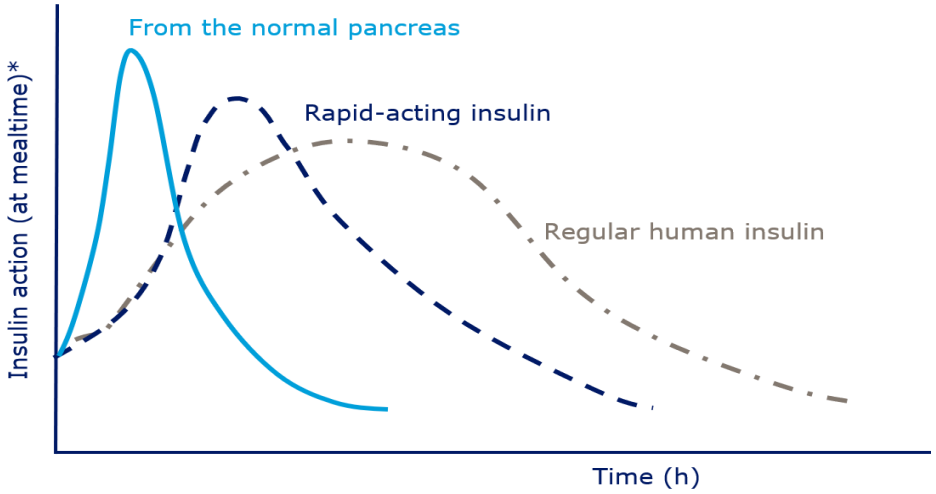
Tight glycaemic control (time in range) is a key treatment parameter

We have covered the clinical landmarks in diabetes care in previous notes, with arguably the single greatest advance being the appreciation of the need to tailor individual insulin therapy to maintain tight glycaemic control (see the DCCT study). Keeping blood sugar levels as close to normal throughout the day (known as time in range) helps prevent common, debilitating, and expensive, complications such as retinopathy, neuropathy, nephropathy, and cardiovascular diseases.

Absorption profile needs to be as close to endogenous insulin as possible

In his presentation, Thomas Pieber of the Medical University of Graz, Austria, highlighted the importance of striving to mimic the physiological profile of endogenous insulin. The use of regular human insulin, whilst a clear advance over prior animal-sourced products, is associated with a significant mismatch in postprandial activity with high glycaemia after a meal and hypoglycaemia later. The fast-acting insulin analogs (such as lispro, aspart, glulisine) have a better profile, with tighter postprandial control and less nocturnal hypoglycaemia. However, there is still a sizeable gap (Exhibit 2) to the endogenous insulin profile and that is the driver for the development of ultra-rapid insulin formulations.

Exhibit 2: Striving to achieve a closer to physiological insulin profile



Source: Adapted from Diabetes Obes Metab 2015;17:1011–20 *Schematic representation

Arecor has two clinical programmes in development

Arecor is progressing two ultra-rapid insulins through a series of Phase I trials. **AT247** is a novel formulation of an existing insulin (100U aspart) that aims to materially accelerate absorption after injection, achieving a profile that very closely approximates healthy (non-diabetic) physiological insulin secretion, giving the desired tighter and more effective management of blood glucose levels. **AT278** is a novel formulation of insulin aspart with the focus on creating a highly concentrated, 500 units/ml, ultra-fast insulin. AT278 recently reported Phase I data that exceeded our expectations (see later), this prompts us to raise its contribution within our valuation model. Discussions with KOLs has strengthened our belief in the potential of the franchise, most notably the prospects for AT278.

AT247: the leading ultra-rapid insulin programme

First AT247 Phase I trial successfully completed…

AT247 is a second-generation ultra-rapid prandial insulin analogue that was examined in a Phase I clinical trial that compared it against Novo Nordisk's NovoRapid (IAsp) and Fiasp (faster IAsp). The double-blind study tested 19 Type 1 diabetics using a standard glucose clamp setting to determine the pharmacokinetic (PK), pharmacodynamic (PD), and safety characteristics of AT247. The full results were published in Diabetes Care February 2021, with AT247 having successfully met all study endpoints and suggesting a best-in-class profile. The relevant profiles and data were discussed at the KOL event and are shown in the graphics and table (Exhibits 3 and 4).

Exhibit 3: AT247 Phase I clinical study PK/PD results

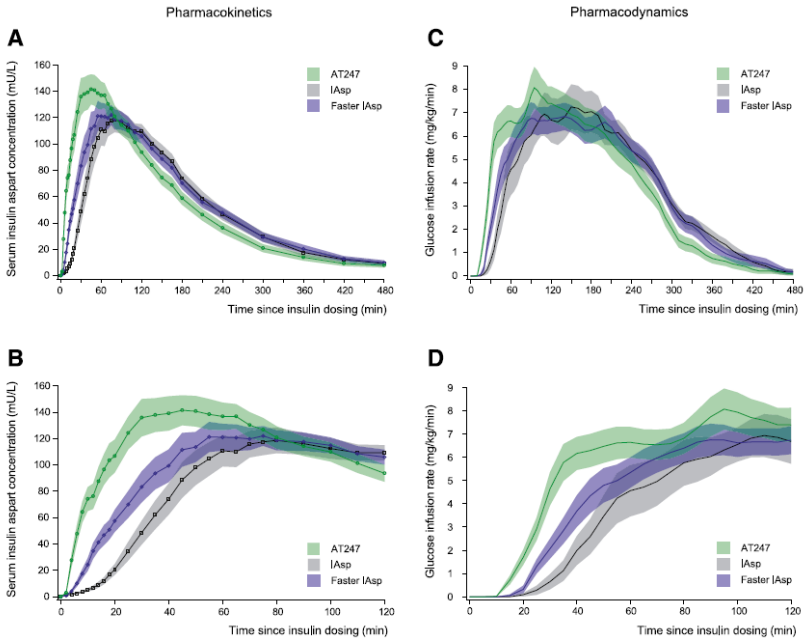


Figure 1—Pharmacokinetic and pharmacodynamic profiles after subcutaneous administration of 0.3 units/kg of a novel insulin aspart formulation (AT247), IAsp, or faster IAsp in men with type 1 diabetes. Serum insulin aspart concentration-time profiles for 8 h (*A*) and 2 h (*B*) postdose, and GIR-time profiles for 8 h (*C*) and 2 h (*D*) postdose. The GIR was averaged over 5-min intervals for the first 2 h, while 10-min intervals were used for the remaining time. Variability bands show the SEM. Number of participants: 19 for AT247 and faster IAsp; and 18 for IAsp.

Source: Svehlikova et al. Diabetes Care 2021: 44: 448-455

...with promising results against NovoRapid and ultra-rapid Fiasp

These data (Exhibit 4) show that AT247 has a superior onset of action and activity throughout the important 120 minutes after dosing vs both NovoRapid and Fiasp. For instance, AT247 was nine minutes faster than Fiasp for onset of action, achieved a three-fold increase in glucose lowering in the first 30 minutes and a two-fold increase in the first 60 minutes, yet was comparable over 480 minutes. As expected, AT247 was well tolerated with no safety concerns seen.

Exhibit 4: Phase I data on onset, offset and overall exposure and glucose-lowering effect

	AT247* $n = 19$	IAsp* $n = 18$	Faster IAsp* $n = 19$	Treatment difference† (95% CI) AT247 − IAsp	*P*	Treatment difference† (95% CI) AT247 − faster IAsp	*P*
Onset of early exposure							
Onset of appearance, min	2.0 (1.0; 3.0)	13.5 (10.0; 17.0)	5.0 (4.0; 7.0)	−11.5 (−14; −8)	0.0004	−2.0 (−5; −2)	0.0003
$t_{Early50\%Cmax}$, min	12.0 (9.0; 17.0)	37.5 (30.0; 41.0)	24.0 (20.0; 28.0)	−23.5 (−31; −19)	0.0004	−12.0 (−14; −7)	0.0004
t_{max}, min	50.0 (40.0; 60.0)	90.0 (75.0; 120.0)	75.0 (65.0; 100.0)	−35.0 (−80; −15)	0.0004	−25.0 (−50; −10)	0.0032
Onset of glucose-lowering effect							
Onset of action, min	17.0 (13.0; 24.0)	37.0 (35.0; 63.0)	23.0 (22.0; 35.0)	−23.0 (−37; −15)	0.0004	−9.0 (−11; −3)	0.0006
$t_{50\%GIRmax}$, min	30.0 (25.0; 45.0)	65.0 (50.0; 90.0)	50.0 (40.0; 60.0)	−32.5 (−50; −20)	0.0004	−20.0 (−25; −5)	0.0155
t_{GIRmax}, min	95.0 (55.0; 135.0)	140.0 (110.0; 172.0)	115.0 (85.0; 150.0)	−30.0 (−55; −15)	0.0061	−30.0 (−60; 25)	0.1292
Offset of exposure and overall exposure							
$t_{Late50\%Cmax}$, min	173.0 (133.0; 223.0)	211.5 (190.0; 287.0)	221.0 (183.0; 258.0)	−32.0 (−58; −15)	0.0015	−27.0 (−85; −15)	0.0017
Time to disappearance, min	427.0 (383.0; 480.0)	462.5 (417.0; 480.0)	474.0 (420.0; 480.0)	−12.5 (−46; 0)	0.1534	−23.0 (−49; 0)	0.0241
C_{max}, mU/L‡	138.2 ± 1.5	122.0 ± 1.4	121.3 ± 1.4	1.15 (0.99; 1.33)	0.0595	1.13 (0.98; 1.31)	0.0863
Duration of glucose-lowering effect and overall glucose-lowering effect							
$t_{Late50\%GIRmax}$, min	280.0 (210.0; 290.0)	295.0 (265.0; 330.0)	290.0 (240.0; 310.0)	−22.5 (−75; 15)	0.0843	−20.0 (−60; 0)	0.2053
GIR_{max}, mg/kg/min	9.1 (5.2; 12.7)	8.0 (6.3; 11.5)	8.4 (7.5; 11.0)	0.53 (−1.82; 3)	0.7911	0.11 (−1.19; 1.43)	1.0000

*Data are presented as median (25th percentile; 75th percentile) or geometric mean ± SD. †Median treatment difference (treatment comparison calculated using the Wilcoxon rank sum test using untransformed parameters). ‡Mean treatment ratios (95% CI) are presented for C_{max} (log-transformed data analyzed by means of a mixed-effects model and results back-transformed to the original scale).

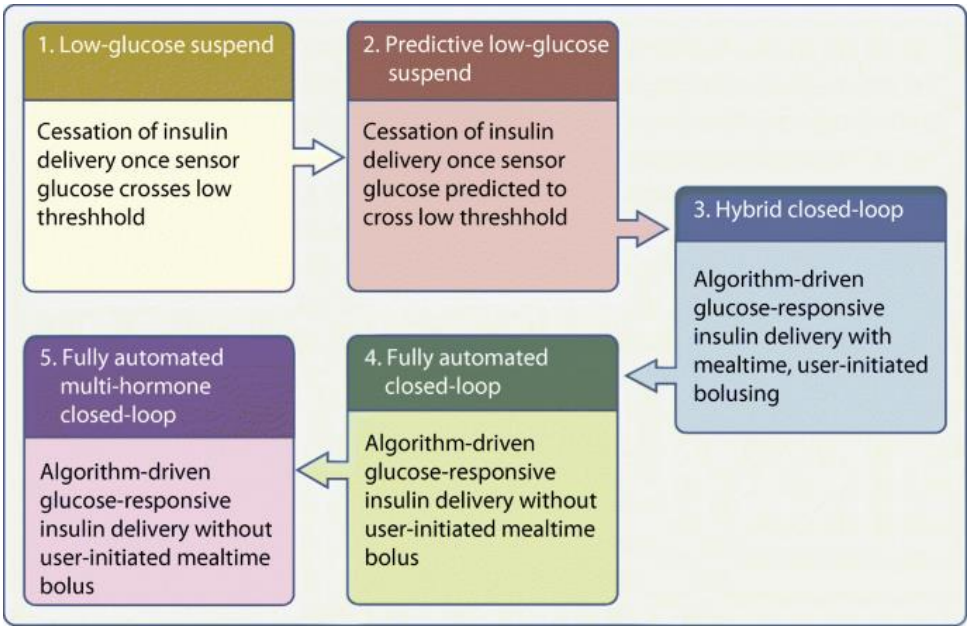
Source: Svehlikova et al. Diabetes Care 2021: 44: 448-455

Pens are currently the mainstay delivery system, but pump devices are advancing rapidly

The importance of such a profile is not simply in improving outcomes in diabetics who are using pen devices (also known as MDI – multiple daily injections) but in enabling the use of fully automated continuous pump devices. Advances in miniaturisation and computing power have seen the introduction of viable continuous glucose monitors (CGM). These allow patients, and clinicians, to assess trends, patterns, and time spent in range in real time. The sensor tests glucose every few minutes and sends an alarm if hypo- or hyper-glycaemia is threatened.

Such devices have been transformative for some patients. In parallel, similar technological advances saw sophisticated, and reliable, wearable pumps developed. These pumps, known as continuous subcutaneous insulin infusion (CSII) therapy, have evolved rapidly and offer near-normal glucose control in previously uncontrolled diabetics.

Exhibit 5: Key milestones towards a truly artificial pancreas



Source: New closed loop insulin systems Boughton & Hovorka Diabetologia 1007-1015 (2021)

A clear need for specialised ultra-fast acting insulins

As these devices approach reality, the remaining obstacles to be addressed are shifting from the physical and software aspects to the characteristics of the insulins that are now required. For instance, the inherent delays in absorption of subcutaneous injected insulin compared with endogenous insulin production means postprandial hyperglycaemia is still a challenge for these closed-loop systems. As the clinicians at the KOL event noted, the pharmacokinetics and pharmacodynamics of current rapid-acting insulins are known to be suboptimal. The new ultra-rapid acting insulins, which have faster onset and offset of action, have the potential to address this issue. Small studies with Fiasp (faster aspart) and Lyumjev (ultra-rapid lispro) have not shown the hoped-for conclusive results. It is for this clear clinical need that AT247 (ultra-rapid insulin) and, increasingly, AT278 (ultra-rapid and ultra-concentrated) appear particularly well suited.

AT278: ultra-rapid and ultra-concentrated insulin

AT278 is the focus of much clinical attention

AT278 is a novel formulation of insulin aspart with the focus on creating a highly concentrated, 500 units/ml (U500), ultra-rapid insulin. There has always been a need for concentrated insulins (eg for insulin control post operatively or post-infection) but the use is now much more mainstream. Such high concentration insulins are expected to become increasingly in demand, reflecting the rising number of Type 2 and refractory Type 1 diabetics requiring higher daily dosing.

Rising obesity rates mean a corresponding rise in daily insulin dosing

A key element driving this is the growing rate of obesity across most geographies, with a BMI of 30 or greater said to contribute 80-85% of the risk of developing Type 2 diabetes. Although the reasons remain unclear, excess abdominal fat is

thought to release pro-inflammatory signals that create insulin resistance (and relative insulin insufficiency). In the UK 28.1% of adults are classified as obese, rising to 63.4% when the overweight are included ; forecasts suggest 26m people will be classified as obese by 2040. In the US the figures are even more dramatic, with obesity prevalence rising from 30.5% in 2000 to 41.9% in 2022. The expectation is that half of all US adults will be obese by 2030.

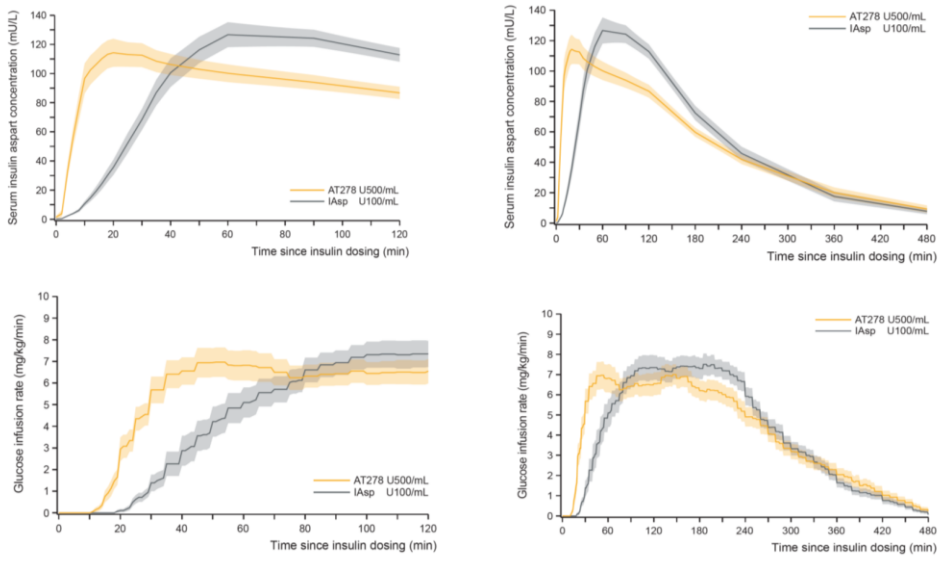
The trend is cascading down from specialist centres to secondary and primary care

Dr Wendy Lane, a diabetes specialist from North Carolina, highlighted how obesity-related insulin resistance is driving increases in daily insulin requirements, pointing out how in 2012 some 35% of Type 2 diabetics needed a daily maintenance of 60U (units), whilst in 2022 the average daily dose has risen to 97U. Similar trends were also seen in Type 1 diabetes, despite the younger demographics and stricter attention to dietary intakes, with 25% having a BMI greater than 30 and 64% with a BMI greater than 25. Yet, even with this growing population, there are only three concentrated bolus insulins available: U500 regular insulin (which has a profile similar to a basal insulin), U200 Humalog, and U200 Lyumjev (all manufactured by Eli Lilly).

AT278 data confirms better than we expected absorption profile

The results from the AT278 Phase I study in Type 1 diabetics were first presented at the Advanced Technologies and Treatments for Diabetes (ATTD) meeting on Thursday 28 April. Dr Thomas Pieber described the results at the KOL seminar (Exhibits 6 and 7). The trial met all primary and secondary endpoints, demonstrating a superior pharmacokinetic (PK) and pharmacodynamic (PD) profile to a comparable dose of lower concentration of NovoRapid (NovoNordisk's gold standard rapid acting insulin). The trial evaluated 38 adults with Type 1 diabetes in an euglycemic clamp setting aiming to establish PK/PD equivalence between a subcutaneous dose of AT278 0.3 U/Kg (500 U/mL) that was five-fold more concentrated than the comparator 0.3 U/Kg NovoRapid (100 U/mL). AT278 matched or exceeded key measures such as glucose lowering, onset of action, and absorption profile, and there were no safety signals.

Exhibit 6: AT278 Phase I clinical study PK/PD results



Source: ATTD April 2022 Pharmacokinetics is the upper pair, Pharmacodynamics the lower

A faster onset despite being five-fold more concentrated

We have stated before how the outcomes are highly impressive and better than we expected. The top-line results showed AT278 has, despite the five-fold greater

concentration, an absorption profile that does not simply match the rapid insulin criteria. Instead, the PK/PD data justifies AT278 classification as an ultra-rapid insulin. AT278 showed enhanced early insulin exposure compared to IAsp, with a six-minute earlier insulin appearance, a 23-minute faster $t_{Early50\%Cmax}$ (time to 50% of maximum insulin concentration in the early part of the PK profile), and a four-fold higher insulin exposure within the first 30 minutes. Looking at accelerated glucose lowering properties compared to IAsp there is a ten-minute earlier onset of action, a 20-minute faster $t_{Early50\%GIRmax}$ (time to early 50% of maximum glucose infusion rate), and a two-fold higher glucose-lowering effect within the first 60 minutes. The overall insulin exposure and glucose-lowering properties were comparable and AT278 was, as expected, well tolerated and safe.

Exhibit 7: AT278 Phase I study: early exposure and glucose-lowering effect

	AT278 n = 38	IAsp n = 38	Treatment difference / ratio (95% CI)	*p*-value
Insulin exposure				
Onset of appearance (min)	3 (3; 4)	9.5 (8; 14)	-6 (-8; -6)	<0.0001
$t_{Early50\%Cmax}$ (min)	7.5 (6; 10)	32 (27; 35)	-23 (-26; -22)	<0.0001
$AUC_{IAsp,0\text{-}30min}$	2 460 (1 580; 3 531)	649 (315; 987)	**4.02 * (3.29; 4.90)**	
$AUC_{IAsp,0\text{-}60min}$	5 288 (3 883; 7 367)	3 471 (2 184; 4 618)	**1.54 * (1.35; 1.76)**	
Glucose-lowering effect				
Onset of action (min)	11.5 (9; 16)	21.5 (14; 27)	-9.5 (-13; -6)	<0.0001
$t_{Early50\%GIRmax}$ (min)	30 (25; 45)	60 (45; 75)	-20 (-30; -15)	<0.0001
$AUC_{GIR,0\text{-}30min}$	45 ± 42	5 ± 9	**8.91 * (5.96; 17.46)**	
$AUC_{GIR,0\text{-}60min}$	241 ± 157	102 ± 117	**2.36 * (1.92; 3.22)**	

Source: ATTD April 2022

Well positioned for both high dosing needs and increasingly compact pump devices

Interestingly, all the seminar participants viewed these results as "fantastic" and felt AT278 offers a step-change in the treatment, management, and dosing of the rising number of patients with high insulin needs. They also expressed the view that AT278 precisely meets the needs of the next generation of more compact insulin devices currently in development. Such positive endorsement from leading industry experts has led us to review our expectations for AT247 and, materially, AT278. Typically, we employ conservative assumptions in our valuation modelling but these discussions with practicing clinicians have raised our confidence that Arecor's emerging diabetes franchise has greater clinical, and commercial, potential than we had originally expected.

Exhibit 8: Arecor diabetes franchise development timelines

Source: Arecor Therapeutics

Valuation

Valuation of £159.8m, 574p per share (from £140.9m, 506p) on increased diabetes confidence

We value Arecor using an rNPV model, explicitly valuing the diabetes franchise, four partnered assets, and the in-house specialty hospital products research programme(s). We have updated our valuation to reflect recent detailed AT278 Phase I data and highly positive KOL commentary that clearly outlined the unmet medical need for a rapid-acting ultra-concentrated insulin. This has resulted in valuation uplift to £159.8m, or 574p per share (from £140.9m and 506p), largely on an increased contribution for AT278. Exhibit 9 summarises the model outputs and underlying assumptions.

Exhibit 9: Arecor rNPV valuation

Programme	Total NPV (£m)	Total NPV ($m)	Success probability	Royalty	rNPV (£m)	rNPV ($m)	rNPV/ share (p)	Notes
AT247 (Type I diabetes)	81.0	105.4	60%	"High single to double-digit"	36.4	47.4	130.9	Peak sales: $358m; Launch year: 2025
AT278 (Type II diabetes)	102.1	132.7	60%	"High single to double-digit"	46.7	60.7	167.7	Peak sales: $516m; Launch year: 2026
AT299 (Diabetes)	15.8	20.6	10%	"Low single digit"	1.6	2.0	5.6	Peak sales: $200m; Launch year: 2028
Research (specialty hospital)	18.2	23.7	20%	"High single to double-digit"	4.3	5.6	15.5	Peak sales: $100m; Launch year: 2025+
AT282 (specialty hospital: Hikma)	51.5	67.0	75%	"High single to double-digit"	37.3	48.5	134.0	Peak sales: $150m; Launch year: 2024
AT307 (speciality hospital: Hikma)	19.9	25.9	60%	"High single to double-digit"	11.1	14.4	39.9	Peak sales: $75m; Launch year: 2025
AT220 (undisclosed biosimilar: partnered)	9.2	12.0	80%	"Low single digit"	6.6	8.6	23.6	Peak sales: $500m; Launch year: 2023
AT292/INBRX-101 (AATD: Inhibrx)	12.8	16.6	30%	"Low single digit"	4.5	5.8	16.2	Peak sales: $390m; Launch year: 2025
Operating costs	(7.0)	(9.1)			(7.0)	(9.1)	(25.1)	
Net cash at FY21e	18.3	23.8			18.3	23.8	65.8	
Total	**321.9**	**418.5**			**159.8**	**207.7**	**574.1**	

Source: Trinity Delta Note: AATD = Alpha-1 antitrypsin deficiency; assumptions include a 12.5% discount factor, £/$ FX rate of 1.30, and 10% taxation from 2026 (UK patent box).

Retaining conservative assumptions

Under this methodology, the rNPVs of the individual R&D projects are assessed and success probabilities adjusted for the clinical, commercial, and execution risks carried. These are summed and netted against operational costs and cash. Success probabilities, based on standard industry criteria for development stage, are flexed to reflect the inherent risks of the individual asset, indication, and development and regulatory pathway. Although the current strategy envisages out-licensing most of Arecor's assets before the later costlier stages of clinical development, we allow for commercial and execution risks which are integral to any asset's intrinsic value. We continue to apply conservative assumptions throughout.

AT278 upgrade reflects the increased confidence

For AT278 we have increased peak sales to $516m (from $424m) given a likely larger market of patients that could benefit from a rapid-acting ultra-concentrated insulin, as outlined during the KOL event and discussed earlier in this report. This is still conservative, given the significant and growing size of the diabetes market.

AT278 now contributes c 29% of our risk-adjusted NPV and, together with AT247, the in-house diabetes franchise is now c 52% of our overall valuation. There could also be upside to AT247, notably with top-line data from the ongoing US Phase I pump study of AT247, expected in H222. Underlying assumptions for other programmes are largely unchanged, albeit we have rolled our valuation forward in time. There could be upside to all of these as progress and updates are made available in due course.

Further value inflection events are expected in near- and longer-term

Key areas which could represent valuation upside include progress of the current pipeline and earlier-stage formulation development collaborations, while the Arestat technology platforms are a source of intangible value underpinning Arecor's business model. Not only will development progress de-risk the pipeline further but it is also likely to reveal more about the commercial terms of partnered programmes. Sensitivities around the terms of these inevitably mean visibility is limited until later in the development process. For in-house assets that are yet to be partnered, more information on their profile could have a positive impact on the deal terms achieved. Hence, until our knowledge improves (especially with respect to the identity of some of the underlying programmes), we employ modest assumptions for launch timings, pricing, and market shares.

Greater visibility, coupled with continued progress, will provide material upside

In addition, we only include very modest risk-adjusted development milestone assumptions for actual and potential licensing deals, with assumed royalty rates at the lower end of management guidance. Limited visibility on the formulation development collaborations means these are not included in our valuation until they convert to longer-term licence partnerships, and hopefully further disclosures are made with respect to key factors such as the identity of the underlying assets, indications to be pursued and likely development timeline. Management expectations for the licencing of one formulation development programme each year therefore provides upside.

Exhibit 10: Summary of financials

Year-end: Dec 31	£'000s	2019	2020	2021	2022E	2023E
INCOME STATEMENT						
Revenues		**748**	**1,698**	**1,158**	**1,442**	**1,612**
Cost of goods sold		0	0	0	0	0
Gross Profit		**748**	**1,698**	**1,158**	**1,442**	**1,612**
R&D expenses		(3,085)	(3,937)	(5,283)	(11,623)	(8,136)
SG&A expenses		(1,416)	(1,642)	(2,523)	(2,382)	(2,416)
Underlying operating profit		**(3,753)**	**(3,880)**	**(6,648)**	**(12,562)**	**(8,940)**
Share-based payments		(201)	(318)	(484)	(508)	(529)
Exceptionals		0	0	(462)	0	0
Other revenue/expenses		898	452	640	1,408	752
EBITDA		**(2,688)**	**(3,259)**	**(6,299)**	**(11,001)**	**(8,046)**
Operating Profit		**(2,855)**	**(3,428)**	**(6,470)**	**(11,154)**	**(8,188)**
Financing costs/income		(15)	(84)	(21)	92	45
Profit Before Taxes		**(2,870)**	**(3,512)**	**(6,976)**	**(11,063)**	**(8,143)**
Adj. PBT		**(3,970)**	**(4,283)**	**(7,153)**	**(12,979)**	**(9,424)**
Current tax income		435	760	756	1,278	895
Net Income		**(2,435)**	**(2,752)**	**(6,220)**	**(9,784)**	**(7,248)**
EPS (p)		**(1.1)**	**(0.2)**	**(0.3)**	**(0.4)**	**(0.3)**
Adj. EPS		**(1.5)**	**(0.2)**	**(0.3)**	**(0.4)**	**(0.3)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		2.3	16.2	23.0	27.8	27.8
Gross margin		*100%*	*100%*	*100%*	*100%*	*100%*
EBITDA margin		*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Underlying operating margin		*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
BALANCE SHEET						
Current assets		**4,998**	**3,822**	**20,495**	**11,401**	**4,784**
Cash and cash equivalents		3,447	2,898	18,316	9,013	2,448
Short-term investments		0	0	0	0	0
Accounts receivable		809	166	1,423	1,501	1,546
Inventories		0	0	0	0	0
Other current assets		742	758	756	887	791
Non-current assets		**452**	**462**	**406**	**377**	**390**
Property, plant & equipment		353	375	328	305	323
Intangible assets		51	38	30	24	19
Other non-current assets		48	48	48	48	48
Current liabilities		**(1,107)**	**(1,408)**	**(2,298)**	**(2,451)**	**(2,567)**
Short-term debt		0	0	0	0	0
Accounts payable		(1,014)	(1,303)	(2,172)	(2,325)	(2,441)
Other current liabilities		(93)	(105)	(126)	(126)	(126)
Non-current liabilities		**(128)**	**(2,102)**	**(105)**	**(105)**	**(105)**
Long-term debt		0	(1,698)	0	0	0
Other non-current liabilities		(128)	(403)	(105)	(105)	(105)
Equity		**4,216**	**774**	**18,498**	**9,222**	**2,502**
CASH FLOW STATEMENTS						
Operating cash flow		**(2,505)**	**(1,857)**	**(5,450)**	**(9,179)**	**(6,410)**
Profit before tax		(2,870)	(3,512)	(6,976)	(11,063)	(8,143)
Non-cash adjustments		389	614	1,156	570	625
Change in working capital		(23)	747	(388)	74	72
Interest paid		0	0	0	92	45
Taxes paid		0	295	758	1,148	991
Investing cash flow		**(65)**	**(49)**	**(68)**	**(124)**	**(155)**
CAPEX		(73)	(52)	(69)	(124)	(155)
Acquisitions/disposals		0	0	0	0	0
Other investing cash flows		9	3	1	0	0
Financing cash flow		**5,317**	**1,774**	**20,931**	**0**	**0**
Proceeds from equity		5,424	0	18,565	0	0
Increase in loans		0	1,840	2,500	0	0
Other financing cash flow		(107)	(67)	(134)	0	0
Net increase in cash		**2,748**	**(132)**	**15,413**	**(9,303)**	**(6,565)**
Exchange rate effects		(6)	(43)	5	0	0
Cash at start of year		705	3,074	2,898	18,316	9,013
Cash at end of year		**3,447**	**2,898**	**18,316**	**9,013**	**2,448**
Net cash at end of year		**3,447**	**1,200**	**18,316**	**9,013**	**2,448**

Source: Company, Trinity Delta Note: Due to subsequent restatement of accounts FY19 relates to the 12 month period ending 31 May 2019.

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