Trinity Delta

Arecor Therapeutics

Update

Continued delivery with key AT278 data due in Q423

20 April 2023

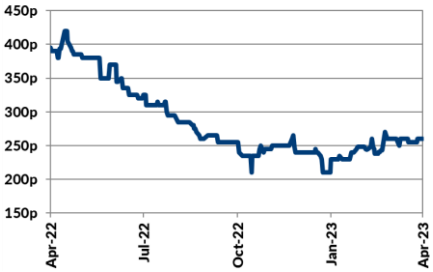
Momentum continues to build across Arecor's pipeline and 2023 should see the first Arestat-based product, AT220, approved and entering a multi-billion market. Partner Hikma has confirmed it will progress AT307 through to commercialisation, with several milestones expected over the coming 18 months. Two new formulation collaborations have been signed, and one has been extended. The diabetes franchise remains in the spotlight with changing US insulin market dynamics. Insulins AT278 (ultra-concentrated, ultra-rapid) and AT247 (ultra-rapid, pump-optimised) have highly promising profiles that should be ideally placed for emerging diabetes needs. AT278 is in a second Phase I trial, with key data expected in Q423. Arecor's formulation expertise underpins both the in-house clinical pipeline and the partnered Specialty Hospital Products programmes. Our updated valuation is £176m, or 575p per share.

Year-end: December 31	2021	2022	2023E	2024E
Revenues (£m)	1.2	2.4	4.9	7.1
Adj. PBT (£m)	(7.1)	(11.7)	(8.9)	(7.9)
Net Income (£m)	(6.2)	(9.1)	(6.9)	(6.5)
EPS (p)	(0.3)	(0.3)	(0.2)	(0.2)
Cash (£m)	18.3	12.8	7.1	2.9
EBITDA (£m)	(6.3)	(10.2)	(7.0)	(6.4)

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

- **Diabetes franchise gaining traction** Arecor's key in-house programmes and the main value drivers are: AT278, an ultra-rapid, ultra-concentrated insulin that is well positioned for the demographic and technology shifts that are underway within diabetes; and AT247, an ultra-rapid, pump-optimised insulin with an ideal profile for "artificial pancreas" pumps. These have both produced encouraging early clinical data. A second Phase I trial with AT278 was recently initiated in Type II diabetes patients, with results expected Q423.
- **AT220, a partnered product, will be first to launch** The late-stage Specialty Hospital Products are mainly partnered, reducing financial risks yet retaining meaningful downstream payments. In January Hikma confirmed it is taking AT307 through the FDA's 505(b)(2) approval pathway, with milestones and royalties due on commercialisation. AT220, an undisclosed biosimilar for a multi-billion market, is also partnered and could be first to launch later this year. Two new formulation collaborations, and an extension to an existing agreement, were signed in the year.
- **First commercial revenues achieved with more to come in 2023** First product sales of £1.0m were from Tetris Pharma in the five-months post-acquisition. We expect these to grow in FY23, and for Arecor to record first AT220 royalties, assuming approval later this year. Cash of £12.8m (FY21: £18.3m) should be sufficient to execute current strategic plans and beyond key value inflection points.
- **Valuation of £176.0m, or 575p per share** Our pipeline rNPV model has been updated to reflect FY22 results, with our Arecor valuation now £176.0m (from £174.5m), or 575p/share) which remains based on conservative assumptions. Continued clinical progress, greater visibility on partnered products (indications, market positioning), and further licensing deals, could result in material uplifts.

Price	260p
Market Cap	£79.6m
Enterprise Value	£66.8m
Shares in issue	30.6m
12-month range	200p-435p
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 platform result in enhanced products with lower development risks and less onerous regulatory approvals.

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Arecor: more than simply a diabetes play

Arecor's Arestat platform underpins the investment case. It is employed to develop enhanced, novel formulations of established drugs which would otherwise be unachievable. This has created a broad and well-balanced portfolio of innovative products that offer similar milestone and royalty streams to classic drug discovery companies, yet with lower development risks and in a less costly and more rapid manner. A mix of partnered and in-house assets with multiple catalysts provide an attractive blend of value inflection points. We view the emerging diabetes franchise as particularly interesting, providing the most upside potential within our valuation. The two lead compounds - AT278, an ultra-concentrated, ultra-rapid insulin, and AT247, an ultra-rapid pump-optimised insulin - are completing Phase I studies. If successful, these could be ideally placed for the notable shifts underway in diabetes therapy. Updating our model for FY22 results lead to a valuation of £176.0m or 575p per share.

Partnering provides a commercially attractive and lower risk pipeline

Arecor's strategy is to manage development risks through striking a balance between in-house and partnered assets. The partnered programmes centre on specialty hospital products and on technology partnerships. The latter includes AT220, an undisclosed biosimilar product under development with a global pharmaceutical company, which is on track for approval in 2023. If launched, AT220 will be the first Arestat formulation to reach the market, triggering a milestone to Arecor, plus royalties on sales. Within specialty hospital products, where development is focused on improving injectable products that have clear issues, partner Hikma recently confirmed it would take AT307 through approval and commercialisation. The timing of the 505(b)(2) regulatory pathway suggests several key milestones will be achieved during the next 18 months. Another two formulation collaborations with major pharmaceutical players were signed, and an additional collaboration is now also in place with an existing, unnamed partner.

In-house diabetes programmes appear well positioned for emerging clinical needs

The in-house programmes centre on diabetes, with two clinically differentiated and commercially promising insulin formulations progressing through Phase I studies. The political uncertainties surrounding the US insulin market, notably centred on affordability and patient access, have dominated the headlines for some time. These are being addressed, with the major players now set to experience some degree of revenue, and profit, visibility over the medium term. The well documented demographic shifts, notably how rising obesity levels are driving Type II diabetes levels, coupled with the technological advances that are transforming the insulin pump sector's outlook, are creating the ideal setting for Arecor's novel AT278, an ultra-rapid, ultra-concentrated insulin, and AT247, an ultra-rapid, pump-optimised insulin.

Cash should be sufficient to execute current strategic plans

Following the Tetris Pharma acquisition in August 2022, Arecor's revenues now also include product sales, largely from Ogluo in Europe, a ready-to-use glucagon auto-injector pen, which we expect to increase in coming years. Steady income is also generated from formulation development partnerships. This year could also see first recurring royalties on AT220 launch. Arecor had cash and equivalents of £12.8m at end-December 2022 (FY21: £18.3m), with our updated forecasts suggesting that this should be sufficient to execute current strategic plans, including the ongoing Phase I trial of AT278, with data expected Q423, and to provide optionality into 2024 as potential future development plans are refined.

Three pillars: platform, pipeline, and partnering

Arestat creates novel products with improved and competitive clinical profiles

Arecor's Arestat formulation technology platform underpins the investment case. Arestat consists of a series of over ten different families of formulation techniques that employ different combinations of excipients and formulation methods to achieve enhanced or superior product features and physical properties. The excipients used are generally well characterised and typically pose no additional safety or regulatory burdens, but skilful modifications can materially alter the physical characteristics of the product (eg lipophilicity vs hydrophilicity). Typically, the focus is on existing biologics, such as antibodies, where superior kinetics can materially improve clinical and patient outcomes. Exhibit 1 summarises Arecor's key development programmes.

Exhibit 1: Summary of Arecor's current pipeline

Source: Arecor Therapeutics

Lower development risk, a well-balanced pipeline, and quicker timelines

Management has actively sought to build a balanced pipeline of both in-house and partnered assets. The aim is to contain development risks, and the associated cash burn, but still retain material upsides as programmes progress towards the market. Although Arestat can be employed on a compound at any stage of development, the reformulation of known drugs also means the risk is lower than for a novel API, and the favourable regulatory environment means that, if required, any clinical trials will be smaller. The partnered programmes bring in revenues from the start, usually as service fees, but the greater income is set to arise from milestone payments and royalties as they progress through development and are commercialised. The in-house programmes are selected for their clinical value add, commercial appeal, likely development costs, and inherent development risks.

Closer look at the commercially important US diabetes market

In this Update note we explore the diabetes programmes, with a focus on the dynamics of the treatment landscape in the important US market, the emerging changes in clinical practices, and the technological progress driving insulin pumps.

The lead in-house programmes address diabetes

A high-profile focus on diabetes, with lead compound AT278 a potentially disruptive insulin

Arecor's two key in-house clinical stage programmes are the ultra-rapid insulins AT278 and AT247, both of which are innovative formulations of insulin aspart, the active ingredient in Novo Nordisk's well-characterised, proven and now off patent Novolog (US)/NovoRapid (ex-US). There are also two further diabetes assets: Ogluo, a ready-to-use glucagon auto-injector pen, which is commercially available in select European countries; and AT299, an insulin co-formulation of pramlintide and insulin, which is in the preclinical stage.

AT278 is unique as both an ultra-fast and ultra-concentrated insulin

AT278 is an ultra-concentrated U-500 (500 units/ml) and ultra-fast acting insulin formulation. Such high concentration insulins are expected to become increasingly in demand, reflecting the rising number of people with Type II and refractory Type I diabetes that require higher daily dosing. The increase in incidence of both Type I and Type II people with diabetes is being driven by rising obesity rates across most geographies, which result in greater incidence of obesity-related insulin resistance, such that average usage for Type II diabetes patients is now 97 units of insulin daily, with a growing number needing 200 units or more. For context, the average adult needs between 0.5 and 1.0 units/kg daily. The challenges in formulating a higher concentration (>200 U/ml) rapid or ultra-rapid acting insulin mean there are no such options commercially available, nor do we know of any in clinical development.

AT247 is an ultra-fast insulin optimised for use in pumps

AT247 is a next-generation ultra-rapid prandial insulin analogue of 100U insulin aspart. It has been specifically formulated to materially accelerate absorption after injection, achieving a profile that closely approximates healthy (non-diabetic) physiological insulin secretion. The goal is to improve control of postprandial glucose and increase time in range (the percentage of time spent in the target glucose range). It is suitable for both Type I and Type II diabetes patients who self-administer insulin either via pen devices (also known as multiple daily injections, MDI) or any insulin pump system. Importantly, AT247's attractive PK/PD profile suggest it has the potential to be an ideal pump insulin, enabling optimal use of automated continuous subcutaneous insulin infusion (CSII) devices, and ultimately a fully closed loop artificial pancreas system.

Previous notes explore many of the key clinical aspects in detail

Two of our prior reports provide an in-depth review of Arecor's diabetes assets, including an overview of clinical data, the current diabetes market, and the potential opportunity and prospects: January 2022 Update and May 2022 Update. Additionally, our more recent December 2022 Outlook presents the complete picture of Arecor's investment case, placing these in-house programmes into the relevant context.

Diabetes incidence: rises driven by Type II diabetics

Diabetes is on the rise in all countries, notably Type II

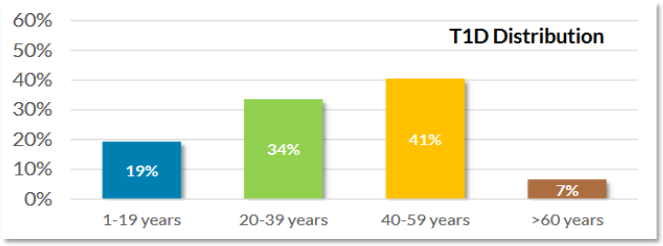
The tenth IDFDA fact sheets show that in 2021 there were an estimated 537m people with diabetes globally. This is projected to increase to 643m by 2030, representing growth of 19.7% over this period, continuing to rise to 784m by 2045, a 46.0% increase from 2021. For commercially important markets, notably Western countries, in North America there were 51m people with diabetes in 2021, projected to rise to 57m in 2030 (+11.8%) and to 63m by 2045 (+23.5%), and in Europe for 2021 there were 61m people with diabetes, with a more modest projected 9.8% increase to 67m in 2030 and a 13.1% rise to 69m in 2045.

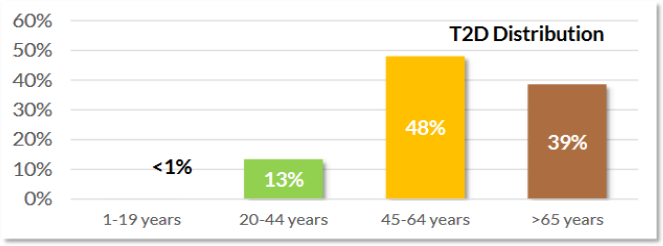
US market influences diabetes company priorities and decisions

The US market may not be the largest in terms of population, or future growth, however its commercial importance remains decisive. Seagrove Partners estimate the diagnosed diabetic population to be 27.9m, of which 1.9m are Type I diabetics and 26.9m are Type II, with forecast growth rates of 3.0% and 4.0% (five-year CAGR) respectively. Additionally, a further 7.5m may be undiagnosed, with these being Type II diabetics. These numbers correlate closely with the CDC estimates of 28.7m diagnosed, 8.5m undiagnosed, and 37.3m total.

Exhibit 2: US diabetes market overview by Type and age

Age Group	T1D Estimate 1.9M Dx'ed	T2D Estimate 26.0M Dx'ed
Infants 0-4	0.7% (13,300)	0% (none)
Children 5-9	3.3% (62,700)	<1% (588)
Youth 10-14	6.7% (127,300)	<1% (5,664)
Adolescents 15-19	8.6% (163,400)	<1% (17,962)
Young Adults 20-39 (T1), 20-44 (T2)	33.6% (638,400)	13.4% (3,478,313)
Middle Aged 40-59 (T1), 45-64 (T2)	40.5% (769,500)	48% (12,492,723)
Elderly 60+ (T1), 65+ (T2)	6.6% (125,400)	38.6% (10,041,967)





Source: Seagrove Partners Blue Diabetes Book. Note: T1D = Type I diabetes, T2D = Type II diabetes

Type I and Type II diabetics share many aspects of treatment but have differing journeys

Exhibit 2 shows the demographics associated with Type I and Type II diabetes. This reflects their differing causes: Type I diabetes is largely caused by the pancreas failing to make sufficient insulin, with a typical early onset (hence it is also known as juvenile diabetes); with Type II diabetes, the pancreas may still produce sufficient insulin but blood sugar regulation (insulin resistance) has been disrupted (previously known as adult-onset diabetes). The cause of Type I diabetes remains uncertain, with genetic, viral, and immune factors thought to be involved. Type II diabetes may also involve genetic elements, but the greater components are obesity and inadequate physical exercise. The rise in childhood obesity means Type II diabetes is increasingly seen in younger age groups.

Type I patients are initiated on some form of insulin injection

Clearly, Type I diabetes patients are initiated on insulin therapy from diagnosis, with the individual patient treatment variations centred around how the intensive management of time in range is achieved. For the majority this is still based on multiple daily injections (MDI), typically using a single bolus long-acting insulin coupled with more frequent injections of a rapid-acting formulation, although increasing numbers are migrating onto automated insulin delivery (AID). The advances in miniaturisation and AI-driven algorithms now allow the full integration of continuous glucose monitoring systems with sophisticated insulin pumps. The patients selected for pump-based therapy currently are those that are difficult to manage and maintain optimal time in range with MDI, yet the Type I "patient journey" is shifting notably towards an earlier and broader adoption of AID.

Type II treatments depend on time point of diagnosis

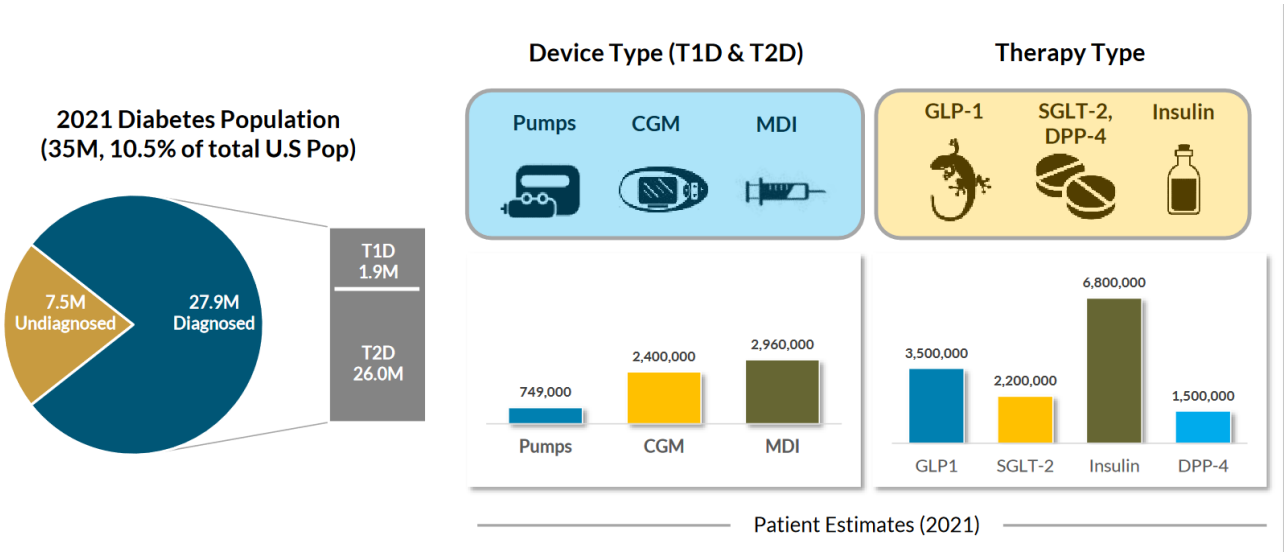
With Type II diabetes the patient journey is dependent upon the point of diagnosis. For many (c 38%) a regimen of increased activity coupled with

improved diet is sufficient to achieve the target HbA1c (blood sugar) levels. Those able to adhere to these lifestyle changes may remain stable for many years, however experience shows that a large proportion progress and require medication. Typically, treatment involves the use of multiple drugs, with the combination selected to best suit a patient's needs. The mainstay is metformin (used in 61% of newly-diagnosed Type II patients), an oral generic with a proven and attractive profile that is well understood. Historically, patients not controlled on metformin and exercise/diet had drugs such as sulphonylureas, thiazolidinediones, and DPP-4 inhibitors (gliptins) added.

Newer classes of Type II drugs are showing impressive results

The improved clinical benefits (including superior HbA1c reductions, cardio-renal protection, and weight loss) seen with newer classes, notably SGLT-2s (Sodium Glucose Transport 2 inhibitors) and GLP-1s (Glucagon-Like Peptide-1 Receptor agonists), have seen these used much earlier and more widely. The SGLT-2 class is gaining clinical traction for its ability to manage multiple Type II comorbidities, especially serious cardiovascular and renal damage, with impressive "real world" data demonstrating the value of this class. Boehringer Ingelheim/Eli Lilly's Jardiance (empagliflozin) and AstraZeneca's Farxiga (dapagliflozin) are the SGLT-2 class leaders. Extensive supportive clinical data for time in range and HbA1c reduction have seen injectable GLP-1s, ie Novo Nordisk's Ozempic (semaglutide) and Eli Lilly's Trulicity (dulaglutide), effectively supplant long-acting insulin as next line treatment for many Type II patient groups. The outcomes for weight loss, c 10% consistently, have made household names of drugs such as Ozempic.

Exhibit 3: US diabetes market overview by means of delivery and therapy



Source: Seagrove Partners Blue Diabetes Book Notes: CGM Continuous Glucose Monitoring, MDI Multiple Daily Injections, GLP-1 Glucagon-Like Peptide 1 receptor antagonists, SGLT-2 Sodium Glucose Transport 2 inhibitors, DPP-4 Dipeptidyl Peptidase-4 Inhibitors

Insulin therapy is expected to be added later in Type II journey

Despite the rise of the GLP-1 and SGLT-2 drug classes, Exhibit 3 shows how the majority of patients (excluding Type II diabetes controlled through diet and exercise alone) are currently treated with multiple daily injections of insulin. Clearly, all Type I diabetes patients require insulin injections but the majority of the c 7m (estimates range from c 5m to over 10m) US patients who use insulin daily are Type II diabetics. Whilst it is hoped that optimised combination therapy with the newer agents will delay, or even negate, the need to introduce insulin for many Type II diabetics, the harsh reality is this patient group will likely remain the largest users of insulin.

Market access: complexities abound for insulin

Whole industry in focus as many US diabetics find a voice and no longer suffer in silence

The US insulin market has been under the spotlight in recent years, becoming the focus of heated debate, both among politicians and the wider public, about pricing and affordability. US patients account for c 16% of the global insulin market yet generate around half of the revenues. This largely reflects the impact of regular and sustained price increases that have resulted in the cost of some insulin formulations tripling over a decade. Criticisms also centre on the perceived oligopoly, as only three manufacturers (Eli Lilly, Novo Nordisk, and Sanofi) supply insulin to the US market. Whilst these are factually correct, the provision and reimbursement of insulin is actually more complicated than for other drug classes.

Some critics see complex and ineffective regulation as a barrier to greater competition

Some observers believe a key factor is the inefficiency of the regulatory system, citing the fact that most of the commonly prescribed insulins now lack patent protection. The argument is that if the FDA were to approve "biosimilars", then the competitive pressures seen when generic versions of small molecules are introduced would take effect. A key anomaly is that, because of their long history, most insulins were approved under the NDA process. In 2020 a dedicated regulatory pathway for biologicals, the Biologics License Application (BLA), was introduced. Subtle, yet clinically important distinctions between the two processes mean there was no simple pathway to approval. In July 2021 the FDA approved the first interchangeable biosimilar insulin (Mylan's Semglee for Sanofi's Lantus), but this required the nature and scope of the clinical and non-clinical studies to be specifically agreed between the FDA and Mylan.

Biosimilars do not generate the same sizeable price falls as generic small molecules

The FDA is addressing these concerns but, in our view, the "genericisation" of insulin would not materially improve competition. Firstly, unlike with most small molecules, the complexities of manufacturing mean few companies can achieve the necessary economies of scale whilst maintaining the required product quality and consistency. It is also worth noting that in most cases with small molecules, the originator's sales decline rapidly and steeply as they are replaced by a multitude of far cheaper generic versions. The experience with biosimilars in other segments is different, with the price discounts generally more modest.

Pen devices do provide competitive barriers but are not the main issue in the US

Delivery devices are also often cited as a factor. In fairness, the majority of pen devices are patent protected and are designed to be used only with a particular type of insulin. This means the respective dedicated insulin cartridges benefit directly from this intellectual property protection. However, this is not a significant contributor since, unlike in Europe where the majority of MDI insulin users have been stabilised on pen systems for some time, in the US nearly two-thirds of MDI patients still happily used vials and disposable syringes as recently as 2016 (this has since declined to c 40%, with pens now at c 60%).

Complex US insulin supply chain and reimbursement creates a unique situation

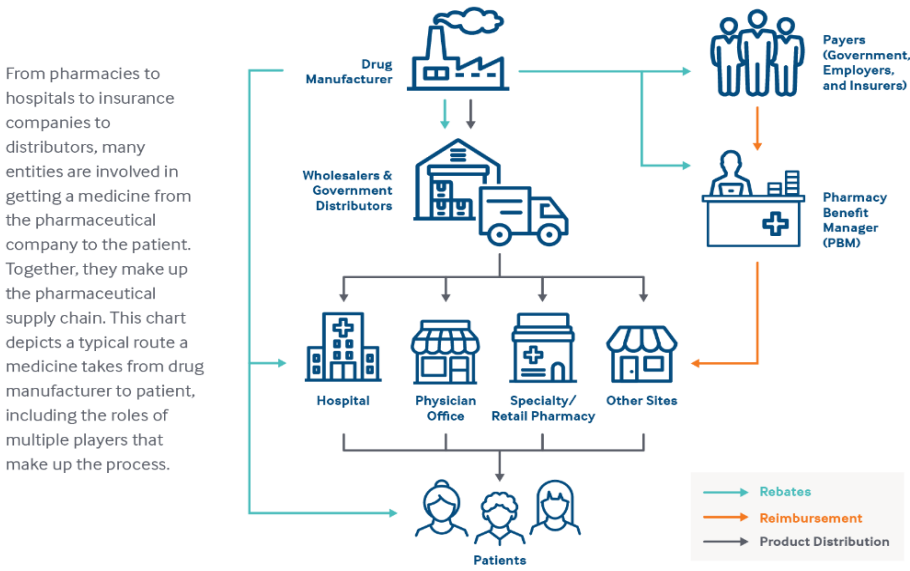
Instead, a major factor lies in the fragmented supply chain and reimbursement process, with the major players' activities distorting the marketplace. The US employs a "mixed system", with healthcare provided through a combination of publicly financed entities (eg Medicare and Medicaid) and private companies (typically health insurance plans). Around 56% of adults have some form of private insurance coverage, usually provided as part of their employment package; c 20% are covered by Medicaid (for a variety of low-income groups); some 14% are with Medicare (for people 65 and older not covered elsewhere); and a further 1% are

covered by other public insurance (such as Veterans Health Administration). The remaining 9% (c 30m) are not covered by either private insurance or public bodies.

PBM power is huge and they can drive volumes and prices

This is where Pharmacy Benefit Managers (PBMs) enter the picture. These are intermediaries who specialise in managing the supply chain for prescription drugs. They manage drug access, procurement, and supply on behalf of health insurers, Medicare Part D and managed care drug plans, large employers, and other payers. Their power comes from controlling prescribing, mainly through formularies, and using this purchasing power to obtain sizeable rebates from manufacturers. The administrative hurdles to prescribe a product not on a formulary are sufficient to have a real negative commercial impact, hence drug companies are incentivised to ensure their key products are easily prescribed and readily reimbursed.

Exhibit 4: The unique role of PBMs in the US purchase and supply chain



Source: Insulin affordability over time, The Commonwealth Fund, September 2020

Formulary inclusion, or worse exclusion, can shift market share

PBMs are aware that formularies have to reflect clinician choices, and products that are well differentiated and offer clear benefits find an easier path to inclusion. Within diabetes care the profiles of the oral drugs, such as GLP-1s and SGT-2s, are such that a choice of several, from different manufacturers, will be included. Unfortunately, US endocrinologists see little differentiation within the various insulin formulations and view several as essentially interchangeable. This has resulted in PBMs being able to extract attractive discounts from a supplier in return for the exclusive inclusion of their insulin product range. Over time, the damaging effect on sales of formulary exclusion has driven fierce pressure for ever greater discounting, with PBMs gaining an increasing share of the list prices.

Active discussions across the political spectrum

The impact and magnitude of these pressures has been documented in a number of studies, including the Senate's Grassley-Wyden report. The PBM space is dominated by three large players: Express Scripts (owned by insurer Cigna), CVS Caremark (part of CVS Health, which also owns health insurer Aetna), and OptumRx (a subsidiary of the insurer UnitedHealth Group). These have, understandably, exploited the perception that the various types of insulins are essentially interchangeable and used tactics employed in commoditised markets to provide volume sales, through prime positioning in formularies, in return for

material discounts. Over time the discounts and rebates have grown to unsustainable levels (80% to 90% of list price), resulting in raising of list prices by manufacturers. The outcome has been that, despite higher list prices, insulin revenues for manufacturers have been flat to negative over the past decade.

Distortions in real market pricing have impacted magnitude of patient co-pays

The downside for patients is that the co-pays (cost sharing provisions that differ across healthcare providers and plans) are typically based on list prices. Hence the typical patient's co-pays have been rising significantly, while the savings negotiated by PBMs have been largely retained and not passed on along the supply chain. The Grassley-Wyden report provides an excellent review of the US prescription healthcare market and how it has become so grossly distorted over time. The situation was clearly not sustainable, with many patients unable to afford such life-dependent medication. Insulin pricing became a feature of the Inflation Reduction Act (IRA) and the momentum for change was set in motion.

All three major players recently have introduced high profile list price cuts

All three manufacturers have taken a number of steps to redress the balance. For example, Eli Lilly cut the prices of its most commonly used insulins by 70% in March 2023. Similarly, Novo Nordisk quickly reduced the prices of several of its insulin ranges by 65% to 75%, as did Sanofi for its popular Lantus product range, with price cuts of 78%. Paradoxically, whilst these headline grabbing price reductions are designed to make their insulins more affordable for many patients (hence pre-empting likely regulation), by rebasing the PBM discounts (assuming this happens) these key manufacturers may find the cuts actually improve the commercial attractiveness of the US insulin market.

Positioning of new insulins: a need for differentiation

Innovation in insulins has not been a major focus

Against this complex and challenging background in the world's largest diabetes market, it is understandable that innovation in insulin formulation has not been a key priority for the main players. Add in the excitement around the newer anti-diabetic classes, particularly the GLP-1 and SGLT-2 products (where clinicians do perceive their superior HbA1C lowering abilities, coupled with material benefits such as weight loss and cardiovascular protection, offer major clinical advances) and the diabetes companies were right to direct their R&D efforts to this greater, and more easily realised, commercial potential.

Technological advances mean a viable artificial pancreas is imminent

Yet this overlooks one of the major transformations underway for not just Type I diabetes patients, but also those difficult to treat Type II patients. We have covered the technological advances that are driving the pump market in previous notes. Briefly, insulin pumps are not new (the first true pump devices were made in the 1970s) but the improvements in continuous glucose monitoring (CGM) and the corresponding miniaturisation of the pump technologies, coupled with the software that allows genuine real-time responses, have led to the current highly sophisticated artificial pancreas (Automated Insulin Delivery) systems.

These are set to transform lives, especially for younger patients

We believe these developments are as important a step change in diabetes care as the landmark Diabetes Control and Complications Trial (DCCT) of 1982-93. Just as DCCT showed intensive insulin management reduced long-term complications (despite an increased risk of hypoglycaemia), so the benefits of AID and the transformation in quality of life will be such that clinical practice will change over the coming decade. Exhibit 5 shows a useful overview of the clinical benefits that

were expected in 2016; even then, the use of only short- or rapid-acting insulin was advocated as a major positive in improving blood glucose level control.

Exhibit 5: Benefits of an insulin pump over equivalent multiple injections

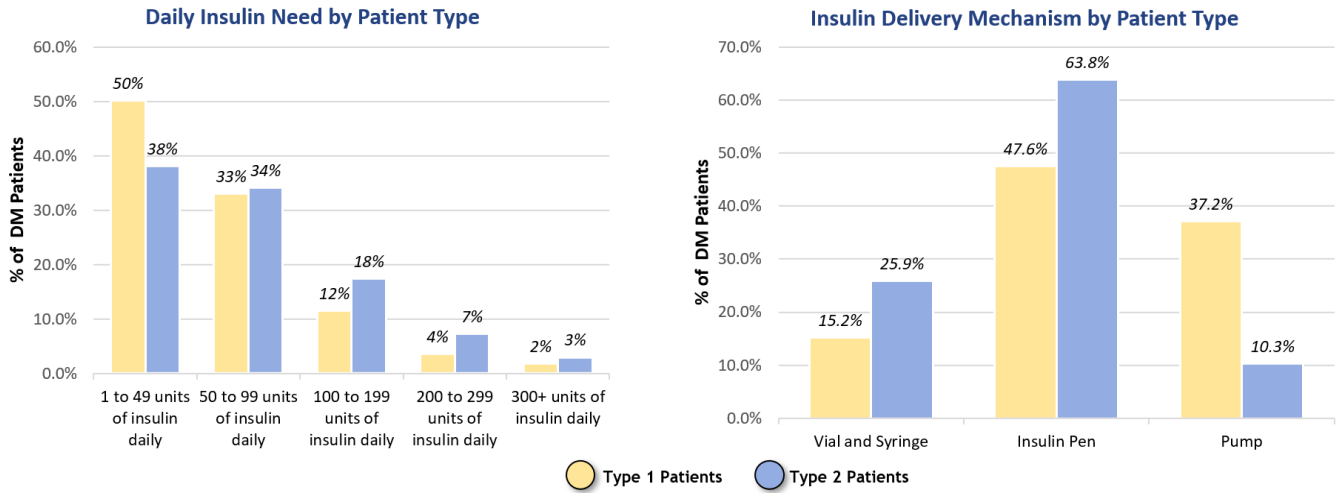
- Programmable insulin delivery allows closer match with physiologic needs
- Uses only short- or rapid-acting insulin, minimizing peaks and absorption-related variability
- Uses one injection site for up to 72 hours, thus reducing variations in absorption and treatment-related burden from multiple injections
- Reduction in glycemic variability and improved glycemic control
- Decreased risk of severe hypoglycemia and need for emergent medical attention
- Reduction in need for hospitalization and cost of care
- Improved quality of life and treatment satisfaction

Source: Adapted from McAdams and Rizvi, Journal of Clinical Medicine 2016, 5(1) 5

Pump adoption is currently mainly by difficult to stabilize Type I patients

Currently c 37% of Type I diabetics (c 650k patients) are using some form of insulin pump, with around 70,000 added during the past year. This compares with a far lower c 10% penetration (although some estimates are as high as 20%) for Type II diabetics. Interestingly, in Europe the majority of Type I diabetes patients use pen devices rather than the vial and syringe that is still a major element in the US. Some commentators believe the better glycaemic control, increased adherence, and improved self-management (especially convenience) seen with pen devices are a contributory factor to slower switching to pumps outside the US. Whilst this may have an impact, we suspect the various reimbursement systems (mainly national in European geographies) may be equally large factors.

Exhibit 6: Insulin market overview



Source: BioStrategies May 2022

Type II pump adoption is picking up momentum

There are c 2.3m Type II diabetes patients on intensive insulin therapy (excluding those who use a simpler basal insulin regimen) in the US, which compares with c 1.5m outside the US. Of these some 100k are already pump users in the US and 175k outside the US, largely due to the difficulties in maintaining their glucose

control. Despite the advent of newer therapies that should materially alter the Type II treatment journey (delaying the need to introduce insulin), growth rates for Type II pump adoption are expected to exceed Type I rates.

An emerging need that will drive a shift in the insulin needed

Estimates do vary but the next five years could see around 425k US Type II diabetes patients on pump therapy. A key differentiator between Type I and Type II pump users is the need for greater insulin levels, mainly due to the complexities of insulin resistance. As Exhibit 6 shows, c 18% of Type I patients require more than 100 units of insulin per day, compared with some 28% of Type II insulin using patients. Importantly, whilst there is a clear shift towards the adoption of pumps, a significant number of patients, c 63% of Type I and c 90% of Type II, still receive their insulin through injections, with most coming from pens.

AT278 and AT247: addressing an evolving need

Both AT278 and AT247 have been discussed extensively in previous notes

AT278 and AT247 are novel ultra-rapid formulations of insulin aspart, the active ingredient in Novo Nordisk's Novolog/NovoRapid (US and ex-US respectively). AT278 is a highly concentrated, 500 units/ml (U-500), ultra-rapid insulin, whilst AT247 is an ultra-rapid prandial insulin analogue that appears to have a best-in-class profile. Their clinical data have been discussed in detail in previous reports (including December 2022 Outlook), with the PK/PD characteristics from the Phase I programmes covered extensively in two earlier notes (January 2022 Update and May 2022 Update).

AT278 addresses the most pressing emerging clinical need

AT278 has the potential to be a disruptive insulin. AT278 is a novel insulin aspart formulation that is both highly concentrated, U-500 (500 units/ml), and ultra-fast acting. As mentioned, high concentration insulins are expected to become increasingly in demand, reflecting the rising number of Type II and refractory Type I diabetes patients requiring higher daily dosing. Higher rates of obesity are a clear factor, the link with Type II diabetes is well-established, but even within Type I, despite the younger demographics and stricter attention to dietary intakes, over 25% have a BMI greater than 30 and c 64% have a BMI greater than 25.

Technical difficulties mean existing market segment is poorly addressed

Notably, even with this clear and growing population need, there are only three concentrated bolus insulins available: Humulin R U-500 (human insulin, Eli Lilly) which has a similar profile to a basal insulin, and two more rapid acting but less concentrated products, Humalog U-200 and Lyumjev U-200 (both lispro, Eli Lilly).

MDI patients are struggling with large insulin volumes, complex regimens, and many injections

AT278 is well positioned to address a clear and existing clinical need for a rapidly-acting concentrated insulin in Type II diabetes and the emerging need in both younger and mature Type I diabetics. For the MDI segment (including both insulin pens and vials/syringe) the immediate benefits centre on reducing injection burden through materially fewer daily injections and with lower volumes, whilst also gaining the improved postprandial glucose control and better time-in-range (including reduced nocturnal hypoglycaemia) that ultra-fast insulins provide.

A far from ideal real-world experience

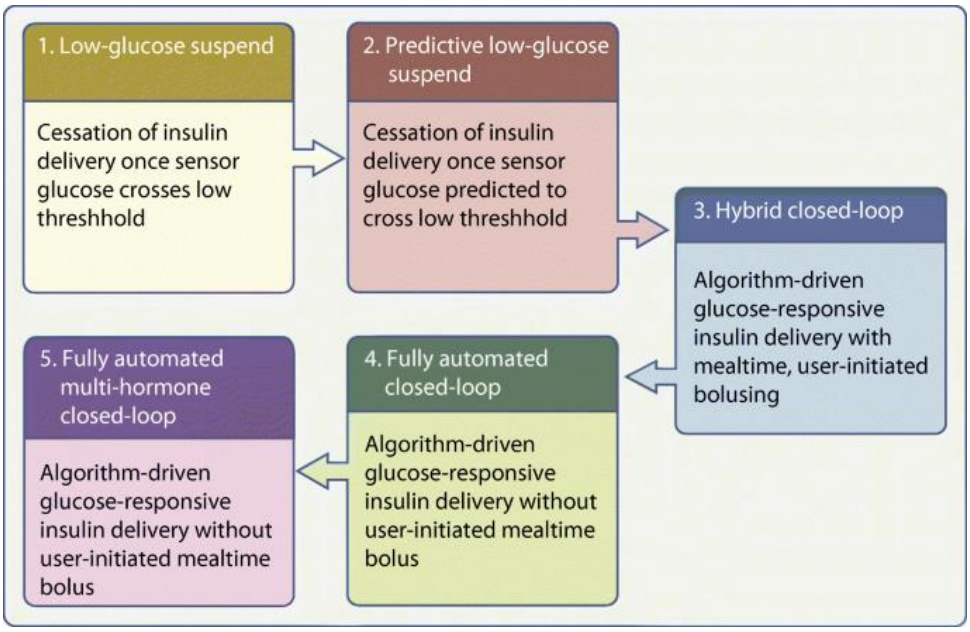
Placing this into a patient's context, when daily insulin doses exceed 200 units, the volume of U-100 insulin needed makes insulin delivery challenging. Standard insulin syringes typically deliver a maximum of 100 units, and insulin pen devices deliver only 60-80 units per injection. Also, injecting doses >1ml in volume can be painful and such larger volumes may alter the insulin absorption. Similarly, the number of injections needed can cause difficulty in maintaining the required

rotation of injection sites. From a clinical perspective, the onset of activity for regular U-500 insulin is c 30-45 minutes, with a time to peak activity of 4-6 hours and a 12-14 hour duration of action. In contrast, AT278 has PK/PD profiles that are ideal for postprandial use, with rapid and predictable absorption.

The larger opportunity is with the advent of advanced pumps

However, despite addressing this current need, the larger commercial opportunity for AT278 could lie in pump applications. We have covered this in prior notes, but the advances in miniaturisation and computing power, coupled with the flexibility, responsiveness, and predictive qualities of the evolving integrating algorithms, means a truly artificial pancreas is within sight (Exhibit 7).

Exhibit 7: Key milestones towards a truly artificial pancreas



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

Needs for pump users will make this more pressing

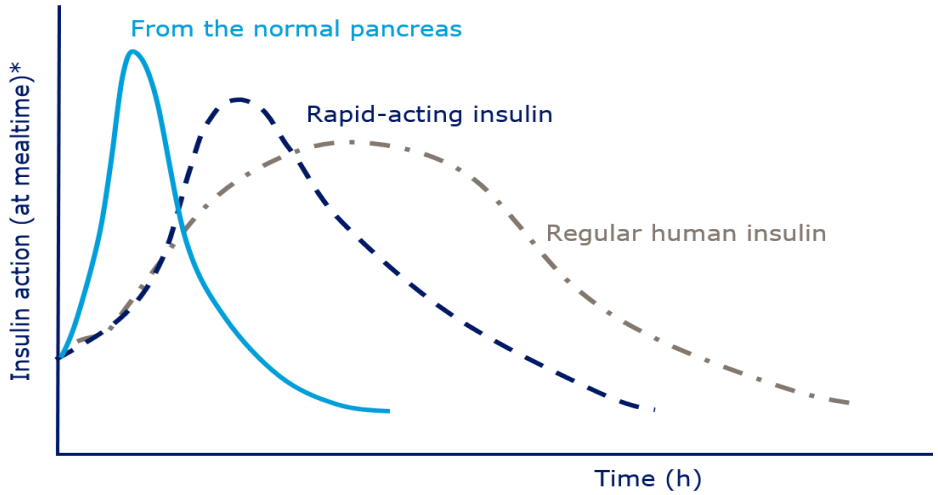
The field of AID remains nascent, with various manufacturers seeking to create the most relevant device for the majority of patients to achieve the best time spent in the glucose target range (70-180 mg/dL), whilst allowing for maximum convenience and flexible lifestyles. Common amongst all is the drive towards miniaturised devices (where their size limits reservoir capacities) and longer wear times (currently 3 days but the trend is towards 7 days), which means higher insulin concentrations (and smaller volumes) are increasingly viewed as key enablers. Importantly, algorithm-driven devices require a really rapid acting insulin to optimise glycaemic control, with a fast response and short duration of action. It is these requirements that place AT278 right in this emerging sweet spot.

AT247 is a true pump-optimised insulin with close to endogenous PK/PD profiles

AT247 is also an ultra-rapid insulin that is ideally suited to use with insulin pumps. A key goal for young Type I diabetes patients is to achieve a time in range of c 95%, with this seen as likely to prevent most of the longer-term complications currently associated with diabetes. For this to happen the artificial pancreas would need an insulin that mimics the profile of physiological insulin as closely as possible, avoiding the existing mismatch in postprandial activity with high glycaemia after a meal, followed by a rebound hypoglycaemia later. We view AT247 as a pump-optimised ultra rapid insulin and, as covered in prior notes, its PK/PD profiles are currently seen as best-in-class. Novo Nordisk has a

development programme addressing similar clinical needs that it terms "ideal pump insulin" (NNC0471-0119) which is progressing through Phase I studies.

Exhibit 8: Striving to achieve a closer to physiological insulin profile



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

AT247's time will come once pumps are better established

From a commercial perspective, AT247 could also be used in the MDI setting where its profile does confer benefit in improving blood glucose control. However, understandably in our view, most endocrinologists would argue that the timing of the injection has a greater influence on the resulting time in range, and so efforts directed to improving patient adherence to the dosing regimen have more impact than selecting the best ultra-fast insulin. Consequently, for AT247, and similarly for Novo Nordisk's ideal pump insulin, the appreciation of the clinical need is still evolving and will only become apparent once the drivers of optimising pump delivered therapy are better understood.

Valuation

We value Arecor at £176.0m, equivalent to 575p per share

We continue to value Arecor using an rNPV model, explicitly valuing the diabetes franchise, partnered assets, and the in-house specialty hospital product research programme(s). We have made no significant changes to our underlying product assumptions, with the valuation simply updated to reflect reported FY22 results, notably the net cash position, and our revised financial forecasts. Our updated valuation is £176.0m (from £174.5m previously), equivalent to 575p per share. An overview of our valuation is provided in Exhibit 9.

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)	104.7	125.7	60%	High single to double-digit	50.4	60.4	164.5	Peak sales: $358m; Launch year: 2025
AT278 (Type II diabetes)	128.7	154.4	60%	High single to double-digit	61.2	73.4	199.7	Peak sales: $516m; Launch year: 2026
AT299 (Diabetes)	20.4	24.5	10%	Low single digit	3.0	3.6	9.9	Peak sales: $200m; Launch year: 2028
Research (Specialty Hospital)	55.0	66.0	30%	High single to double-digit	16.5	19.8	54.0	Peak sales: $350m; Launch year: 2025+
AT307 (Speciality Hospital - Hikma)	30.0	35.9	75%	High single to double-digit	20.9	25.1	68.2	Peak sales: $100m; Launch year: 2025
AT220 (undisclosed biosimilar - partnered)	11.2	13.5	90%	Low single digit	9.6	11.5	31.4	Peak sales: $500m; Launch year: 2023
AT292/INBRX-101 (AATD - Inhibrx)	18.5	22.2	50%	Low single digit	9.1	10.9	29.6	Peak sales: $515m; Launch year: 2026
Tetris Pharma/Ogluo	7.9	9.5	100%	N/A	7.9	9.5	25.8	Peak sales: $10m; Launch year: 2021
Operating costs	(15.4)	(18.4)			(15.4)	(18.4)	(50.2)	
Net cash at FY22	12.8	15.4			12.8	15.4	41.8	
Total	**402.6**	**483.2**			**176.0**	**211.2**	**574.7**	

Source: Trinity Delta Note: AATD = Alpha-1 antitrypsin deficiency; assumptions include a 12.5% discount factor, £/$ FX rate of 1.20, and 10% taxation from 2026 (UK patent box).

Significant upside with clinical data and improved visibility

Our valuation continues to be based on conservative assumptions, and there could be significant upside across a number of areas. These include the diabetes programmes AT278 and AT247, which are the main value drivers, where we expect further clinical data this year. Approval of AT220 and disclosure of the partner and underlying product could lead to refined forecasts, as could visibility on progress with Hikma partnered AT307.

No value attributed to the inherent value in potential new licences and the platform itself

We do not attribute a value to the technology formulation development collaborations due to limited visibility surrounding the underlying assets, and the potential economics. We also do not provide an indicative valuation of the Arestat technology platforms. Nevertheless, we highlight that Arecor has a solid track record of formulating clinically and commercially attractive compounds and of striking commercially astute licensing deals.

Financials

Three revenue streams with varying predictability

Arecor now generates the majority of its revenues from three sources: (1) steady income from formulation development partnerships; (2) licensing agreements which include upfront payments and variable milestones that are contingent on development progress and commercialisation, on which we typically have limited visibility; and (3) product sales, mainly from Ogluo in Europe, following the acquisition of Tetris Pharma in August 2022.

FY22 saw growing formulation development revenues and first product sales

Revenues in FY22 were £2.4m (FY21: £1.2m) comprising £1.4m of formulation development (FY21: £1.2m) and £1.0m in product sales (FY21: nil). Product sales relate to Tetris Pharma, mainly Ogluo sales in select European countries, for the five-months post-acquisition. There were no milestones recorded in FY22 (FY21: nil) albeit the transfer of AT307 to Hikma in January 2023 was a milestone triggering event. Arecor also recorded £1.1m (FY21: £0.6m) of other operating income as part of a £2.8m grant awarded from Innovate UK in March 2021.

R&D increased with clinical trial investments, whilst SG&A rose with Tetris Pharma spend

Operating expenses for FY22 were £14.1m (FY21: £8.3m), or £13.7m when excluding non-recurring costs (FY21: £7.8m) with the increase driven by both R&D investment and SG&A spend. R&D grew to £8.6m (FY21: £5.4m) driven by the US Phase I trial of AT247, which completed in October 2022, and the start of the EU Phase I trial of AT278, which initiated in December 2022. Meanwhile, SG&A spend increased to £5.4m (FY21: £2.9m), as this now includes Tetris Pharma related costs; we estimate FY22 Arecor SG&A spend (ex-Tetris Pharma) of c £3.1m, suggesting costs remain controlled with only a very modest absolute uptick (FY21: £2.9m). Pre-tax loss was £10.4m (FY21: £6.9m), with a net loss of £9.1m (FY21: £6.2m) due to an R&D tax credit benefit of £1.3 (FY21: £0.8m).

Operating expenses will focus on increasing commercial investment for Tetris Pharma and the AT278 Phase I trial

We conservatively forecast FY23e product sales of £3.0m (FY22: £1.0m but only including five-months of sales post-acquisition; we estimate proforma FY22 Tetris Pharma sales of c £1.7m) and we also anticipate first royalty revenues from FY23e onwards assuming partnered-product AT220 receives regulatory approvals. We anticipate a broadly similar level of investment in FY23e, with operating expenses of £13.4m (FY22: £13.7m excluding non-recurring costs). With a full-year of Tetris Pharma costs to be consolidated in FY23e, coupled with increasing investment into Tetris Pharma commercial activities, including costs to support Ogluo's European marketing plans, we forecast an uptick in SG&A spend to £7.1m but a more modest increase to £7.9m in FY24e. In terms of R&D, with the AT278 Phase I trial initiated during FY22, but the AT247 Phase I trial now largely complete, we forecast R&D spend of £6.3m in FY23e and £6.6m in FY24e, albeit the latter is largely illustrative and future R&D investment will depend on clinical trial plans, likely to be refined during the course of this year and as data become available.

Cash should be sufficient to execute current strategic plans

With cash and equivalents at end-December 2022 of £12.8m (FY21: £18.3m), our updated forecasts (Exhibit 10) indicate that Arecor has sufficient funds to execute on current strategic plans, including the ongoing Phase I trial of AT278, with data expected Q423, and to provide optionality into 2024 to prepare for potential future development plans, as these are refined. Our forecasts do not assume any potential conversion(s) of pre-licence technology partnerships to longer-term licence agreements, nor any uncertain milestones. Hence partnering and/or licence income from upfront payments, or development milestones, or higher revenues from product sales and royalties, could extend the runway.

Exhibit 10: Summary of financials

Year-end: Dec 31	£'000s	2020	2021	2022	2023E	2024E
INCOME STATEMENT						
Revenues		**1,698**	**1,158**	**2,403**	**4,943**	**7,057**
Cost of goods sold		0	0	0	0	0
Gross Profit		**1,698**	**1,158**	**2,403**	**4,943**	**7,057**
R&D expenses		(3,937)	(5,386)	(8,613)	(6,287)	(6,602)
SG&A expenses		(1,642)	(2,389)	(5,039)	(7,126)	(7,899)
Underlying operating profit		**(3,880)**	**(6,617)**	**(11,249)**	**(8,471)**	**(7,443)**
Share-based payments		(318)	(484)	(503)	(523)	(539)
Exceptionals		0	(462)	(400)	0	0
Other revenue/expenses		452	640	1,132	720	308
EBITDA		**(3,259)**	**(6,268)**	**(10,244)**	**(6,954)**	**(6,404)**
Operating Profit		**(3,428)**	**(6,439)**	**(10,517)**	**(7,752)**	**(7,135)**
Financing costs/income		(84)	(21)	83	64	36
Profit Before Taxes		**(3,512)**	**(6,945)**	**(10,434)**	**(7,688)**	**(7,099)**
Adj. PBT		**(4,283)**	**(7,122)**	**(11,669)**	**(8,930)**	**(7,946)**
Current tax income		760	776	1,309	786	594
Net Income		**(2,752)**	**(6,169)**	**(9,125)**	**(6,902)**	**(6,505)**
EPS (p)		**(0.2)**	**(0.3)**	**(0.3)**	**(0.2)**	**(0.2)**
Adj. EPS		**(0.2)**	**(0.3)**	**(0.4)**	**(0.3)**	**(0.2)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		16.2	23.0	28.9	30.7	31.1
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		**3,822**	**20,515**	**17,455**	**11,847**	**7,455**
Cash and cash equivalents		2,898	18,316	12,806	7,110	2,862
Accounts receivable		166	1,423	2,167	2,031	1,934
Inventories		0	0	1,131	1,486	1,488
Other current assets		758	776	1,351	1,220	1,172
Non-current assets		**462**	**406**	**4,371**	**4,019**	**3,772**
Property, plant & equipment		375	328	838	855	904
Intangible assets		38	30	3,485	3,115	2,820
Other non-current assets		48	48	48	48	48
Current liabilities		**(1,408)**	**(2,267)**	**(3,927)**	**(3,346)**	**(3,173)**
Short-term debt		0	0	0	0	0
Accounts payable		(1,303)	(2,141)	(3,725)	(3,144)	(2,971)
Other current liabilities		(105)	(126)	(202)	(202)	(202)
Non-current liabilities		**(2,102)**	**(105)**	**(582)**	**(582)**	**(582)**
Long-term debt		(1,698)	0	0	0	0
Other non-current liabilities		(403)	(105)	(582)	(582)	(582)
Equity		**774**	**18,549**	**17,317**	**11,938**	**7,472**
CASH FLOW STATEMENTS						
Operating cash flow		**(1,857)**	**(5,450)**	**(9,367)**	**(6,251)**	**(5,264)**
Profit before tax		(3,512)	(6,945)	(10,434)	(7,688)	(7,099)
Non-cash adjustments		614	1,156	624	1,256	1,234
Change in working capital		747	(419)	(291)	(800)	(77)
Interest paid		0	0	0	64	36
Taxes paid		295	758	734	917	642
Investing cash flow		**(49)**	**(68)**	**(1,371)**	**(445)**	**(484)**
CAPEX		(52)	(69)	(389)	(445)	(484)
Acquisitions/disposals		0	0	(1,091)	0	0
Other investing cash flows		3	1	109	0	0
Financing cash flow		**1,774**	**20,931**	**5,159**	**1,000**	**1,500**
Proceeds from equity		0	18,565	5,648	1,000	1,500
Increase in loans		1,840	2,500	0	0	0
Other financing cash flow		(67)	(134)	(489)	0	0
Net increase in cash		**(132)**	**15,413**	**(5,579)**	**(5,696)**	**(4,248)**
Exchange rate effects		(43)	5	69	0	0
Cash at start of year		3,074	2,898	18,316	12,806	7,110
Cash at end of year		**2,898**	**18,316**	**12,806**	**7,110**	**2,862**
Net cash at end of year		**1,200**	**18,316**	**12,806**	**7,110**	**2,862**

Source: Company, Trinity Delta. Note: FY24e R&D is largely illustrative pending development plans

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