Trinity Delta

# Arecor Therapeutics

Update

## AT278 ultra-concentrated insulin superior to benchmarks

20 May 2024

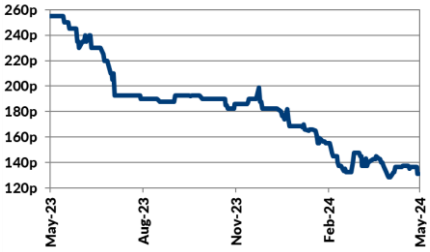
**Arecor's lead compound AT278, a unique ultra-rapid and ultra-concentrated insulin, has successfully shown superiority to benchmark fast-acting or concentrated insulins in a Phase I study in Type II diabetes (T2D). This follows a similarly positive outcome in a previous Phase I study in Type I diabetics (T1D). Demonstrating AT278's clinical efficacy in difficult-to-treat overweight/obese T2D patients confirms the validity of the formulation, shows its profile is attractive for T2D patients with high insulin needs, as well as being ideally suited for the emerging needs of "next generation" insulin pumps. Continued development is strongly supported by the data and unmet patient needs, and the focus will now be on the optimal strategy to further advance AT278. Our updated valuation is largely unchanged at £179m, or 584p/share.**

| Year-end: December 31 | 2022 | 2023 | 2024E | 2025E |
|---|---|---|---|---|
| Revenues (£m) | 2.4 | 4.6 | 6.8 | 11.2 |
| Adj. PBT (£m) | (12.0) | (10.7) | (8.2) | (5.4) |
| Net Income (£m) | (9.3) | (8.6) | (7.1) | (4.4) |
| EPS (p) | (0.3) | (0.3) | (0.2) | (0.1) |
| Cash (£m) | 12.8 | 6.8 | 0.1 | (3.7) |
| EBITDA (£m) | (10.2) | (8.7) | (7.1) | (4.4) |

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

- **Positive data from Phase I Type II diabetes study** Topline data from a key Phase I trial in overweight and obese T2D patients, who are typically more difficult to treat, show that AT278 is superior to both the benchmark rapid insulin NovoRapid (100IU) and to concentrated Humulin (500IU). AT278 is an ultra-high concentration insulin that also has ultra-fast absorption. These data support the view that AT278 has a unique profile that is ideally suited to the changing diabetes landscape.
- **Ideally positioned to address emerging needs** Diabetes is a growing global issue, and patients with high insulin needs are becoming increasingly prevalent. However, this demographic is poorly served by existing insulins and devices (pens/pumps). Whilst there have been impressive technological advances within insulin pump delivery systems (known as AID), miniaturisation and longer wear times will be key to drive uptake from currently low levels, particularly in T2D. This can only be achieved with an ultra-rapid and ultra-concentrated insulin like AT278.
- **Data support continued development** Continued future development of AT278 is strongly supported by the positive Phase I data and the growing unmet needs within diabetes. Management will now need to assess the optimal development plan, subject to funding, which could include conducting future studies alone or with a partner. Given the importance of an insulin such as AT278 to enable next generation devices, strong relationships with device manufacturers will be key, in our view; Arecor already has a separate collaboration in place with Medtronic.
- **Valuation of £179m, or 584p per share** Our rNPV valuation is updated for a number of factors (described later), albeit the AT278 probability is unchanged as we assumed Phase I success. Our updated rNPV is £179m (584p per share). Continued progress with the diabetes franchise, growing royalties on AT220, and execution of further collaborations and partnerships, could all have significant upside.

| | |
|---|---|
| Price | 131.0p |
| Market Cap | £40.1m |
| Enterprise Value | £52.4m |
| Shares in issue | 30.6m |
| 12-month range | 124.3p-260p |
| 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 results in enhanced products with lower development risks and less onerous regulatory approvals.

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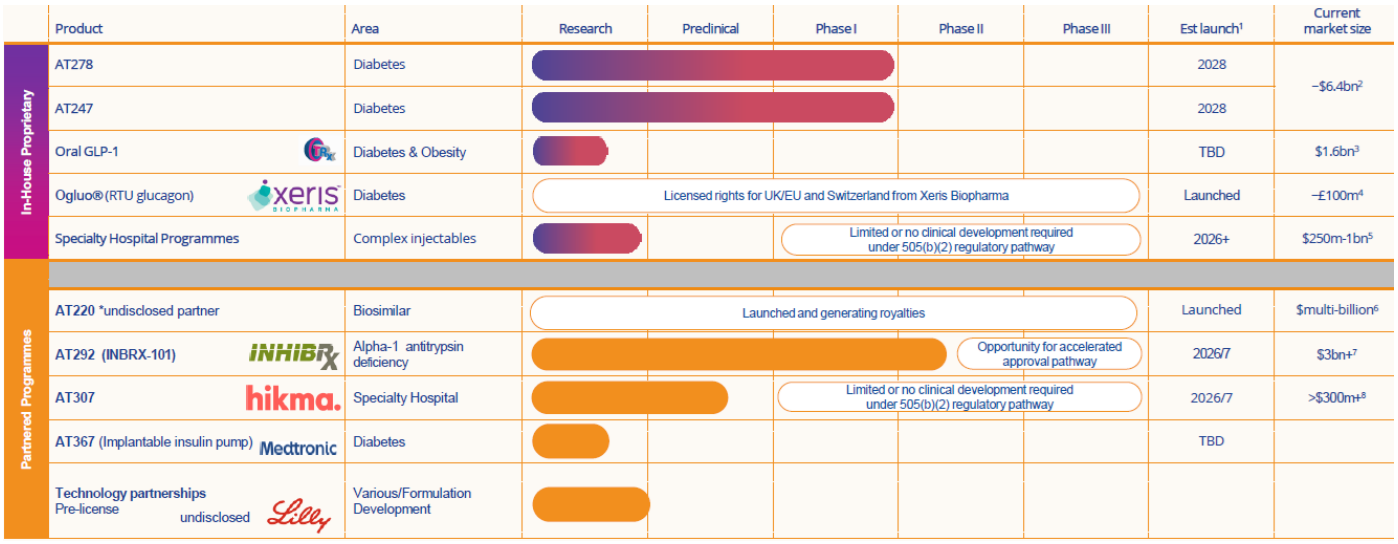
# Arecor: Data confirm attractive AT278 profile

**Arecor's near-term investment case centres on its diabetes franchise, notably AT278, an ultra-rapid and ultra-concentrated insulin. AT278's absorption profile is well suited to the needs of Type II diabetic patients who require higher daily doses of insulin and, importantly, could be a key enabler for the development of "next-generation" insulin pumps. The Phase I study in overweight/obese Type II diabetics, a particularly challenging study population, showed AT278 was superior to the current benchmark insulins. AT278 is a 500IU insulin and, despite its much higher concentration, was able to better the absorption of both 100IU NovoRapid (NovoLog in the US), the gold standard rapid insulin, and high concentration Humulin-R 500. These results, if replicated in Phase II trials, suggest AT278 could be the first disruptor insulin in several decades and is ideally placed for the sizeable shifts underway in the diabetes market. Investor focus should now turn to the format, and cost, of the next development phase to progress AT278 towards approvals, and on potential partnering options. Our updated Arecor valuation is £179m, equivalent to 584p a share.**

### Positive AT278 outcome in Phase I Type II diabetic study confirms attractive profile

The success of AT278 in the Phase I study in overweight/obese Type II patients is a significant achievement. Typically, this patient group is challenging, with variable body composition often impacting results. The replication of the findings of the earlier Phase I study in otherwise healthy Type I diabetics confirms the validity, and value, of the Arestat formulation. In this note we summarise the diabetes market dynamics, the size of the opportunities, the treatment shifts that are already happening, and how AT278 could be the disruptive insulin that enables key elements of the evolution. However, Arecor is more than simply AT278; Exhibit 1 shows the broad pipeline of opportunities being progressed.

**Exhibit 1: Summary of Arecor's current pipeline**




Source: Arecor Therapeutics

### Several partnered programmes on market or in late-stage development

Arecor's three most advanced partnered assets are: AT220, an undisclosed partnered biosimilar that is the first product employing the Arestat technology to launch; AT307, a specialty hospital product licenced to Hikma; and INBRX-101, a late-stage clinical orphan disease drug with Inhibrx/Sanofi.

## The opportunities for Arecor's diabetes franchise

**A valuable diabetes franchise is coming together**

Arecor's diabetes franchise centres on two proprietary clinical-stage programmes that address the emerging need of AID (Automated Insulin Delivery) devices: AT278, an ultra-rapid and ultra-concentrated insulin, and AT247, an ultra-rapid insulin that closely approximates physiological insulin. Additionally, Arecor has recently signed a collaboration with Medtronic to develop a high concentration, thermostable insulin for use with their next-generation peritoneal implantable pump (May 2024 Lighthouse). There is also an earlier co-development deal with TRx Biosciences to develop an oral GLP-1 (March 2024 Lighthouse), and the commercial product Ogluo, which is sold in Europe via subsidiary Tetris Pharma.

**Dynamic market as technology drives seismic shifts…**

Several of our prior reports provide an in-depth review of Arecor's diabetes assets, including detailed clinical data, the current status of the diabetes market, the potential opportunity and prospects (January 2022 Update, May 2022 Update), and importantly, a US market overview (April 2023 Update). Collectively these present a comprehensive picture of the rapid technological changes and clinical developments in progress, detailing how Arecor is poised to potentially disrupt the current insulin market oligopoly. Also, our November 2023 Outlook explains Arecor's investment case and contextualises its in-house diabetes assets.

**…which AT278 is well placed to exploit and to drive**

In this note, without duplicating previous work, we aim to recap briefly and update on the various device and pump markets, as well as the developing clinical needs. The main message is that AT278 is well positioned to not simply benefit from these technology developments, but actually be one of the key enablers.

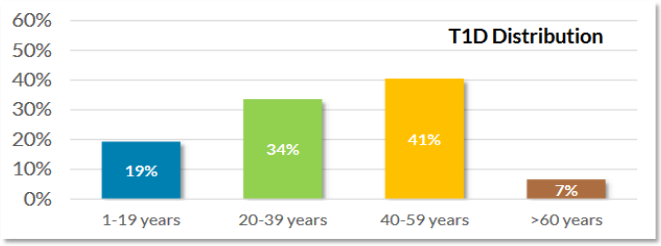
## Diabetes on the rise globally, driven by Type II

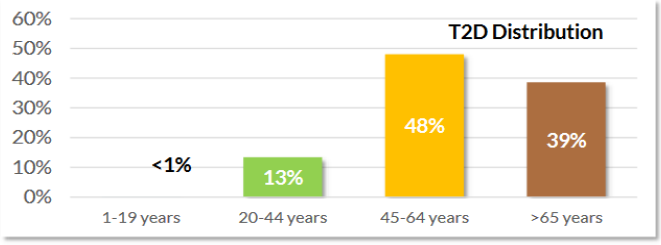
**Diabetes is a large and growing problem globally**

Diabetes is a growing global problem, with patient numbers forecast to rise to 643m by 2030 and to 784m by 2045. For commercially important markets, in North America the cases are expected to rise to 57m in 2030 and 63m by 2045, and in Europe a more modest increase to 67m in 2030 and 69m in 2045.

### 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, Dx'ed = diagnosed

**US market is the most important commercially, with considerable opportunities**

The US market may not be the largest in terms of cases, or future growth, however its commercial importance remains decisive. The diagnosed diabetic population in the US is thought to be c 27.9m, of which c 1.9m are Type I diabetics and c 26.0m are Type II, with growth rates of 3.0% and 4.0% (five-year CAGR), respectively. Additionally, a further c 7.5m may be undiagnosed, with these typically including early Type II diabetics. Exhibit 2 shows the patient breakdown by age group for Type I and Type II diabetics.

**Type I diabetes incidence is rising but Type II is soaring**

The patient populations reflect their differing causes: Type I diabetes largely results from the pancreas failing to make sufficient insulin, with a typical early onset (thus it was 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. Rising childhood obesity means Type II diabetes is increasingly seen at younger ages.

## Insulin essential for Type I, used frequently in Type II

**AID is coming of age as various elements are being integrated**

Type I diabetes patients are initiated on insulin therapy from diagnosis, with variations in individual patient treatment centred around achieving and managing time in range. For the majority this is still based on multiple daily injections (MDI), using a single bolus long-acting insulin coupled with more frequent injections of a rapid-acting formulation (typically 3 times a day with meals), although increasing numbers are migrating onto automated insulin delivery (AID). AID uses rapidly acting insulins, without a basal element, delivered by continuous infusion to respond to changes in glucose levels. The advances in miniaturisation and AI-driven algorithms now allow the full integration of continuous glucose monitoring (CGM) systems with sophisticated insulin pumps. The Type I patients selected for pump-based therapy currently are those that are difficult to manage and maintain optimal time in range with MDI, yet the "patient journey" is shifting towards an earlier and broader adoption of AID.

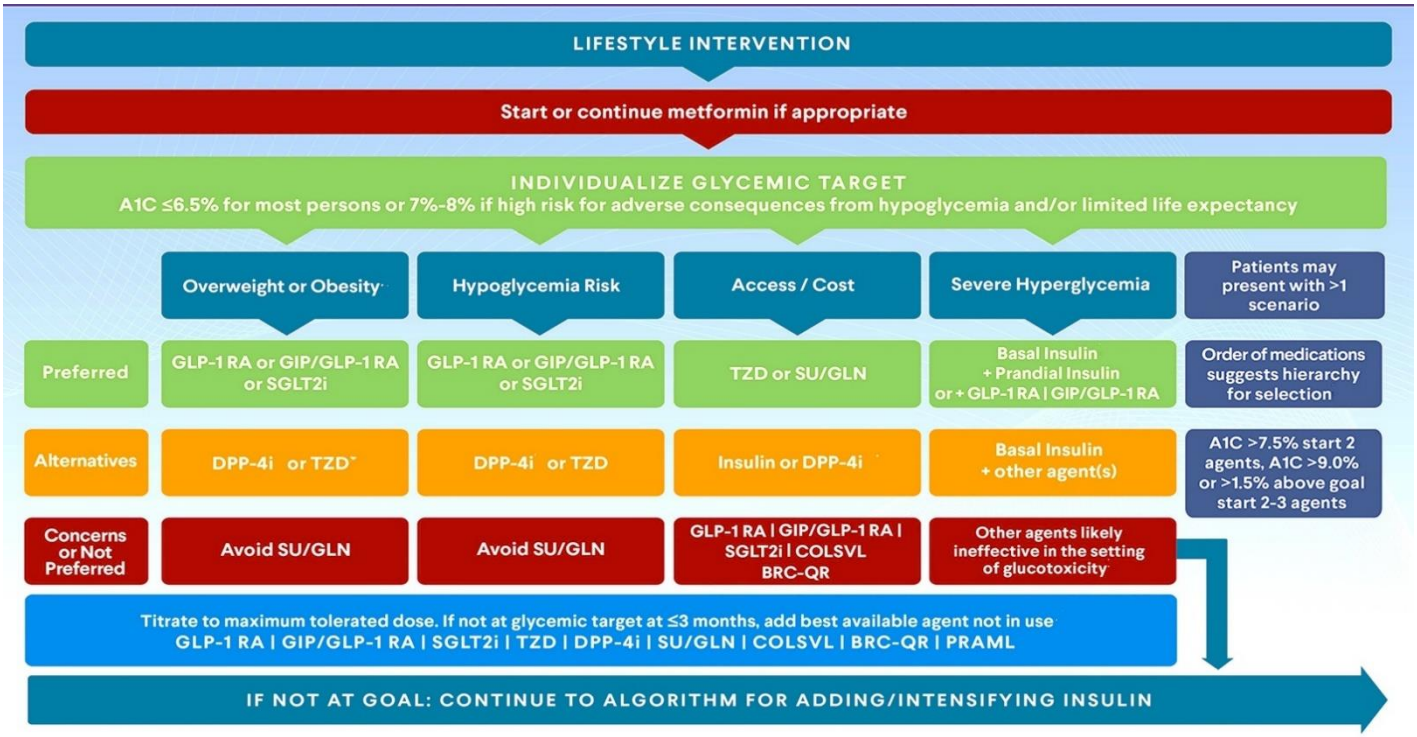
**Type II diabetes therapy is set to alter materially as new drug classes are adopted…**

With Type II diabetes the patient journey depends on the point of diagnosis. Lifestyle modifications underlie all interventions. 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. Normally treatment involves the use of multiple drugs, with the combination selected to best suit a patient's needs. Exhibit 3 shows the 2023 AACE (American Association of Clinical Endocrinology) glucose-centric algorithm for glycaemic control.

**…with GLP-1s set to enter much earlier in the treatment cascade**

The mainstay is metformin (used in c 61% of newly-diagnosed Type II patients), an oral generic with a proven profile that is well understood. However, we expect the downstream cascade to change materially over time. 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, in particular, GLP-1s (Glucagon-Like Peptide-1 Receptor agonists), should result in the complications-centric model gaining importance, with these drug classes being used much earlier and far more widely.

**Exhibit 3: AACE Glucose Centric Algorithm for Glycaemic Control 2023**




Source: American Association of Clinical Endocrinology Consensus (AACE) 2023

**Despite the impressive efficacy of GLP-1s in Type II, insulin will remain a key treatment option**

All Type I diabetes patients require insulin injections, but the majority of patients who use insulin daily are Type II (estimates vary by geography but typically 3x to 5x as many). It is in Type II patients that the future role of insulin creates debate. As mentioned, the clinical data supporting improved time in range and consistent HbA1c reductions, coupled with benefits such as weight loss and cardiovascular protection, should see GLP-1s, eg Novo Nordisk's Ozempic (semaglutide), Eli Lilly's Trulicity (dulaglutide) and Mounjaro (tirzepatide), effectively supplant long-acting (basal) insulin as next line treatment for many Type II patient groups. Many hope that optimised combination therapy with these newer agents will delay, or even possibly negate, the need to introduce insulin for many Type II diabetics; however, the harsh reality is this patient group will likely remain the largest users of insulin.

## Technology advances are driving insulin pump delivery

**The undoubted promise of AID is being realised as advances in technologies converge**

The past decade has seen one of the major treatment transformations not just for Type I diabetes patients, but also those difficult-to-treat Type II patients. We have previously covered the technological advances driving the pump market in earlier notes. Briefly, insulin pumps are not new (the first true pump devices were made in the 1970s) but improvements in continuous glucose monitoring (CGM) that allow the assessment of trends, patterns, and time spent in range in real time, and the corresponding miniaturisation of pump technologies, coupled with the defining advances in software and controller algorithms that allow genuine real-time responses, have led to the current highly sophisticated "artificial pancreas" (Automated Insulin Delivery is the term preferred by regulators) systems.

**AID can deliver unequivocal improvements in diabetes control across all groups**

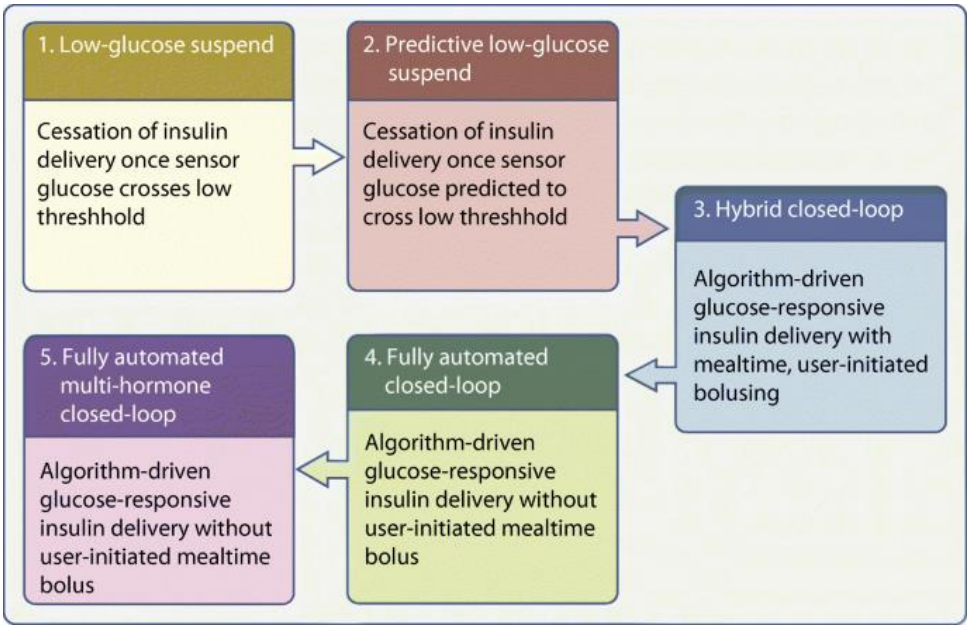
We have stated before that we believe these developments are as important a step change in diabetes care as the landmark Diabetes Control and Complications Trial (DCCT) of 1982-93. Just as DCCT showed intensive insulin management

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. Despite the widespread use of improved MDI (Multiple Daily Injections) regimens, only a minority of Type I patients currently meet widely accepted glycaemic goals. Extensive clinical data, coupled with rising "real world" evidence, is showing AID systems unequivocally improve glycaemic outcomes across all age groups, in all genders, and regardless of diabetes duration, prior insulin delivery modality, or baseline glycated haemoglobin (HbA1c) levels.

**The rate of AID adoption is set to rise as benefits, short and long term, become clear**

Whilst many of the improvements in clinical outcomes are expected to accrue over the longer term (eg quantifiable reductions in retinopathy, neuropathy, nephropathy, and cardiovascular complications), several extensive studies have shown the reduction in acute complications such as severe hypoglycaemia (SH) and diabetic ketoacidosis (DKA) can make AID therapy cost-effective over the near term too. From a patient's perspective (and their families) the improvements in quality of life, reduced diabetes burden, decreased fear of hypoglycaemia, and normalisation of daily routines are seen as major drivers of adoption.

**Exhibit 4: Key milestones towards a truly "artificial pancreas" (AID)**




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

**A long and tortuous journey but the "artificial pancreas" is within sight of commercial reality**

The path to a fully automated closed-loop system (Exhibit 4) has required significant advances in many diverse technologies. The first step was the creation of compact monitors that were able to measure glucose levels consistently without blood draws. This required a great deal of clinical work to ensure glucose measurements in the interstitial fluid were reliable indicators of the levels seen in blood. There is still work to be done to achieve faster response times and that is a development need that is being addressed. The pump manufacturers have also undertaken a substantial amount of work to create compact, reliable pumps that deliver insulin accurately and consistently. Concurrently, the financial investment in software that coordinates these disparate components has been significant, and over a prolonged period, but the incremental improvements have resulted in systems that can genuinely approximate the "artificial pancreas".

**New insulin profiles needed to allow these novel systems to work to their potential**

Having achieved these milestones, the development focus is shifting onto the elements that should make a difference in the clinic rather than the laboratory. To date the pumps have been developed with the best available rapid insulins, with Novo Nordisk's NovoRapid/NovoLog being viewed by many as the gold standard. However, the critical need of the next generation pump is for ultra-rapid insulins that can be absorbed from the sub-cutaneous site in as close a profile to physiological insulin as possible. This need is reflected in Arecor's development of AT247, an ultra-rapid insulin, whose absorption profile does approximate physiological insulin. Importantly, AT278 has a similar absorption profile yet is also five times as concentrated, a factor that is set to alter the way the pump industry can make more compact devices and still deliver extended wear times.

**Nearing the goal of automating the management of diabetes**

The goal of the device industry has been to automate the process of managing diabetes completely. Although the vision of what was needed to deliver effective AID systems (a broad term that includes closed-loop systems) was known and well-articulated, its development had to follow a deliberate stepwise process. This reflects the diversity of elements that have to combine seamlessly, consistently, and accurately. Hence individual hardware systems, such as CGM devices and insulin pumps, were refined, tested, and approved first. Once proven, these were connected with the control software that is, arguably, the most critical enabling technology. Several types of algorithms have been developed, including model predictive control (MPC), proportional integral derivative (PID), and fuzzy logic (FL) controllers. The scrutiny and approval of control software for diabetes control was a novel challenge for regulators, which understandably took time to address.

## Compact glucose monitors are critical enablers

**Advances in glucose monitoring have been impressive, with more to come in near-term**

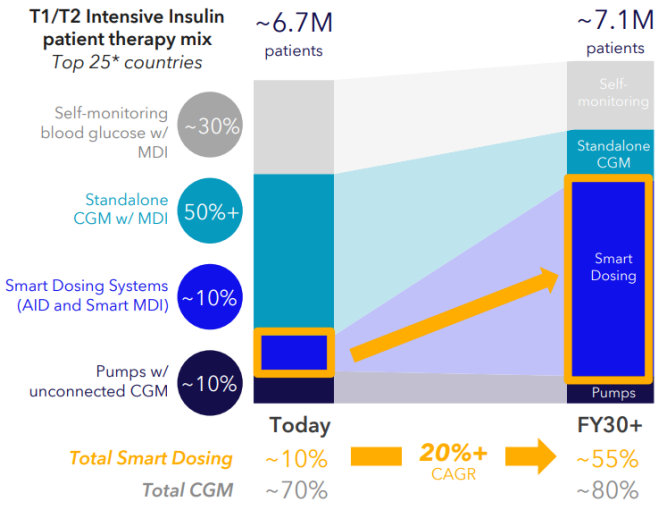
The CGM and pump suppliers split into two very distinct camps, with the major exception being Medtronic. The CGM field is relatively concentrated and is dominated by a number of well-established players such as: Dexcom, with their G7 sensor; Abbott, with the FreeStyle range; Senseonics, with Eversense (distributed by Ascensia); Roche, with the Accu-check range. Medtronic spans the segments, with the Guardian sensor range, InPen Smart insulin pen, and MiniMed insulin pump and infusion sets. The CGM segment has existed longer than the pump equivalent, and consumer needs have been well articulated for some time. A common theme among patients and clinicians, when asked about current CGMs, is the desire for better accuracy but, significantly, the key demand is longer sensor wear times. This has led manufacturers to develop devices that can last a year before a sensor change is required, with fewer calibrations, and with genuinely compact dimensions. In terms of size, the CGM market is estimated at US$11.6bn in 2024 and forecast to reach US$21.3bn by 2029, growing at 12.8% CAGR.

## AID uptake driven by Type I but Type II to push volumes

**AID market is dominated by a handful of US players…**

The insulin pump segment is younger and less consolidated, but with three major players: Medtronic, with their MiniMed range; Tandem Diabetes Care, with the t:slim platform; and Insulet, with the well-regarded Omnipod platform. These have the resources to develop their system platforms and undertake the preparatory work to integrate glucose monitoring and control software effectively. They also have the infrastructure and market presence to drive adoption of their products into what we expect will become a more competitive and mature mass market.

**Exhibit 5: Medtronic expects Smart Dosing conversion to drive growth**




Source: Source: Medtronic at 42nd JP Morgan Healthcare Conference January 2024

**...with smaller players tending to have a technical edge**

Smaller players have their place, with innovation typically their key differentiator, and these include: Ypsomed, with the mylife brand; Beta Bionics, with the iLet Bionic Pancreas; Eoflow, with the Eopatch; Sooil (arguably the originators of the first commercial pump), with the Dana system; CeQur, with the CeQur Simplicity; and VeCentra with their Kaleido product. Roche is also active in the pump space but despite its considerable resources, has yet to make a sizeable impact, which is not, in our view, typical of their corporate character.

**The insulin pump market is valued at $6.1bn and set to grow to $21.7bn by 2032**

The size of the pump market is defined by the number of patients who require daily insulin; this excludes the Type II population who use insulin as part of IIT (Intermittent Insulin Therapy). The IDF statistics place this as c 64m globally, of which c 11m are in the commercially relevant markets (including the US and Top five Europe). Estimates vary but Insulet sees this 11m split 45% Type I and 55% insulin intensive Type II patients, breaking down into c 1.5m Type I and c 2.5m Type II (basal-bolus) in the US, and c 3.5m Type I and a further c 3.5m insulin intensive Type II patients in the international markets. In value terms, the insulin pump market is estimated at US$5.3bn in 2023, rising to US$6.1bn in 2024, and growing to US$21.7bn by 2032, an increase of 17.2% CAGR.

**Early adopters are happy, but majority want compact size and long wear times**

Currently c 37% of Type I diabetics (c 700k 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 for Type II diabetics. The mainstay of this uptake are the early adopters, who often have specific needs driving their decisions, but this is set to change as the limited market launch activities previously undertaken by most pump players transition to comprehensive marketing programmes that address the wider insulin user community. In a similar way to the more mature CGM segment, over time we expect patient and clinician "needs and wants" will shift decisively towards greater ease of use, more discreet and compact sets, and longer wear times.

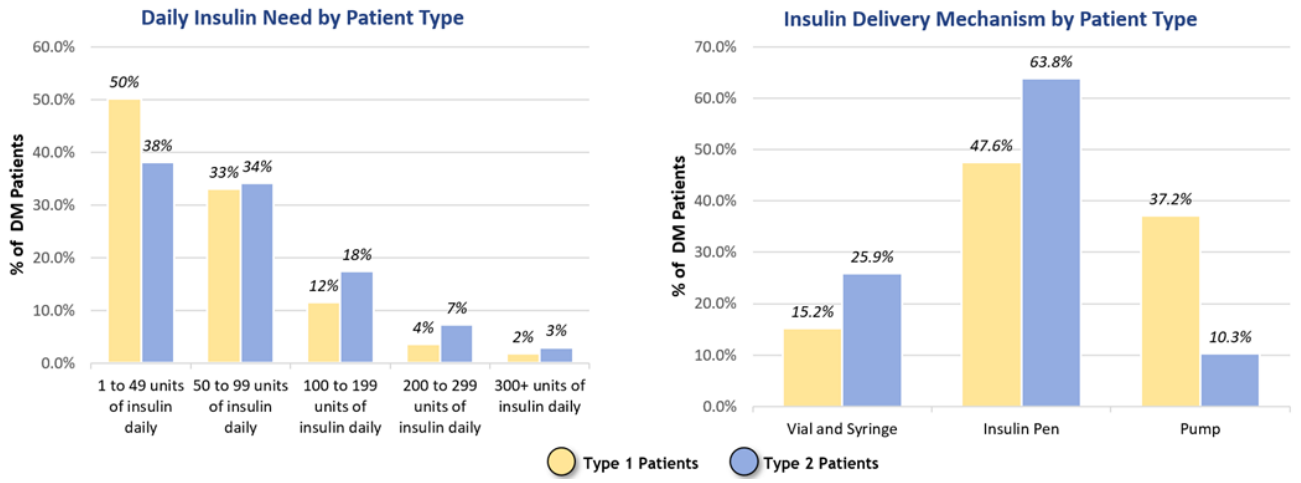
## Type II pump users have differing needs to Type I

**Type II pump user uptake set to exceed Type I, despite GLP-1**

There are some 100k Type II diabetes patients who are already pump users in the US and 175k outside the US, largely due to the difficulties in maintaining their

glucose control. As mentioned, the debate about the GLP-1 class and their role in materially altering the Type II treatment journey, especially in delaying the need to introduce insulin, has seen many observers question the likely growth rates for Type II pump adoption. However, even under somewhat pessimistic scenarios, we expect the growth rates for Type II users to exceed the Type I rates.

**Exhibit 6: Insulin market overview**




Source: BioStrategies May 2022

**Type II need much larger volumes of insulin than Type I**

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 quantities, 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 c 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, mainly via pens.

**Limited reservoir size means wear times are compromised for Type II patients**

The reservoir size of most integrated pump systems is between 1.8ml and 3.0ml (equivalent to 180-300 units) of fast-acting 100IU insulin. With half of Type I patients needing 50IU or less, and a further third needing between 50IU and 99IU, these patients have a pump wear time ranging from six days to only two to three days, with four days on average. Whilst this falls below the desired one-week wear time, mentioned earlier, for most Type I patients it does not override the significant benefits that accrue with pump use. In contrast, a meaningful proportion of Type II diabetics require 100IU or more daily. This means a wear time of two, possibly, three days, is the maximum currently achievable. For these patients the benefits of a pump become marginal compared to the inconvenience of replenishing the reservoir.

**High dose insulin users should not be overlooked**

Ignoring the evolving need for the new pump applications for a moment, high concentration insulins are expected to become increasingly in demand due to the rising number of Type II and refractory Type I diabetics that require higher daily dosing. As Exhibit 6 above shows, the majority of both Type I and, in particular, Type II diabetics use insulin pens and clinical evidence shows they are stable and reasonably well controlled. The currently available high concentration insulins are not prandial insulins, for example Humulin-R 500 is an intermediate acting insulin (an absorption profile that lies between a mealtime prandial insulin, such as

NovoRapid and Fiasp, and the basal insulins, such as Lantus and Levemir) and not suited for most "basal-bolus" regimens.

**Need for an ultra-concentrated and ultra-rapid insulin is clear**

Consequently, high dose requiring patients need to use multiple injections of lower strength insulin, with much higher injection volumes. This brings challenges such as injection site rotation, discomfort, and quality of life. These patient groups have historically been overlooked but their numbers are growing, and they clearly need a high concentration insulin that also has a postprandial rapid absorption profile suitable for standard "basal-bolus" injection regimens.

## Clinicians and device industry look to future needs

**A suitable insulin is needed to enable the desired for smaller pumps with longer wear times**

As mentioned earlier, as AID systems approach mainstream commercial reality, the remaining obstacles to be addressed are moving from the physical and software aspects to the characteristics of the insulins 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 closed-loop systems. Endocrinologists and clinicians in both Europe and the US acknowledge that the pharmacokinetics (PK) and pharmacodynamics (PD) of the current rapid-acting insulins are suboptimal. Newer ultra-rapid acting insulins, with faster onset and offset of action, have the potential to address this issue. However, small studies with Fiasp (faster aspart) and Lyumjev (ultra-rapid lispro) have not shown the hoped-for conclusive results. More importantly, there are no commercially available ultra-rapid insulins that could make the industry drive towards more compact, discreet pumps and the desire for longer wear times a reality. It is against this background that AT278 appears ideally positioned.

## AT278 is well placed to address these emerging needs

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

Arecor's key in-house clinical stage programme is the ultra-concentrated and ultra-rapid insulin AT278, a novel formulation of insulin aspart, the active ingredient in Novo Nordisk's NovoLog (US)/NovoRapid (ex-US). As outlined, AT278 is well positioned for the demographic and technology shifts underway within diabetes, especially in addressing the needs of high-dose Type II diabetics and providing the ideal profile for "next generation" AID pump systems.

**Previous Phase I trial in T1D demonstrated superiority to the benchmark insulin**

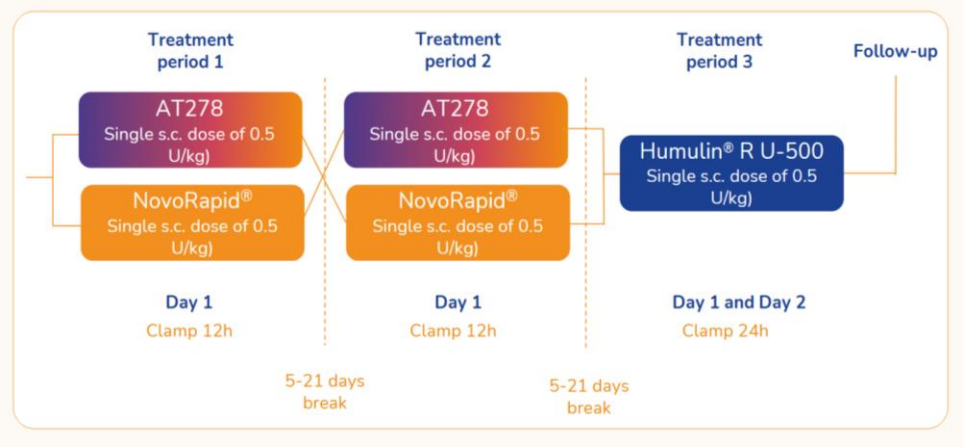
Phase I data from a 38 patient trial in otherwise healthy Type I diabetics show a very promising and highly differentiated profile (September 2021 Lighthouse). This trial evaluated adults with Type I diabetes in an euglycaemic clamp setting and met all primary and secondary endpoints, demonstrating a superior pharmacokinetic (PK) and pharmacodynamic (PD) profile to a comparable dose of lower concentration of NovoRapid (the gold standard rapid-acting insulin).

**Superiority in Type II patients supports AT278's attractive clinical positioning**

The latest topline data relate to a second Phase I trial evaluating 42 patients with Type II diabetes, a population whose overweight/obese nature can result in marked variabilities in outcomes. The study design (Exhibit 7) followed a standard cross-over format but had the added comparator of a high concentration insulin, Humulin-R 500. The trial met the primary endpoint of non-inferiority to NovoRapid in terms of glucose lowering, and also met all secondary endpoints, which importantly included demonstrating superiority to both NovoRapid and to Humulin in terms of faster insulin absorption (PK/PD profile). Detailed data are expected to be presented at a future diabetes conference. This confirms that

AT278 has the potential to be a disruptive insulin as an ultra-concentrated U-500 (500 units/ml) and ultra-fast acting insulin formulation, addressing the needs described earlier for both existing high dose insulin patients using pen injectors and the emerging wants of AID system manufacturers.

### Exhibit 7: Phase I study in 42 Type II overweight/obese Type II diabetics




Source: Arecor

**Continued AT278 is strongly supported by the data, with management to refine optimal next steps**

Following the positive Phase I data, management will now need to assess the optimal future development plan, which will be subject to funding, and could include conducting future studies alone or with a partner. Given the importance of an insulin like AT278 to enable next generation devices, strong relationships with device manufacturers will be key, in our view, with Arecor already having a separate collaboration in place with Medtronic.

## Valuation

**We value Arecor at £179m, equivalent to 584p per share**

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. Our valuation has been updated to reflect revised launch dates for the diabetes franchise, with this change offset by a more rapid ramp to peak sales for AT220 given it is the first commercial biosimilar of the originator product, plus unwinding of the AT220 risk-adjustment, together with rolling forwards in time. Our updated valuation is essentially unchanged at £179m, equivalent to 584p per share. An overview of our valuation, together with key assumptions, is provided in Exhibit 8.

**Exhibit 8: Arecor rNPV valuation**

| Programme | NPV (£m) | NPV ($m) | Success probability | Royalty | rNPV (£m) | rNPV ($m) | rNPV/ share (p) | Notes |
|---|---|---|---|---|---|---|---|---|
| **Diabetes franchise** (AT278 and AT247) | 153.3 | 184.0 | 60% | High single to double-digit | 92.0 | 110.4 | 300.4 | Peak sales: c $875m; Launch year: 2028 |
| **Research** (Specialty Hospital) | 64.7 | 77.7 | Various | High single to double-digit | 21.3 | 25.6 | 69.6 | Various with peak sales of $20-80m; Launch year: 2026+ |
| **AT307** (Hikma) (Specialty Hospital) | 27.9 | 33.5 | 80% | High single to double-digit | 22.3 | 26.8 | 73.0 | Peak sales: $65m; Launch year: 2026 |
| **AT220** (undisclosed biosimilar - partnered) | 14.8 | 17.8 | 100% | Low single digit | 14.8 | 17.8 | 48.4 | Peak sales: $500m; Launch year: 2023 |
| **AT292**/INBRX-101 (AATD - Inhibrx) | 21.3 | 25.5 | 50% | Low single digit | 10.6 | 12.8 | 34.7 | Peak sales: $515m; Launch year: 2026 |
| **Tetris Pharma/Ogluo** | 13.7 | 16.4 | 100% | N/A | 13.7 | 16.4 | 44.6 | Peak sales: $10m; Launch year: 2021 |
| Operating costs | (2.6) | (3.1) | | | (2.6) | (3.1) | (8.5) | |
| Net cash | 6.8 | 8.1 | | | 6.8 | 8.1 | 22.0 | |
| **Total** | **299.9** | **359.9** | | | **178.9** | **214.7** | **584.2** | |

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

**Upside on Specialty Hospital rNPV as deals are executed…**

The Specialty Hospital rNPV consists of a blend of assets based on the framework outlined in our November 2023 Outlook, with various launch timelines and probabilities. This also now includes the undisclosed ready-to-dilute formulation of a high-value oncology product, which was under co-development with an unnamed global player (previously broken out as standalone asset) as the option to an exclusive worldwide development and commercialisation licence has not been exercised. Hence the product is now retained within Arecor's in-house portfolio. We assume a steady flow of new assets into the portfolio, with upside as partnerships are executed.

**…whilst diabetes remains the main value driver**

The diabetes franchise (consisting largely of AT278 and AT247) remains the main value driver for Arecor and there could be material upside as development progresses and data become available. The partnered and commercial assets together could represent a meaningful source of future income with potential upside on AT220 as in-market sales build and the potential peak sales opportunity becomes better understood. We do not attribute a value to the technology formulation development collaborations, nor do we provide an indicative valuation of the Arestat technology platform.

## Financials

**Revenues continue to diversify**

Arecor's revenues in FY23 grew to £4.6m (FY22: £2.4m), and continue to diversify, with these now including first royalties following launch of AT220. Revenues now stem from four main sources:

- **Formulation development £0.9m (FY22: £1.4m):** this is relatively steady income from various partnerships.
- **Licensing agreements £0.7m (FY22: £nil):** this includes non-recurring upfront payments and variable milestones that are contingent on development progress and commercialisation. In FY23 these included: (1) £0.1m on the transfer of AT307 to Hikma; (2) an undisclosed milestone for a novel enhanced formulation of INBRX-101; and (3) an undisclosed milestone on the first commercial sales of AT220.
- **Royalties £26k (FY22: £nil):** These are the first recurring royalties on AT220 following EU launch in November. AT220 is believed to be Fresenius Kabi's Tyenne (biosimilar tocilizumab), with EU launch timing matching disclosures from Fresenius. US approval of Tyenne (both IV and subcutaneous) was received on 5 March 2024, and it was launched on 15 April. According to Fresenius' Q124 results presentation in May, Tyenne is the first marketed tocilizumab biosimilar, with originator Roche's Actemra generating CHF2.6bn of sales in FY23. Tyenne has now been launched in 12 European countries and the US, and by February had reached 15% market share in Germany and 12% market share in Spain. Royalties on AT220 should increase in FY24e and beyond, in our view, as in-market sales grow, particularly following US launch.
- **Product sales £2.9m (FY22: £1.0m):** these are driven by Tetris Pharma and largely consist of Ogluo sales in the UK and Europe.

**Revenues are set to grow driven by Ogluo sales and recurring AT220 royalties**

We expect revenues to grow in the coming years driven by product sales, mainly Ogluo as commercial roll-out continues in Europe and awareness and access increases, and AT220 royalties (described above). Our forecasts also include modest milestone income (albeit we do not include any income from a potential deal on AT247/AT278) and formulation development revenues, although these are not key to growth. We forecast £6.8m revenues in FY24e, which includes £4.4m from product sales, and £11.2m in FY25e, with £7.6m from product sales.

**SG&A set to increase to support Tetris Pharma sales growth, whilst R&D will depend on future development plans**

R&D spend decreased to £6.0m in FY23 (FY22: £8.6m) with the trial of AT278 nearing completion. Beyond this, and pending future development plans, we assume a base level of operating R&D spend, forecasting £4.5m in FY24e, which includes some residual spend on the ongoing AT278 trial, decreasing further to £3.9m in FY25e, albeit these are largely illustrative. SG&A spend increased to £8.9m in FY23 (FY22: £5.6m), which included a full year of Tetris Pharma spend. We forecast a fairly modest increase to £9.8m in FY24e, with a larger uptick to £12.1m in FY25e to support Tetris Pharma sales growth.

**Cash is sufficient to complete the ongoing AT278 trial and to start preparing development plans**

Arecor had cash and equivalents (including short-term investments) of £6.8m at end-December 2023. Our updated forecasts (Exhibit 9) indicate that Arecor has sufficient funds to complete the Phase I trial of AT278, and to provide optionality to prepare for potential future development plans as these are refined.

## Exhibit 9: Summary of financials

| Year-end: Dec 31 | £'000s | 2021 | 2022 | 2023 | 2024E | 2025E |
|---|---|---|---|---|---|---|
| **INCOME STATEMENT** | | | | | | |
| **Revenues** | | **1,158** | **2,403** | **4,573** | **6,793** | **11,207** |
| Cost of goods sold | | 0 | 0 | 0 | 0 | 0 |
| **Gross Profit** | | **1,158** | **2,403** | **4,573** | **6,793** | **11,207** |
| 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) |
| **Underlying operating profit** | | **(6,617)** | **(11,591)** | **(10,317)** | **(7,553)** | **(4,721)** |
| Share-based payments | | (484) | (503) | (638) | (657) | (670) |
| Exceptionals | | (462) | (171) | 0 | 0 | 0 |
| Other revenue/expenses | | 640 | 1,250 | 1,142 | 0 | 0 |
| **EBITDA** | | **(6,268)** | **(10,171)** | **(8,679)** | **(7,087)** | **(4,354)** |
| **Operating Profit** | | **(6,439)** | **(10,512)** | **(9,175)** | **(7,553)** | **(4,721)** |
| Financing costs/income | | (21) | 88 | 274 | 34 | 0 |
| **Profit Before Taxes** | | **(6,945)** | **(10,424)** | **(8,901)** | **(7,520)** | **(4,720)** |
| **Adj. PBT** | | **(7,122)** | **(12,006)** | **(10,681)** | **(8,177)** | **(5,391)** |
| Current tax income | | 776 | 1,164 | 347 | 409 | 309 |
| **Net Income** | | **(6,169)** | **(9,260)** | **(8,554)** | **(7,111)** | **(4,411)** |
| | | | | | | |
| **EPS (p)** | | **(0.3)** | **(0.3)** | **(0.3)** | **(0.2)** | **(0.1)** |
| **Adj. EPS** | | **(0.3)** | **(0.4)** | **(0.3)** | **(0.3)** | **(0.2)** |
| **DPS (p)** | | **0.0** | **0.0** | **0.0** | **0.0** | **0.0** |
| Average no. of shares (m) | | 23.0 | 28.9 | 30.6 | 30.8 | 31.2 |
| | | | | | | |
| **BALANCE SHEET** | | | | | | |
| **Current assets** | | **20,515** | **17,477** | **11,170** | **5,016** | **1,468** |
| Cash and cash equivalents | | 18,316 | 4,765 | 5,093 | 93 | (3,720) |
| Short-term investments | | 0 | 8,041 | 1,659 | 0 | 0 |
| Accounts receivable | | 1,423 | 2,215 | 3,189 | 2,870 | 2,870 |
| Inventories | | 0 | 1,131 | 771 | 1,580 | 1,870 |
| Other current assets | | 776 | 1,325 | 458 | 473 | 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** | **3,073** | **(668)** |
| | | | | | | |
| **CASH FLOW STATEMENTS** | | | | | | |
| **Operating cash flow** | | **(5,450)** | **(10,780)** | **(5,841)** | **(6,493)** | **(3,639)** |
| Profit before tax | | (6,945) | (10,424) | (8,901) | (7,520) | (4,720) |
| Non-cash adjustments | | 1,156 | 569 | 884 | 1,089 | 1,037 |
| Change in working capital | | (419) | (1,659) | 891 | (490) | (290) |
| Interest paid | | 0 | 0 | 0 | 34 | 0 |
| 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)** | **0** | **0** |
| Proceeds from equity | | 18,565 | 5,648 | 0 | 0 | 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** | **(5,000)** | **(3,813)** |
| Cash at start of year | | 2,898 | 18,316 | 4,765 | 5,093 | 93 |
| **Cash at end of year** | | **18,316** | **4,765** | **5,093** | **93** | **(3,720)** |
| **Net cash at end of year** | | **18,316** | **12,806** | **6,752** | **93** | **(3,720)** |

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

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## Disclaimer



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