Trinity Delta

Avacta

Update

Building on Therapeutic and Diagnostic foundations

10 May 2023

Avacta's two proprietary platforms, Affimer proteins and pre|CISION, are central to its plans to create novel diagnostic and therapeutic products. Recent operational and strategic developments during 2022 lay the foundations for unlocking value from its Therapeutics and Diagnostics divisions. Further data from lead asset AVA6000 should confirm the clinical utility of pre|CISION, with a wider portfolio being readied to exploit the platform's tumour-specific activation. An M&A-led growth strategy, leveraging both internal capabilities and the Affimer platform, should create a self-sustaining Diagnostics business. News flow over the next 18-24 months provides multiple value-inflection points. Our valuation is £641m, equivalent to 228p/share.

Year-end: December 31	2021	2022	2023E	2024E
Revenues (£m)	2.9	9.7	21.2	22.1
Adj. PBT (£m)	(24.1)	(27.0)	(39.0)	(41.0)
Net Income (£m)	(26.3)	(39.2)	(42.1)	(44.2)
Adj.EPS (p)	(8.7)	(10.1)	(13.5)	(13.5)
Cash (£m)	26.2	41.8	16.9	(8.2)
EBITDA (£m)	(26.7)	(24.4)	(28.7)	(31.4)

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

- **Funded to key value-inflection points** End-March 2023 cash of c £39m provides ample balance sheet flexibility to progress the Therapeutics pipeline, notably establishing proof-of-concept for the pre|CISION platform through AVA6000 clinical data, and to explore potential Diagnostics M&A opportunities to supplement the £24m Launch Diagnostics acquisition. The latter was a key use of proceeds from the £64m (gross) October 2022 fund raise (via a £7m placing, a £2m open offer, and a £55m convertible bond). Successful clinical outcomes for Therapeutics, and scale up of Diagnostics, represent significant value-inflection points.

- **Seeking proof-of-concept in Therapeutics** Avacta's Therapeutics Science Day gave an overview of its platforms, early-stage pipeline, and wider context on innovations in targeted oncology. Lead asset, AVA6000, a targeted pre|CISION prodrug of doxorubicin, has started dosing cohort five in the Phase Ia trial. Emerging data indicates a clean safety profile and supports the mechanism of action; if the anticipated improved efficacy and reduced toxicity is shown in later-stage trials, this will validate the approach for multiple additional development programmes.

- **Seeding a self-sustaining Diagnostics business** The transformational acquisition of Launch Diagnostics provides a platform on which to build an integrated European Diagnostics business. Avacta plans to add products and capabilities through M&A and leveraging its own internal infrastructure (established over the pandemic) and Affimer platform to further differentiate these in vitro diagnostic (IVD) products.

- **Valuation of £641m, or 228p per share** Our sum of the parts valuation of Avacta includes an rNPV of lead clinical asset AVA6000 (£64m, 22.8p/share), aggregate rNPVs for the Affimer and pre|CISION platforms (£275.7m, 98.1p/share and £279.0m, 99.3p/share respectively), and a diagnostics DCF (£33.2m, 11.8p/share). Upside should be unlocked with AVA6000 progress and as the Affimer technology is incorporated into the emerging Diagnostics strategy.

Price	112.0p
Market Cap	£316.4m
Enterprise Value	£277.4m
Shares in issue	275.4m
12 month range	97.0p-187.9p
Free float	86.0%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	AVCT.L
Corporate client	Yes

Company description

Avacta owns two novel technology platforms: Affimer and pre|CISION. Affimer proteins are antibody mimetics being developed as diagnostic reagents and oncology therapeutics. pre|CISION improves potency and reduces toxicity of cancer drugs by only activating them inside the tumour. Successful clinical trials would be transformative for Avacta.

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Avacta: a wealth of inflection points in sight

Over the course of 2022 Avacta made financial, operational, and strategic progress in exploiting its proprietary technology platforms across both Therapeutic and Diagnostic applications. The pre|CISION platform underpins the near- and medium-term prospects of Avacta's Therapeutics business, with emerging pharmacokinetic/pharmacodynamic data and tumour biopsy results from the Phase I study of lead asset AVA6000 effectively validating the pre|CISION platform's tumour targeting potential and providing the blueprint for an extensive pipeline of related products. The second pre|CISION asset, AVA3996, could enter the clinic within 12 months. Avacta's Diagnostics M&A-led growth strategy, seeded with the Launch Diagnostics acquisition, and complemented by internal capabilities and the proprietary Affimer platform, should create a self-sustaining Diagnostics business. Updating our model following FY22 results lifts our Avacta valuation to £641m, equivalent to 228p per share, vs £587m or 221p per share previously.

Two powerful and versatile platforms create a broad and diverse development pipeline

Over the past two years Avacta has advanced the demonstration of the potential of its two proprietary technology platforms, pre|CISION and Affimer proteins, in creating novel diagnostic and therapeutic products. These platforms can also be combined to produce highly flexible novel synergistic combinations, potentially addressing some of the limitations with currently available targeted therapies.

AVA6000, the lead pre|CISION programme, is progressing through early clinical trials

The pre|CISION platform allows for selective tumour-specific activation of chemotherapy drugs, offering potentially enhanced efficacy and reduced systemic toxicities. The first pre|CISION asset AVA6000, a FAPα activated doxorubicin chemotherapy, is currently enrolling the fifth dose cohort in its Phase Ia study. Early data show a clean safety profile and support its mechanism of action; planning is underway for later-stage trials to focus on soft tissue sarcomas (STS).

Affimers have the specificity of an antibody without the limitations

Affimer proteins are next-generation antibody mimetic protein scaffolds that offer enhanced attributes to equivalent antibodies across therapeutic and diagnostic applications, with characteristics such as better stability, greater versatility, and ease of production. Affimer protein use in clinical applications is currently being progressed mainly via partnerships and collaborations, although their optimisation in diagnostic applications has been demonstrated through the rapid creation of the AffiDX SARS-CoV-2 point-of-care COVID LFT and will be leveraged through Avacta's 'buy and build' diagnostics strategy.

Therapeutics provides the driver of longer-term value…

In our view, Avacta's Therapeutic opportunities are the real driver of longer-term value. However, due to the early stage of these programmes and the long development timescales as required by regulators (which we explore later in this note) investors will have to display patience. Nevertheless, there will be several value inflection points during the development process, not least once proof of concept is demonstrated with Phase II data; from partnering potential; and pipeline expansion.

…but Diagnostics opportunities should not be over-looked

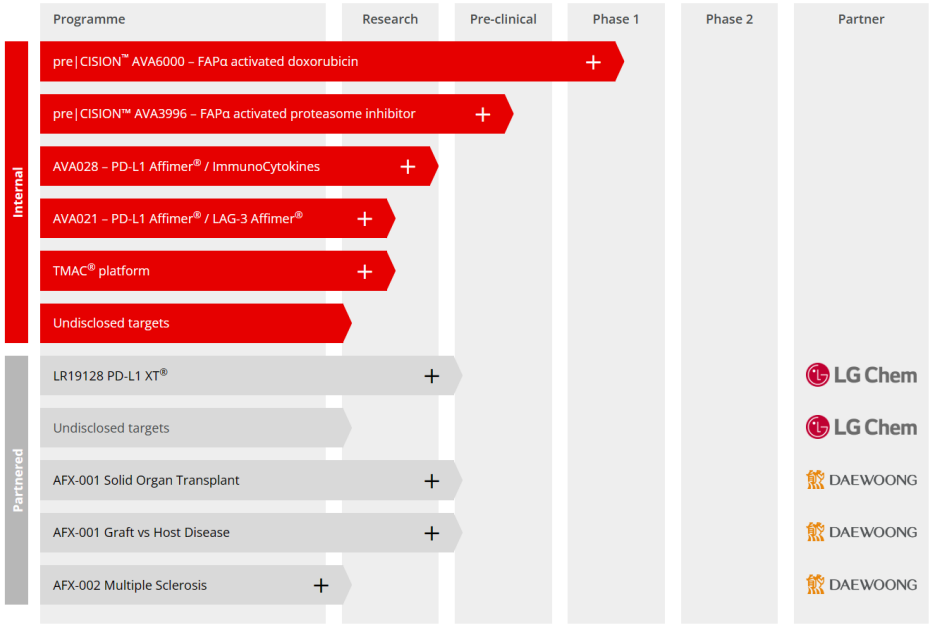
Avacta's Diagnostics division should provide more near-term news flow. Further deals are expected following the execution of the first acquisition, Launch Diagnostics in October 2022. The highly fragmented European diagnostics sector provides manifold opportunities for Avacta to add products and capabilities and create a self-sustaining fully integrated Diagnostics business.

Therapeutics Science Day: a major post-period event

Esteemed KOL panel provided an overview of opportunities, developments, and prospects

Avacta hosted a Therapeutics Science Day in February 2023, where speakers associated with the company (CEO, Alastair Smith; CSO, Dr Fiona McLaughlin; and Dr Andrew Saunders, Medical Advisor) joined international oncology experts (Dr Krishna Komanduri, Professor and Chief of the Division of Hematology and Oncology, University of California San Francisco, and a member of Avacta's Scientific Advisory Board; and Dr William Tap, Chief of the Sarcoma Medical Oncology Service, Memorial Sloan Kettering Cancer Center, New York, and a leading global expert in soft tissue sarcoma) to provide an overview of Avacta's platform technologies and the current therapeutics pipeline (Exhibit 1), as well as considering recent innovations in targeted oncology, the challenges that have been overcome and those that remain, and speculating on how the sector may develop over the next decade.

Exhibit 1: Avacta Therapeutics pipeline



Source: Avacta

Clear clinical and commercial potential for both platforms

The overarching theme of the day was on how Avacta's pre|CISION and Affimer platforms could be applied as enabling technologies to develop differentiated and innovative cancer therapeutics. In the case of pre|CISION, these include targeted therapies including for difficult to drug targets, with the current primary indications for the pre|CISION platform being cytotoxic regimens where, despite proven efficacy, their utility as monotherapy and in combination is limited by systemic exposure causing debilitating side-effects. Understandably much focus was centred on lead clinical programme AVA6000, a pre|CISION enabled FAPα targeted doxorubicin, with the presentation of interim data (see later) confirming its mechanism of action, as well as background on the current and future treatment strategies for likely lead indication soft tissue sarcoma (STS) from Dr William Tapp. We highlight that AVA6000 has an important role, effectively acting as proof of concept for the use of the pre|CISION platform in therapeutics.

Validation of Affimer platform expected within 12-18 months

As novel non-antibody scaffolds, applicability of the Affimer platform is broad both in terms of the disease areas that could be addressed and the Affimer

therapeutics that could be developed, including multi-specific immunotherapies and next-generation cell therapies. Avacta's focus is currently on developing multi-specifics, novel tumour microenvironment-activated drug conjugates (TMACs), and combinations with pre|CISION chemotherapies. However, given this breadth of potential applications, several fully funded collaborations have been signed that exploit the Affimer platform's versatility and represent additional or incremental indications, provide expertise relevant to in-house programmes and, crucially, are useful external validation of the platform's potential. These include an Affimer-based drug development collaboration with LG Chem Life Sciences and the AffyXell Therapeutics joint venture with Daewoong Pharmaceuticals.

Affimer versatility means in-house development alone is not enough

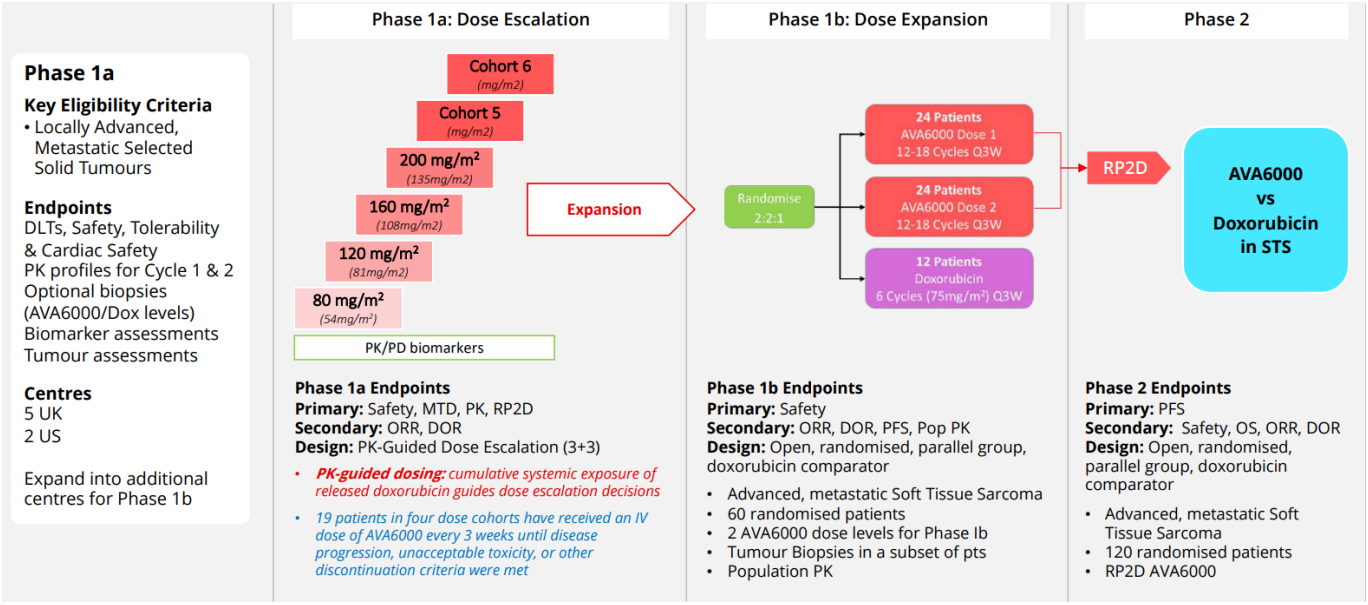
While less emphasis was placed on the Affimer pipeline, reflecting its preclinical status, we believe that as data emerge, the Affimer platform could help address some of the opportunities for cell therapies in oncology as laid out by Dr Krishna Komanduri. These include potential applicability to both solid tumours and haematological cancers, and decreasing the proportion of patients who relapse through the creation of more personalised immunotherapies which can overcome the challenges of a hostile tumour micro-environment. Equally importantly, Affimer-based drugs may have a role to play in reducing the cost of such therapies so that they can be accessed by more patients and be more widely reimbursed.

Therapeutics: an update on the pre|CISION pipeline

AVA6000 is in the spotlight

The principal progress in the Therapeutics division in FY22 relates to Avacta's lead asset AVA6000. AVA6000 employs the pre|CISION substrate to create a tumour-targeted form of doxorubicin. It is a FAPα activated prodrug of doxorubicin that is only activated at the tumour site, where FAPα is typically highly concentrated unlike in healthy tissues, thus minimising systemic toxicities (notably cardiotoxicity and myelosuppression). Life-threatening cardiotoxicity is a major limitation with doxorubicin; as it is correlated with cumulative doxorubicin dose, this effectively limits treatment to only six cycles (typically 60-75mg/m² every three weeks until 450mg/m² is reached).

Exhibit 2: Phase I and II study design for AVA6000 in patients with advanced metastatic solid tumours



Source: Avacta

Phase Ia dose escalation study is continuing

AVA6000 is currently under evaluation in a Phase Ia dose escalation trial (ALS-6000-101) in metastatic solid tumours, which recently dosed the first patient in the fifth dose cohort (250mg/m^2) following favourable safety and tolerability data generated to date from prior cohorts. We note that escalation to a fifth cohort is outside the original clinical trial protocol, thus required protocol amendment and MHRA approval which now allows for up to seven cohorts of three to six patients each. Dosing is continuing at higher levels to identify the maximum tolerated dose (MTD) which will inform the dose level(s) for the Phase Ib dose escalation portion of the trial and subsequent studies (Exhibit 2).

Interim data are very encouraging

The interim data from 19 patients dosed across four cohorts, presented at the Therapeutics Science Day, indicate that AVA6000 has a predictable safety profile across the 80-200mg/m^2 dose range, with the most frequent adverse events being Grade 1-2 nausea, fatigue, and decreased appetite. Additionally, the PK exposure data suggest that dependant on dose, AVA6000 could potentially be used for 12-18 treatment cycles, allowing increased dosing duration.

Safety and toxicity profiles appear promising

PK data also support AVA6000's mechanism of action: the preferential release of the active chemotherapeutic in tumour tissue using FAP specificity to activate doxorubicin. Systemic doxorubicin levels were shown to be considerably lower vs a standard 75mg/m^2 doxorubicin dose, and this was further supported by tumour biopsies from six patients across three cohorts showing higher concentrations of doxorubicin vs systemic plasma levels at the same 24-hour timepoint. Doxorubicin exposure (AUC, area under the curve) and maximal concentrations (Cmax) were substantially reduced across doses.

US trial centres now open for patient recruitment

Patients in the first four cohorts of the Phase Ia study have been enrolled at UK centres, although Avacta has an open US IND and recently confirmed the opening of the first two centres: Memorial Sloan Kettering Cancer Center (MSK) in New York and Fred Hutch Cancer Center in Seattle. This should accelerate patient recruitment into the remaining Phase Ia cohorts and, once the recommended dose is identified, into the dose expansion portion of the trial which will confirm safety and tolerability and explore preliminary anti-tumour activity. In late April, the company confirmed the dosing of the first US patient in ALS-6000-101.

Soft tissue sarcoma selected as the primary indication to be studied

Metastatic soft tissue sarcoma (STS) has been selected as the Phase II indication as advanced STS tumours are known to be highly FAPα positive and doxorubicin is the current first-line therapy in this patient population. However, doxorubicin efficacy (progression-free survival, PFS, of four to six months; overall survival, OS, of 12 to 15 months; and a typical objective response rate, ORR, of 10-15%) leaves considerable room for improvement.

A clear clinical need, with doxorubicin a central therapy

As outlined at the Therapeutics Science Day by Dr William Tap, STS are a heterogeneous group of around 100 different malignancies defined by varied genetic mutations. Doxorubicin is the gold standard first-line treatment option, despite its limited efficacy and less than ideal safety profile, although subsequent lines of therapy are more varied. After a period of clinical failures in STS, it was the smaller, more targeted clinical studies carried out in specific genetically defined patient sub-types that lead to the development and approval of around ten new therapies over the past decade.

Phase Ib data could provide first efficacy insights, stimulating wider industry interest

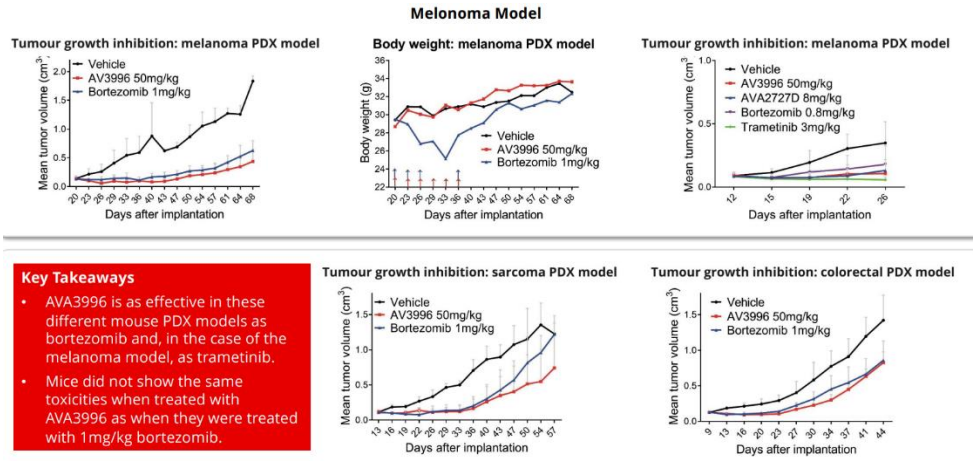
Further positive data for AVA6000 and the establishment of clinical proof of concept should boost industry interest in pre|CISION technology as well as

expanding its application to additional established and effective chemotherapies where there is potential to similarly reduce toxicities and improve the therapeutic window. Partnerships could come in various forms: for example, they could result in the out-licensing of AVA6000 (or other pipeline assets) for an upfront payment, royalties on net sales, plus potential clinical development, regulatory and commercialisation milestones, or alternatively could expand the use of pre|CISION technology to applications outside of those that Avacta is prioritising in-house.

AVA3996 is in preclinical development and is completing IND studies

Avacta's second single-agent pre|CISION-based chemotherapeutic, AVA3996, is a FAP-activated proteasome inhibitor that is a prodrug of an analogue of Takeda's multiple myeloma drug Velcade (bortezomib). AVA3996 offers the prospect of reducing the dose limiting toxicities (peripheral neuropathy, thrombocytopenia) which constrain Velcade use to multiple myeloma and mantle cell lymphoma. The Therapeutics Science Day also covered positive preclinical data showing flatlining tumour growth in patient-derived xenograft melanoma mouse models (Exhibit 3) with additional data presented in a poster at the American Academy of Cancer Research (AACR) 2023 meeting. AVA3996 is currently in IND-enabling studies, with Phase I clinical trials expected to start in 2024.

Exhibit 3: AVA3996 in vivo efficacy in multiple tumour models



Source: Avacta

Diagnostics: building a self-sustaining business

Launch acquisition prepares the ground for a fully integrated diagnostics business

The October 2022 acquisition of Launch Therapeutics was the first major transaction in Avacta's M&A-led growth strategy for its Diagnostics division. The aim is to create a self-sustaining fully integrated Diagnostics business through acquiring complementary capabilities or products, geographical expansion, and leveraging both Avacta's internal expertise (particularly the product development, regulatory, and compliance infrastructure established during the COVID-19 pandemic) and its proprietary Affimer platform (to optimise product performance and economics). Funding is in place following the October 2022 £64m (gross) fundraise which, post the £24m Launch Diagnostics acquisition cost, left an end-March 2022 cash position of c £39m. This provides ample balance sheet flexibility to explore various potential Diagnostics opportunities.

Bolt-on acquisitions are now expected

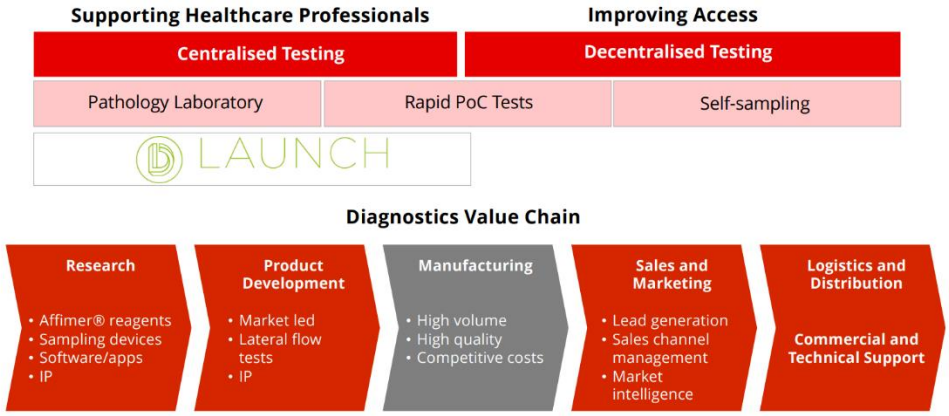
A pipeline of potential acquisition targets in the European diagnostics sector has been identified and management is planning for subsequent bolt-on acquisitions that help scale up and accelerate the build out of a broad IVD (*in vitro* diagnostics)

product portfolio for both consumer and professional use. The opportunities to consolidate within a highly fragmented European sector suggests the next steps will be to augment the product offering further, procure routes into new markets, and strengthen the UK and European infrastructures.

Diagnostic opportunities have been covered in prior notes

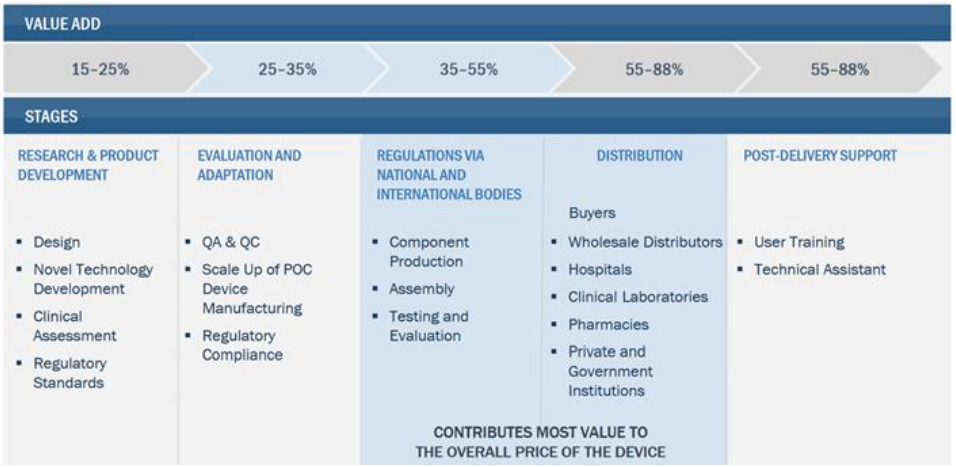
Our Diagnostics focused December 2022 Update provides background on the structural changes in the diagnostics testing industry which have been accelerated by the COVID-19 pandemic (through emphasising the importance of point of care, POC, testing and, specifically, LFTs or lateral flow tests), and on how Launch Diagnostics fits into, and enables Avacta's broader diagnostics strategy. Avacta has previously outlined its ambitions to expand into decentralised testing in several key areas: respiratory infections, cardiovascular disease, cancer, and general health and well-being. With in-house new product development expertise and regulatory processes already in place (validated by ISO13485 accreditation), plus the Launch Diagnostics distribution capabilities, the creation of a diagnostics business that provides access to the entire value chain (Exhibits 4 and 5) could be achievable via a combination of in-house development and/or additional M&A.

Exhibit 4: Diagnostics value chain - markets, applications, and customers



Source: Avacta

Exhibit 5: Diagnostics value chain – typical value gained across the process



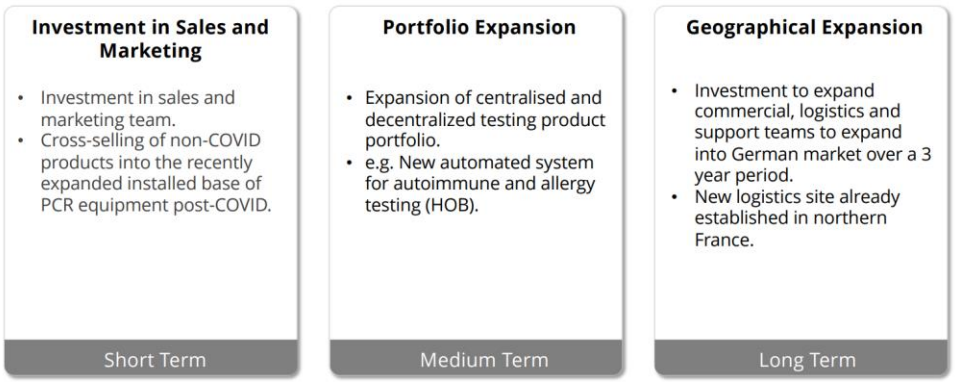
Source: MarketsandMarkets – Point of Care & Rapid Diagnostics Market January 2021

Launch is financially and strategically important

The Launch Diagnostics acquisition should be transformational for Avacta. As the UK's largest independent IVD distributor it provides Avacta with established sales channels into the centralised testing market, in particular hospital pathology

laboratories in the UK and France. From a financial perspective, the c £4m in revenue booked by Avacta from October (of the total FY22 Launch Diagnostics non-COVID-19 revenues of £16.5m) significantly boosted its Diagnostics' division revenues (FY22: £4.17m vs FY21: £0.78m). However, it is also strategically important, as Avacta has identified several growth opportunities (Exhibit 6) which should boost sales and margins. These plans include expanding the product range, investing in the sales teams, cross-selling to new customers gained during the pandemic, and, most impactfully, expanding geographically, particularly into Germany, Europe's largest diagnostics market.

Exhibit 6: Launch Diagnostics growth opportunities



Source: Avacta

"Buy and build" to create scale, breadth and relevance

Avacta's 'buy and build' strategy includes acquisition and innovation as central tenets in its quest to establish a fully integrated IVD business. The primary focus is on acquiring profitable businesses that develop and/or distribute immunodiagnostic and molecular diagnostic tests primarily for the professional use market, to add additional products to its portfolio and/or expand the routes to market. To help grow market share and provide a competitive edge, Avacta's Affimer platform will be leveraged to further differentiate this product offering. This strategy in the context of a fragmented European market with broad potential opportunities, both across the value chain and by end use, could deliver a uniquely positioned Diagnostics business.

Drug development: what it is and how to value it

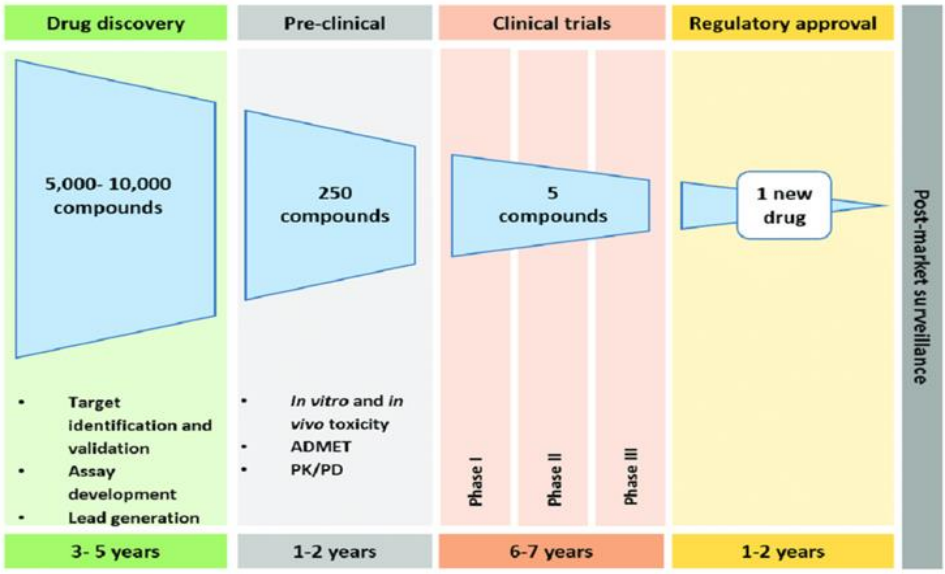
Valuing drug development is very different to valuing a large pharma company…

Investing in a drug development company, whether a biotech or emerging pharmaceutical company, requires a different approach to when considering the value inherent in a "large pharma" company. By definition, a large pharma company has recurring revenues, driven by established therapeutic franchises and supported by skilled sales and marketing teams. The resulting cashflows, whether assessed as EBITDA, net income, or simply operating cashflow, can be analysed and scored in many ways to produce rankings against related peers (geographic or therapeutic) and other industry sectors. Often the pharmaceutical sector's performance is driven by macro issues as much as specific micro factors. In this context, an assessment of a particular company's R&D pipeline does form an important element of a valuation, but it is one of many considerations.

…with the R&D pipeline being the major focus

In contrast, for a drug development company the R&D pipeline is the key factor; hence understanding the drug discovery, development, and approval process is critical. Importantly, as a small company's pipeline is usually narrower and more focused (meaning a clinical disappointment can materially impact the valuation), more effort is devoted in assessing the pipeline constituents, seeking nuanced scientific and clinical insights that can help determine likely outcomes. Interestingly, despite being more complex, biological compounds carry a lower risk in the earlier stages of clinical development than an equivalent small molecule drug candidate. The importance of such facts influences how a pipeline's rNPV (risk-adjusted net present value) is calculated, where even small variations in risk assessments in the model can result in large swings in the eventual outcomes.

Exhibit 7: The key stages in developing a new drug



Source: Adapted from Di Masi Tufts University, FDA, and PhRMA

Rates of programme attrition are still surprisingly high

Drug development is complex, costly, time-consuming, and highly regulated by individual country drug licensing authorities. The hurdles that need to be overcome to demonstrate efficacy and, particularly, safety mean the rate of attrition is high. Numerous studies have shown that for each drug approved some thousands of candidates must be assessed, with the process taking an average of 10-12 years (Exhibit 7). Estimates vary, depending on the analysis methods, but

the average development expenditure for each NCE (new chemical entity) drug approved is now comfortably over $1bn, although this also factors in the cost of development failures as well as the successes. It should also be noted that not all drugs that are approved become commercial successes. Hence striving to optimise every aspect of the processes is, understandably, a major focus for all involved.

Discovery is often viewed as a separate and discrete activity

The process starts with discovery. Novel targets are constantly being sought by researchers in large pharma companies or, increasingly, specialised academic centres. The continuing advances in understanding genomics, and the consequent downstream cascade, has provided a wealth of new target opportunities but traditional methods, such as classical pharmacology and even serendipity, still play a role. Once a suitable target is identified it has to be "druggable", not only must it modify the disease pathway as predicted but it has to be able to be made into a viable product. Numerous steps, involving many scientific disciplines, are then employed to screen and identify a series of compounds, with an optimised compound (plus back-ups) selected for preclinical assessments.

Preclinical requires a well-disciplined and precise approach

The preclinical stage is the essential link from discovery to initiating clinical trials in humans. Although each programme will differ, providing insights that are indication-specific, many common elements are required for regulatory purposes. The studies are broad, addressing aspects such as optimising the lead candidates, determining pharmacokinetic (PK) and pharmacodynamic (PD) profile, establishing the absorption, distribution, metabolism, and excretion (ADME) properties, and seeking relevant signals for expected efficacy and toxicities. This stage consists of a combination of cell-based and animal studies and all work must comply with Good Laboratory Practices (GLP) and regulatory requirements. The resulting data packages are examined to support an FDA Investigational New Drug (IND) application (or a UK Clinical Trial Authorisation, CTA) to initiate human studies. These data also form a key part of any eventual product approval, whether a New Drug Application (NDA) or a Biological Licence Application (BLA) request.

Clinical trials: their role and their significance

Three main clinical phases:

Clinical development consists of three stages: Phase I (increasingly viewed as Phase Ia and Ib), Phase II (also split into IIa and IIb), and the large Phase III trials. Post-approval studies are sometimes referred to as Phase IV. Phase I trials are usually not randomised or blinded in oncology (hence subject to inherent biases), but can be in non-oncology indications. However best practice (if appropriate) is for all subsequent studies to be randomised, comparator controlled, double-blind, multi-centre trials in relevant patients.

Phase Ia focus is on safety and toxicity

Phase I studies are the first studies to be performed in humans and are designed to confirm if the preclinical data can be replicated, with the focus on safety, ADME, side-effects, and tolerability. The patient numbers are small and, in most indications, Phase I is performed in healthy volunteers; however, oncology Phase I studies enrol patients due to ethics considerations where drug side-effect profiles (either of the investigational drug candidate and/or the standard-of-care in a combination trial) are deemed too toxic for healthy volunteers. Phase Ia usually consists of single ascending dose studies, with the 3+3 design being common. Three patients are tested sequentially, starting with the lowest dose (predicted from preclinical results) with each subsequent cohort receiving a higher dose until pre-calculated PK safety levels or intolerable side effects are reached. This is used

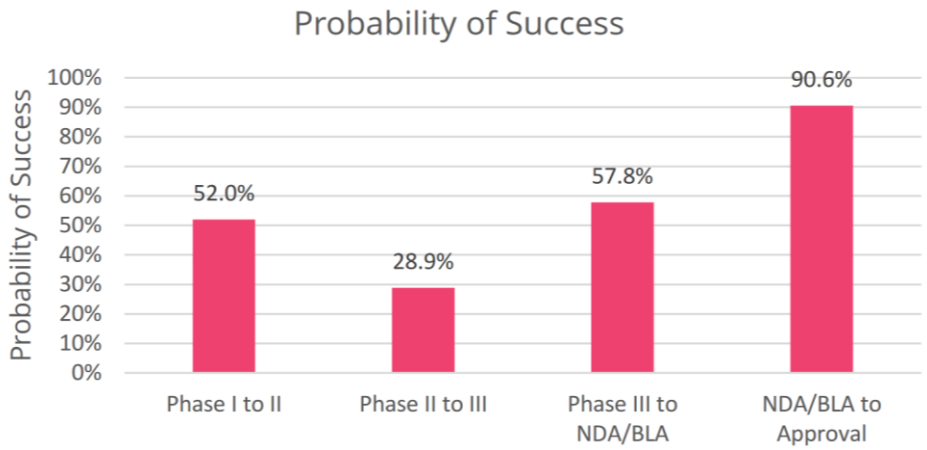
to establish the maximum tolerated dose (MTD) and helps determine the dose employed in later studies.

Phase Ib can often provide the first insights into likely efficacy

Phase Ib studies use multiple ascending doses, with patients being administered a pre-determined number of doses. Again, the focus is on safety and tolerability, while also starting to investigate in further detail the indication(s) of interest and potentially providing early efficacy signals. Drug safety, the medical risk to the patient, is usually determined by objective criteria (eg drug PK and metabolism) which may cause harm to the patient and this can be assessed by laboratory tests, vital signs, incidence of clinical adverse events, or by other safety tests specified in the clinical trial protocol. Tolerability, on the other hand, is the degree to which a drug's side-effects can be tolerated by the patient, and the likelihood that the patient can, or wants to, adhere to the dose schedule or intensity.

In oncology settings, Phase Ib data are useful in guiding the recommended dose for Phase II (RP2D), which is often lower than the MTD because the MTD is defined in a four-week window, whereas toxicities, especially of gene- and immune-targeted drugs, may emerge with longer term use. Additionally, Grade 2 side effects such as diarrhoea or mucositis, which may be tolerable for a short period of time, can become intolerable with ongoing dosing.

Exhibit 8: Overall clinical phase sequential transition success rates



Source: Biomedtracker and Pharmapremia 2020 Note: all diseases, all modalities

Phase II is where the efficacy profile should become clearer…

Phase II studies begin if Phase I data does not reveal unacceptable toxicity, and while the emphasis in Phase I is on safety, the focus of Phase II is on efficacy. The aim of Phase II is to obtain preliminary data on whether the drug works in patients with the disease targeted, hence it is often viewed as the "proof of concept" stage. This data will determine whether a programme either proceeds into registration trials or is discontinued. Unfortunately, many programmes fail at this stage (Exhibit 8). In Phase II efficacy is tested in a larger number of patients, sufficient to reassure that any effect is likely to be replicated in the later, larger, and more expensive, studies. For some indications, such as rare diseases or life-saving treatments, a well planned and executed Phase II programme can provide sufficient high-quality data to act as the pivotal registration study.

…as the trials are typically designed with efficacy endpoints

This clinical stage is commonly viewed as two categories, Phase IIa and Phase IIb, although there is no standard definition to differentiate between them and their applicability may depend on the compound under development. Phase IIa trial programmes usually involve 50 to 100 patients that are representative of the

target population(s). The primary and secondary endpoints reflect the desired activity and efficacy profiles, with confirmation (or otherwise) of the appropriateness of dosing and the degrees of toxicities experienced earlier. These are usually randomised controlled trials, with the resulting data viewed as more robust (and reproducible) than previous studies. In controlled trials, patients receiving the drug are compared with similar patients receiving a different treatment; usually a different drug considered to be 'standard of care' for that indication and patient characteristics. These results, if positive, help determine the positioning of the drug, with much greater visibility on dosing and applicability, and so are used to fine tune the target indications.

Phase IIb trials are often the most illuminating, hence providing value inflection points

Phase IIb consists of larger, 100 to 300 patients, and longer, up to two years, clinical trials. These are undertaken in the now well-defined patient groups with the aim of exploring the degrees of efficacy and establishing the side-effect profile. For most indications, these data confirm the drug's clinical and commercial attractiveness and provide the evidence to support progression into the expensive Phase III trial programmes. For smaller companies this is the major value inflection point for their lead programme, with the difference between a clear success and a marginal failure often determining the company's, and management's, future.

End of Phase II regulatory meetings define the design of Phase III

At the end of Phase II, the sponsor (company developing the drug) and regulatory agencies schedule a meeting to discuss and agree how the large-scale should be designed and conducted. The frequency of meetings between sponsor and regulatory agency vary but the two most common meeting points are the end of Phase II meeting and prior to the submission of the NDA.

Phase III are larger and more representative of clinical practice

If everything has worked as hoped and evidence of efficacy is shown in Phase II, Phase III studies begin and are designed to validate Phase IIb findings but in a much larger population of relevant patients. Phase III studies are viewed as the definitive assessment of the drug candidate: they gather more information about safety and effectiveness, studying different populations and different dosages and possibly using the drug in combination with other drugs. The size and duration of these studies depend largely on the indication (eg chronic vs acute) and its epidemiology (incidence and prevalence of the disease) and will usually compare the NCE (new chemical entity) with the appropriate standard of care as a control. The number of patients can be as little as 300 but complex trial programmes involving thousands of patients are not uncommon. Similarly, study duration can range from a single year to many years (with long term follow ups).

Painstaking planning is essential to create the regulatory submission packages

The planning for such programmes is complex, with specialised statistical analysis to ensure the trials are structured and of sufficient size (ie powered to provide increased confidence that result is not a false positive or negative) to answer the relevant clinical questions. Typically, the regulatory agencies require two large randomised, well controlled, double-blind, multi-centre trials for an initial approval; although, regulatory discussions with the sponsor define what clinical data and specific clinical trial programme is required to support the approval of a drug. Any label extensions require additional specific studies. Running such global, multi-country Phase III trials requires experienced teams and deep pockets; hence it is usual for smaller development companies to partner with larger players for this stage. Despite all the planning and prior work to understand how an NCE should perform, a troublingly high proportion of programmes still fail at the approval stage. This is usually due to a failure in producing the required data to

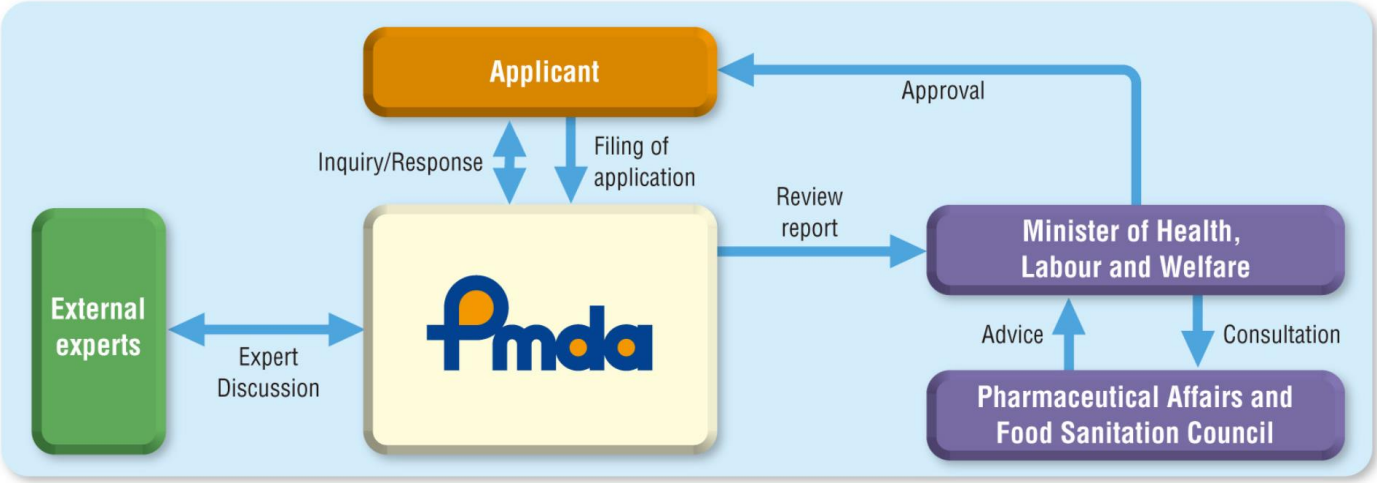
support a regulatory approval and can be various reasons ranging from incorrect patient population selection to the study design.

Regulatory approvals: a number of different pathways

FDA is viewed as the gold standard approval agency

After successfully navigating the tortuous clinical development stages, the drug candidate is ready for submission for regulatory review. The three main agencies are the FDA (Food & Drug Administration) in the US, EMA (European Medicines Agency) in Europe, and PDMA (Pharmaceutical and Medical Devices Agency) in Japan. Exhibit 9 shows a simplified view of the key steps involved using the PDMA as an example.

Exhibit 9: Simplified overview of a typical review process for a drug or medical device application



Source: Pharmaceutical and Medical Devices Agency (Japan)

All agencies offer a variety of approval pathways, reflecting differing clinical and patient needs as well as the drug's status (eg NCE or generic/biosimilar). However, all of the regulatory processes require a huge amount of documentation, chronicling the proposed drug's development pathway with much additional information, including CMC (Chemistry, Manufacturing, Controls) data.

Many approval pathways are available

The FDA has implemented an array of flexible routes to facilitate approval, and, in view of the US's commercial importance, it is worth examining these in more detail. The FDA standard route for a small molecule NCE is the NDA (New Drug Application) and for a biologic product it is a BLA (Biologicals Licence Application). These are reviewed by different divisions within the FDA but obviously share many commonalities.

NDA has three related pathways depending on compound status

The NDA was first introduced in 1938, over time evolving into the comprehensive review it has become. Once a file is submitted, the FDA has 60 days to determine whether it is sufficiently complete to review. The standard review should last 10 months, with the goal that 90% of submissions are processed in this timeframe. The usual NCE route is known as a 505(b)(1); however, drugs that have a similar active ingredient to an already approved drug can use a less onerous (and potentially quicker) route known as 505(b)(2), if agreed by the FDA. Bioequivalent drugs (true generic copies of patent expired NCEs) use much of the originator drug's data and follow an Abbreviated New Drug Application (ANDA) or 505(j).

Several accelerated pathways for novel compounds

Additional accelerated pathways, to address specific patient needs, have been introduced. In all of these, the FDA provides additional guidance and support to the applicant company. None of these programmes are mutually exclusive and any combination is permissible:

- **Priority Review** was first authorised in 1992 for drugs that have completed a suitable clinical trial programme and should result in a significant improvement in safety and efficacy compared to existing therapies. Here the review goal is reduced from 10 months to six months.
- **Fast Track** designation is aimed at drugs that show superior efficacy, avoid serious side effects, decrease clinically significant toxicity, and/or address an emerging or anticipated public health need when compared to existing treatments. A key benefit of Fast Track is more meetings with and support from the FDA to ensure the appropriate data required for approval is clarified quickly. Drugs in the Fast Track pathway are eligible for accelerated approval and priority review if relevant criteria are met.
- **Accelerated Approval** was introduced in 1992 and updated in 2012. Usually, it applies to drugs for life-threating illnesses for which there are inadequate or no treatment options. An example is an oncology drug that shows a meaningful therapeutic benefit over available therapies in clinical studies using a surrogate or intermediate endpoint. Often a conditional approval is given, with a requirement for confirmatory post-marketing trials. If the endpoints are not met, the label is altered or drug withdrawn. This route has been associated with materially faster approvals.
- **Breakthrough Therapy** designation is often granted where preliminary human experience suggests a substantial improvement over available treatment. A "rolling review" is encouraged (as is in Fast Track), with the sequential submission of discrete portions of the NDA as they complete. Both Fast Track and Breakthrough Therapy designations have to be requested formally from the FDA, with guidance provided beforehand as to likelihood of success.

Surrogate markers can be a useful measure that supports Accelerated Approval but also need later confirmation

We note that timely access to drugs that improve quality of life and/or survival is key to patients. Using cancer as an example, measurement of clinical endpoints such as improvement in overall survival does take time so patients may be willing to accept uncertainty about the magnitude of such benefits in exchange for early access to promising drugs, particularly where other treatment options are limited (ie for certain cancers, or for late-stage treatment-refractory patients). The FDA's Accelerated Approval pathway outlined above covers this scenario, and the FDA may grant an approval if the drug candidate can show improvements in surrogate measures in clinical trials which are reasonably likely to predict actual clinical benefit (ie improved survival or quality of life). Cancer-related surrogate measures include changes in tumour size or time to progression of cancer. Such surrogate measures may ultimately be shown to predict meaningful clinical benefit, but this is not always the case, hence the requirement for confirmatory studies.

Early, meaningful discussions with FDA are essential

Selection of the most appropriate pathway(s) has become increasingly complex, with specialist consultants usually required to navigate the optimal route to satisfy all the relevant regulatory agencies in the most effective manner. The key factor is to engage early, as soon as robust efficacy data becomes available, with the

appropriate departments at the main agencies. We reflect this in our modelling, where (with few exceptions) we do not assume any accelerated approval pathway is employed until we have sufficient data from suitable double-blind, controlled trials to assess the likely clinical benefit.

Peak sales and success rates: their key roles in valuation

Many individual considerations needed to build a good rNPV

The value of any DCF (discounted cash flow) calculation is intrinsically linked to the quality of the underlying assumptions. This is particularly the case when a rNPV (risk-adjusted net present value) methodology is employed to assess a drug company's R&D pipeline. There are many variables that need to be examined, and their relative importance alters over time, such that a rNPV model should be dynamic and responsive, being able to identify and capture the key determinants of value at that particular point. Creating a useful and representative rNPV model is time consuming, both in assessing what the most appropriate variables are and estimating their relative contributions.

For drug rNPVs sales potential and success probabilities are key

The two major determinants of a drug programme's value are expected peak revenues and the clinical success probabilities. For investment analysis, as opposed to drug industry resource prioritisation, elements such as discount rates and timelines are essentially the same across the sector, as is a programme's life cycle, with relatively small variations between companies. It is worth emphasising that rNPV models are calculated over a product's expected life span (there is no terminal value); for instance, at patent expiry a small molecule faces "cliff face" generic competition whereas a biological would see more gradual sales erosion as biosimilars enter the market.

Exhibit 10: Factors in estimating therapy market sizes and likely revenues

- **Estimate potential market size for each geography, compare existing product revenues with current patient population, examine the incidence (number of new potential patients each year) and prevalence (total number of potential patients at any one time);**
- **Estimate the addressable market size, comparing number of patients currently diagnosed and those currently treated (will this change?);**
- **Examine likely penetration, pricing, competitive landscape (current and in future), expected patient compliance, known treatment needs, clinical adoption rates, and reimbursement environment;**
- **Review at each clinical phase transition.**

Source: Trinity Delta

Start sales forecast with simple assumptions and elaborate as clinical profile becomes clearer

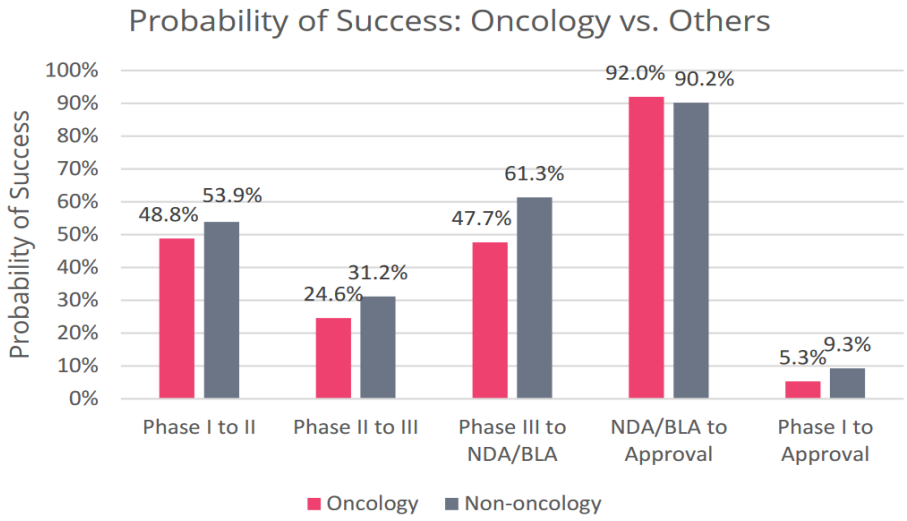
The forecasting of peak sales potential becomes more detailed as the clinical profile becomes clearer. This is usually started by examining the lead indication's existing market size, the patient numbers, currently available treatments and future competitive landscape, the pricing environment, expected adoption rates and ease of reimbursement. Once Phase II is reached there should be greater visibility on the clinical benefits and likely positioning. With this a fuller picture can be built that includes more detailed epidemiological data on the selected indication(s), including changes in treatment rates that could be achieved with a

competitive novel drug. The more detailed "top down" assumptions can be compared to a simple "bottom up" approach, acting as a reality check.

Success probabilities have become more accurate and meaningful

Determining the appropriate likelihood of approval for a development programme is key metric for a rNPV. Traditionally the likelihood of successfully progressing through each clinical stage through to approval was assessed by examining historic public domain data, which meant earlier phase failures were under-represented as companies did not always disclose these. Extensive and sustained work by academic centres, such as Tufts University's Center for the Study of Drug Development (CSDD), has brought more detailed and rigorous phase transition rates that differentiate between disease areas, therapeutic classes, mechanism of action, and novelty. In the past decade the quality of the data have improved, with Biomedtracker (used in BIO's periodic updates) a valuable source of near real-time success and attrition rates.

Exhibit 11: Oncology phase transition success rates and LOA 2011 to 2020



Source: Biomedtracker 2020 Notes: LOA is likelihood of approval

Oncology success rates are low despite sustained industry effort

Cancer is one of the largest areas for industry research, consistently accounting for around a third of all clinical trials. Looking at oncology programmes, the results for the 2011 to 2020 period (Exhibit 11) show that oncology programmes have one of the lowest success rates compared to the other 14 disease categories for every developmental clinical transition and overall likelihood of approval (LOA).

Regulatory agency focus on supporting the approval process is apparent

The disappointing news is that the equivalent transition scores for the 2006 to 2015 period (from BIO's 2016 report) are 62.8% Phase I to Phase II, 24.6% Phase II to Phase III, 40.1% Phase III to NDA/BLA, and 82.4% NDA/BLA to approval, with a Phase I to Approval LOA of 5.1%. The area where oncology programmes perform well, against both historical and peer comparisons, is in regulatory approvals; suggesting efforts by the various regulatory agencies to improve the availability of cancer drugs for patients is bearing fruit.

Biologics have better success rates than small molecules

Picking out snippets from BIO's 2021 report, immune-oncology drugs tend to have better success rates than traditional oncology programmes, with the notable feature being a Phase II to Phase III transition rate of 42.0% (vs 24.6%) which drives a Phase I to approval LOA of 12.4% (vs 5.3%). This is borne out by the biologics group having higher transition rates and overall LOAs across all phases than their equivalent NCEs (mainly small molecules). This correlates well with the

higher valuations attributed to biologics development companies relative to their small molecule peers.

An example: how we value the pre|CISION pipeline

AVA6000 key point will be Phase II, acting as proof of concept for both product and platform

The lead pre|CISION programme, AVA6000, is completing Phase Ia trials which are designed to determine the optimal dose for future studies and confirm that the safety profile seen in preclinical studies can be replicated in humans. First signs of efficacy are typically seen in the patients taking part in the Phase Ib trial. The AVA6000 active ingredient, doxorubicin, is well characterised so the major uncertainty concerns the pre|CISION technology itself. Early data, albeit from a small patient population, suggests its PK/PD profiles are behaving as predicted. However, regulatory agencies will require further data to be sufficiently confident that the pre|CISION platform is safe, delivers the drug to the tumour site, cleaves in sufficient amounts to deliver therapeutically active doxorubicin, and clears the body (both the dissociated parts and any uncleaved residue) as predicted.

Success probability of 10%, compares with 5.3% for comparator drugs

We believe approval for AVA6000 will be sought through the FDA's 505(b)(2) pathway, exploiting existing data files for doxorubicin, and providing the required data to demonstrate pre|CISION's mode of action, safety, and efficacy. This could typically be achieved with two reasonably powered Phase IIb/III trials. We make no assumptions regarding any form of expedited approval until proof of concept is demonstrated in Phase II trials. Whilst Phase Ib results should provide a useful indication of likely efficacy, it is the structure and patient numbers of the Phase II programme that form the basis for demonstrating that AVA6000 and consequently the pre|CISION platform works as anticipated. Placing all these elements together, we arrive at a risk adjustment of just over 10% (which we round down). This compares favourably with the equivalent risk factor for a small molecule oncology NCE, reflecting a lower risk profile as the active drug is known.

AVA3996's rNPV calculated when IND completes and Phase I trials start

In contrast, AVA3996, a pre|CISION activated prodrug of an analogue of Takeda's multiple myeloma drug Velcade (bortezomib), is still completing preclinical studies. Here both the active and the delivery platform are as yet unproven. This novelty means the approval pathway will be the usual NDA 505(b)(1) route, which normally requires two larger Phase IIb/III clinical trials. At this stage with uncertainty surrounding the development timelines, coupled with the number of other unknowns, means we have too many variables to make anything more than an educated guess at likely value. The key points in establishing greater visibility will be an IND approval, and start of Phase I studies, and, importantly, AVA6000's Phase II results providing proof of concept for the pre|CISION platform.

Industry standards are employed but flexed to reflect individual programme features

Hence our model currently consists of an rNPV of the lead clinical asset and an aggregate rNPV for the remainder of the proprietary platforms, Affimer proteins and pre|CISION. We deliberately employ conservative assumptions throughout. The success probabilities are based on standard industry criteria for the respective stage of clinical development but, importantly, flexed to reflect the individual programmes. These still consider the inherent risks of platforms that are as yet unproven in human studies. From a valuation perspective, the first inflection point occurs when a programme enters human studies, with the next, and more significant, one being when Phase II results are known.

Valuation

We continue to value Avacta using an rNPV model for Therapeutics and a DCF for Diagnostics

Our Avacta sum-of-the-parts valuation includes an rNPV of the lead clinical asset AVA6000, an aggregate rNPV for the remainder of the proprietary platforms (Affimer and pre|CISION), and a DCF valuation of Launch Diagnostics, which are netted against near-term operating costs. We include last reported net cash, excluding the Convertible Bond (CB) as we assume this will be settled in shares. Our valuation has been rolled forward in time and updated to reflect FY22 results, while maintaining the key underlying assumptions that underpin each component. This results in a valuation of £641m, equivalent to 228p/share (199p fully diluted for future shares to settle the CB).

We value Avacta at £641m, equivalent to 228p per share (199p per share diluted)

Our updated valuation is shown in Exhibit 12. We employ conservative assumptions throughout and, as stated earlier, while the success probabilities are based on standard industry criteria for the respective stage of clinical development we flex these to reflect the inherent risks of platforms that are as yet clinically unproven. More details on the methodology are in our December 2022 Update. We envisage revisiting our models as news flow on AVA6000's clinical progress is released and, importantly, as further plans for the Diagnostics business emerge.

Exhibit 12: Avacta sum of the parts valuation

Programme	Total NPV (£m)	Total NPV ($m)	Success probability	rNPV (£m)	rNPV ($m)	rNPV/ share (p)	Notes
AVA6000 (doxorubicin prodrug)	667.4	800.9	10%	64.0	76.8	22.8	Royalty: 15%; Launch yr: 2026; Peak sales $1.5bn
pre|CISION platform (various preclinical)	1811.2	2173.4	10%	279.0	334.8	99.3	Royalty: 15%; Launch yr: 2027+
Affimer platform (various preclinical assets & diagnostics)	2295.2	2754.2	6%	275.7	330.9	98.1	Royalty: 20%; Launch yr: 2028+
Diagnostics	33.2	39.9	100%	33.2	39.9	11.8	Launch Diagnostics
Operating costs	(52.8)	(63.3)		(52.8)	(63.3)	(18.8)	
Net cash	41.8	50.1		41.8	50.1	14.9	At FY22
Total	**4,796.0**	**5,755.2**		**641.0**	**769.1**	**228.1**	

Source: Trinity Delta Note: assumptions include a 12.5% discount factor, £/$ FX rate of 1.20

Progress with AVA6000, details on AVA3996, and diagnostics M&A could lead to upside

The pre|CISION platform is an important component of our valuation and the lead project, on which we have the most visibility, is AVA6000. Positive outcomes for AVA6000 would not only drive an increase in its rNPV, but also materially act as validation for, and de-risk, the pre|CISION platform. Our pre|CISION platform valuation is based on an indicative value, with progress therefore resulting in sizeable upside potential. In addition, as preclinical asset AVA3996 advances into clinical development, this could lead to a refining of forecasts; currently, AVA3996 is incorporated within the pre|CISION platform valuation. Finally, as the diagnostics M&A strategy emerges, with additional bolt-on acquisitions potentially driving higher sales and profitability, and as the Affimer technology is incorporated, the inherent value in this platform should unlock and be realised.

Financials

Revenues driven by first few months of Launch Diagnostics, plus milestones

Avacta's FY22 revenues were £9.65m (FY21: £2.94m) with the Therapeutics Division contributing £5.48m (FY21: £2.16m) and the Diagnostics Division £4.17m (FY21: £0.78m). Therapeutics revenues were mainly derived from milestones achieved under collaborations with LG Chem (£1.65m cash receipt) and AffyCell (£3.6m in additional equity in the JV) and funded FTE reimbursement from partners. The increase in Diagnostics revenue reflected the contribution from Launch Diagnostics from October onward (£3.97m in revenue) with the remainder from a smaller number of custom Affimer reagent projects given the focus of internal resources on developing future diagnostic tests.

SG&A included initial Launch Diagnostics spend, whilst R&D was well controlled

FY22 R&D spend was lower at £11.10m (FY21: £13.48m), although SG&A increased to £11.23m (FY21: £8.14m) due to the Launch Diagnostics acquisition (incurring admin expenses of £1.43m) and scale up of operations in both divisions (Diagnostics: product development capabilities; Therapeutics: infrastructure to support a clinical stage business). Avacta reported an adjusted EBITDA loss of £15.09m for FY22 which when adding back depreciation and amortisation, share based compensation, and the share of losses from the AffyXell JV translated into an operating loss of £32.65m (FY21: adjusted EBITDA loss of £21.74m and operating loss of £29.08m). The March 2022 sale of the Animal Health Division, including £0.86m upfront and a deferred contingent consideration of up to £1.43m (£0.72m was recognised in FY22), resulted in a £0.31m profit on disposal.

Cash of £41.8m boosted by the £61.3m fundraise; CB accounting is complex but is largely non-cash

End-December 2022 cash and equivalents stood at £41.78m (end-June 2022: £17.02m; end-December 2021: £26.19m), boosted by the £61.3m (gross) fundraise in October 2022 (£55m in convertible bonds issued at 95% of the principal for gross cash proceeds of £52.25m plus £9m from the equity placing). Cash at end-March 2023 is c £39.0m following receipt of £2.8m in FY21 R&D tax credits. At-end December 2022 the £55m senior, unsecured Convertible Bond (CB) was held on the balance sheet with a value of £57.83m (debt value of £18.73m; derivative fair value of £39.1m). For more details on the CB see our December 2022 Update. Following the second amortisation on 21 April 2023, the outstanding CB value is £46.8m. For the purposes of our model, we assume the CB and coupon are repaid over the five years in shares priced at 118.75p ie. non-cash movements, resulting in total repayment by October 2027.

FY23e will include a full year of Launch Diagnostics

Our FY23e revenue forecast is £21.2m incorporating core Avacta revenues, plus a full year of revenues from Launch Diagnostics, where we include unchanged core revenues of £17.0m (see our December 2022 Update for more details on our assumptions for Launch Diagnostics). We conservatively forecast only a slight increase in total FY24e revenues to £22.1m. We expect both R&D and SG&A to increase in FY23e, with SG&A notably including a full year of Launch Diagnostics costs. For FY24e we forecast a more modest increase in both. This drives an Operating Loss of £32.1m in FY23e and £34.3m in FY24e, and a Net Loss of £42.1m in FY23e and £44.2m in FY24e.

Cash should be sufficient beyond key AVA6000 newsflow

Our updated forecasts, shown in Exhibit 13, suggest that Avacta has sufficient cash well into 2024, albeit this does not factor in any future potential Diagnostics M&A. However, this should be more than sufficient to reach key value inflection points, notably with AVA6000 over the next 12-18 months.

Exhibit 13: Summary of financials

Year-end: Dec 31	£'000s	2020	2021	2022	2023E	2024E
INCOME STATEMENT						
Revenues		**2,144**	**2,941**	**9,653**	**21,211**	**22,072**
Cost of goods sold		(962)	(924)	(2,410)	(10,144)	(10,938)
Gross Profit		**1,182**	**2,017**	**7,243**	**11,067**	**11,133**
Manufacturing expenses		0	(2,143)	0	0	0
R&D expenses		(9,715)	(14,301)	(12,150)	(18,225)	(20,048)
SG&A expenses		(6,996)	(9,598)	(13,136)	(19,434)	(19,643)
Underlying operating profit		**(15,529)**	**(24,025)**	**(18,043)**	**(26,591)**	**(28,557)**
Share-based payments		(3,070)	(5,058)	(7,490)	(5,468)	(5,741)
Exceptionals		(217)	0	(7,112)	0	0
Other revenue/expenses		0	0	0	0	0
EBITDA		**(14,921)**	**(26,707)**	**(24,408)**	**(28,746)**	**(31,434)**
Operating Profit		**(18,816)**	**(29,083)**	**(32,645)**	**(32,059)**	**(34,298)**
Financing costs/income		(46)	(111)	(8,997)	(12,411)	(12,485)
Profit Before Taxes		**(18,862)**	**(29,194)**	**(41,642)**	**(44,470)**	**(46,783)**
Adj. PBT		**(15,575)**	**(24,136)**	**(27,040)**	**(39,002)**	**(41,042)**
Current tax income		2,464	2,820	2,102	2,369	2,606
Discontinued operations		(2,494)	58	351	0	0
Net Income		**(18,892)**	**(26,316)**	**(39,189)**	**(42,100)**	**(44,177)**
EPS (p)		**(8.4)**	**(10.5)**	**(15.3)**	**(15.4)**	**(15.4)**
Adj. EPS		**(6.0)**	**(8.7)**	**(10.1)**	**(13.5)**	**(13.5)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		225.6	249.5	255.4	273.7	286.3
BALANCE SHEET						
Current assets		**53,254**	**34,736**	**55,551**	**30,952**	**5,584**
Cash and cash equivalents		47,911	26,191	41,781	16,897	(8,202)
Accounts receivable		2,895	4,327	5,579	5,811	5,442
Other current assets		2,200	4,029	6,510	6,577	6,636
Non-current assets		**14,208**	**12,266**	**37,098**	**34,509**	**32,382**
Property, plant & equipment		2,696	2,612	7,798	6,535	5,601
Intangible assets		9,417	7,925	26,324	24,998	23,805
Other non-current assets		2,095	1,729	2,976	2,976	2,976
Current liabilities		**(3,781)**	**(4,368)**	**(9,784)**	**(6,829)**	**(5,371)**
Short-term debt		0	0	0	0	0
Accounts payable		(3,491)	(3,731)	(8,423)	(5,468)	(4,010)
Other current liabilities		(290)	(637)	(1,361)	(1,361)	(1,361)
Non-current liabilities		**(1,752)**	**(1,412)**	**(64,427)**	**(51,027)**	**(40,627)**
Long-term debt		0	0	(57,829)	(44,429)	(34,029)
Other non-current liabilities		(1,752)	(1,412)	(6,598)	(6,598)	(6,598)
Equity		**61,929**	**41,222**	**18,438**	**7,605**	**(8,031)**
CASH FLOW STATEMENTS						
Operating cash flow		**(10,642)**	**(20,506)**	**(16,432)**	**(24,161)**	**(24,361)**
Profit before tax		(18,862)	(29,194)	(41,642)	(44,470)	(46,783)
Non-cash adjustments		4,702	7,529	21,614	21,191	21,091
Change in working capital		722	(1,130)	3,873	(3,174)	(1,130)
Interest paid		42	17	75	(11)	(85)
Taxes paid		2,754	2,272	(352)	2,302	2,547
Investing cash flow		**(21,899)**	**18,703**	**(25,042)**	**(723)**	**(738)**
CAPEX on tangible assets		(1,665)	(1,314)	(709)	(723)	(738)
Acquisitions/disposals		(217)	0	(24,333)	0	0
Other investing cash flows		(20,017)	20,017	0	0	0
Financing cash flow		**51,647**	**232**	**56,904**	**0**	**0**
Proceeds from equity		51,902	522	8,868	0	0
Increase in loans		0	0	48,836	0	0
Other financing cash flow		(255)	(290)	(800)	0	0
Net increase in cash		**19,106**	**(1,571)**	**15,430**	**(24,884)**	**(25,099)**
Cash at start of year		8,788	27,894	26,191	41,781	16,897
Cash at end of year		**27,894**	**26,191**	**41,781**	**16,897**	**(8,202)**
Net cash at end of year		**47,911**	**26,191**	**(16,048)**	**(27,532)**	**(42,231)**

Source: Company, Trinity Delta Note: Revenue forecasts do not include products that have not yet been approved or launched.

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