Diamyd® on track for Phase III with 50% LOA, targeting a multibillion-dollar market as a precision medicine game changer

As of September 15th, 2020, the company that was founded in 1984 delivered convincing top-line data – in line with medical consensus view of implementing precision medicine – consistently supporting positive effect of the first-in-class disease-modifying diabetes vaccine Diamyd® in a genetically defined group. The patient group constitutes approximately 40% of patients with type 1 diabetes (T1D) and is delineated by patients positive for the human leukocyte antigen DR3-DQ2 haplotype and GAD autoantibodies. The fresh prospective topline-data from the Phase IIb study DIAGNODE-2 has now verified the genetic patient group as responder to Diamyd®, giving the company sufficient cumulative scientific and clinical basis to pursue the genetically defined patient group into a pivotal Phase III study and motivate its associated financing risk.

Going forward with the genetically well-defined patient group reduces the impact of disease heterogeneity considerably, addressing a very significant reason why previous late-stage clinical trials have failed.

The stock has moved 174% YTD and the company is trading at SEK 4.5bn. Insiders have not sold shares. Mark Atkinson, a board member of Diamyd®, a medical researcher best known for his contributions to research seeking to predict, prevent, and cure T1D, the author of over 500 publications and one of the world's most cited diabetes researchers recently increased his holding in the company.

Clearly money will always follow science, in this instance a disease-modifying therapy for diabetes. On the backdrop of a pioneering treatment for an already huge and growing patient population with significant direct and indirect healthcare costs, the underpinnings are in place which triggers a significant revenue stream and would concurrently translate into hyper-growth for the stock.

We initiate coverage with an Outperform rating. With a 50% LOA for the lead candidate Diamyd® and 18% LOA for Remygen® our risk-adjusted DCF valuation results in a value for Diamyd Medical of SEK 100 per share, corresponding to an equity value of approximately SEK 6.6 bn non diluted. While awaiting further detailed data on the Phase IIb secondary endpoints, the stock should reach our target price in twelve months ahead assuming a data consistent trend across these endpoints and pivotal Phase III study set up to start enrolment.

DIAMYD MEDICAL

OUTPERFORM

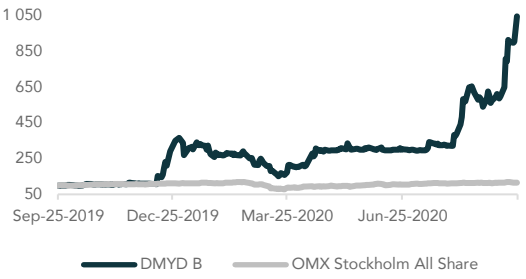
Initiating Coverage

Target price: SEK 100
Current price: SEK 68.2
Implied upside potential: 47%

Diamyd Medical at a glance

Diamyd Medical is a clinical stage pharmaceutical company addressing unmet medical needs in type -1 diabetes with its first-in-class disease-modifying therapies. Its lead candidate Diamyd® is an antigen-specific immunomodulating vaccine targeting new-onset T1D on track for Phase III. Remygen® is an oral regenerative and immunomodulatory therapy targeting type-1 and type-2 diabetes in a clinical Phase I/IIa trial (ReGenerate-1).

Share price development (index= Sep 25, 2019)



Key Data	As per 2020-09-25
Ticker	DMYD B
Share price (close)	SEK 68.2
Free float	72.2%
Market cap	SEK 4.5bn
Website	www.diamyd.com
Average daily volume (Aug 17 – Sep 25)	SEK 30.8m

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Contents

Emerging science forming consensus in favor of precision medicine for type 1 diabetes

Like neurodegenerative diseases, such as Alzheimer's Disease, the field of type 1 diabetes (T1D) has for long been considered a graveyard of projects, and consequently a no-go zone for investors. Scientific and technological advancements in neuroscience have, however, sparked new, particular interest in the field among the industry and investors, demonstrated by significant investments to advance preventative and disease modifying agents against diseases with substantial unmet medical need and market potential. The Swedish company BioArctic (OM:BIOA B) serves as an example of a company in that field with an attractive stock growth trajectory on the back of progress through clinical development and industrial partnerships. Comparable to neuroscience, the field of T1D is also undergoing an intense knowledge inflection point, where emerging science and technology rapidly improves the understanding of biology and pathogenesis, providing new translational directions to increase the likelihood of advancing new disease-modifying therapies through trials into clinical practice. We predict that the knowledge gains in such an area characterized by a huge unmet medical need, no new therapies since insulin in 1922, and enormous market potential, will trigger a new broad industry and investor interest for disease modifying therapies; money will always follow the science. With that, we believe that diabetes has the potential to witness advancements in the '20s corresponding to that in oncology over the last decade.

A significant reason for the translational impasse of disease-modifying agents in the T1D field is due to failure of assessing the impact of disease heterogeneity clinical trials. The science is, however, today at a new medical consensus regarding the heterogenous population within the T1D field. The new recent thesis is based on categorization of patients by underlying biological mechanisms, defining and understanding genetic variations in T1D, and thus replacing the disappointing "one size fits all" approach. This realization comes after a period of unprecedented change in clinical trial medicine, with increasing emphasis on individualization and precision in complex, heterogenous diseases; for instance asthma, a prototypical example in which the delineation of patients based on pathophysiological pathways have proved critical for advancing a new age of precision-based asthma medications. Furthermore, precision medicine has also shown significant success in oncology where immunotherapies such as pembrolizumab (Keytruda) targets tumors that express specific biomarkers. There is consequently a strong case for precision medicine for T1D patients, supporting Diamyd Medical's approach and placing it at the forefront of the new medical consensus.

In line with medical consensus view of implementing precision medicine, Diamyd Medical has recently reported findings from analyses consistently supporting positive effect of its lead candidate, first-in-class disease-modifying diabetes vaccine Diamyd® in a genetically defined group, corresponding to approximately 40% of patients with type 1 diabetes (T1D). This group consists of patients positive for the human leukocyte antigen (HLA) DR3-DQ2 haplotype and GAD autoantibodies. Fresh prospective topline-data from the Phase IIb study DIAGNODE-2 has now verified the genetic patient group as responder to Diamyd®, giving the company sufficient cumulative scientific and clinical basis to pursue the genetically defined patient group into a pivotal Phase III study and motivate its associated financing risk.

Diamyd® is an antigen-specific immunotherapy and one of very few treatments ever evaluated that has shown effects on both preserving endogenous insulin production, reducing the need for external insulin as compared to other treatments, while at the same time lowering HbA1c thus preserving normal blood glucose level. Compared to other late-stage, disease-modifying or preventative T1D therapies such as the anti-CD3 antibody Teplizumab (Provention Bio, market cap SEK 6bn), Diamyd® has a favorable safety profile, modulating the immune system rather than suppressing it. The vaccine has been evaluated without any safety concerns in clinical trials encompassing more than 1,000 individuals. This is an important factor to recognize, making Diamyd® a commercially viable and sustainable treatment alternative for T1D patients, particularly in a COVID-19 era. T1D patients are commonly risk groups of infectious diseases, and the disease burden is greatest among children and adolescents, thus highlighting the need for safe treatments that do not suppress the immune system and are viable for the long term.

However, Provention Bio's development of Teplizumab provides further support for Diamyd Medical's approach, substantiating the importance of applying precision medicine approaches, i.e. delineating patients based on defined pathophysiological pathways and underlying genetic predispositions, in the development of disease-modifying T1D treatments. Provention Bio has demonstrated that subgroups defined by HLA and zinc transporter 8 autoantibodies are differentially responsive to the drug. The company is currently in regulatory phase with an expected completion of BLA filing for at risk patients in Q4.

Follow the science. Diamyd Medical's clinical development legacy is not a symptom of lacking internal capabilities, but rather - just as for other companies in the field - a symptom or reflection of the disease knowledge status in the field. Recent knowledge gains in the field, forming the new medical consensus view, provides new translational directions to increase the likelihood of advancing new therapies through trials into clinical practice, and Diamyd Medical is successfully advancing accordingly.

Recognition among specialist 'big league' and prospective Phase IIb data lend credibility to the science of Diamyd®

Diamyd® is based on the protein GAD65, an endogenous antigen and validated target in the pathology of T1D. The protein is expressed by pancreatic beta cells and a common target by the immune system as nearly 80% of T1D patients have antibodies against GAD, leading to destruction of the insulin-producing beta cells. Diamyd®'s mode of action is to induce GAD65-specific immunomodulation to slow or prevent autoimmune destruction of pancreatic beta cells by inducing tolerance to GAD65 through the skewing of the immune response from a tissue degrading T helper cell type 1 response to a benign, anti-inflammatory reaction. An important advantage of antigen-specific immunomodulation is the potential for a high safety profile, which has been confirmed and contrasts with the toxicities of less specific, bazooka approaches of immunosuppressive therapies applied to T1D autoimmunity.

During the past year, the company has demonstrated that a patient's genetic predisposition of the gene family HLA (human leukocyte antigen), influences the

responsiveness to Diamyd®. The HLA complex plays an important role in the regulation of the immune system through antigen presentation and immune tolerance. A large-scale retrospective meta-analysis, comprised of more than 500 patients from three placebo controlled randomized clinical trials in Europe and USA, demonstrated a highly significant, clinically relevant and dose-dependent effect of Diamyd® on preserving endogenous insulin production in the genetically defined group of type 1 diabetes positive for HLA DR3-DQ2. The fact that DR3-DQ2 is known to confer high risk of developing T1D and has previously been associated with autoimmunity to GAD, substantiates the scientific rationale for the therapeutic potential of Diamyd®. The science, data and analyses behind these findings have achieved a stamp of credibility, recognition and spread among the specialist and scientific elite through peer-reviwed publication of results in Diabetologia, the specialist journal of the European Association for the Study of Diabetes (EASD). EASD is the largest medical scientific association in Europe and the American Diabetes Association counterpart.

Additional analyses of conducted prevention studies are consistent with the results from the meta-analysis, corroborating the reliability of the findings and the strength of the scientific rationale. Most importantly, however, topline data from the recent prospective, randomized, double-blind, placebo-controlled Phase IIb study DIAGNODE-2 verified the genetically defined patient group as a responder to Diamyd®, with statistically significant ($p<0.01$) treatment effect demonstrated on preservation of beta cell function (endogenous insulin production) at 15 months post-diagnosis, as measured by meal stimulated C-peptide. The comprehensive dataset from analyses and the prospective results are scientifically consistent and cohesive, substantiating the scientific rationale that translates into clinical effects.

Bear in mind that DIAGNODE-2 was initiated prior to the company's knowledge of how underlying genetic predisposition could influence trial outcomes and treatment responsiveness, meaning that the trial, and the primary study endpoint of meal stimulated C-peptide, was not designed to solely include the defined genetic group. Consequently, it not surprising that the primary endpoint, considering the entire trial population, was not met. However, this does not mean that the results reported from the genetically defined group lack scientific strength and are irrelevant. This case is rather on the contrary: Why? As emerging analyses supported that Diamyd® is effectively working in a genetically defined group, the statistical analysis plan and trial protocol of DIAGNODE-2 was updated with predefined endpoints to include analysis of this patient population as part of topline. It is important to understand and recognize that this statistical approach is highly differentiated from a subsequent post hoc analysis, producing results of substantially higher scientific impact and regulatory value. To that end, it is highly notable that a statistically significant ($p < 0.01$) treatment effect was observed in the predefined group of patients positive for the HLA DR3-DQ2 genotype, corresponding to 46 patients out of 103 evaluated. This scenario was the best possible outcome of the study given the recent knowledge of genetics influence on Diamyd® responsiveness.

DIAGNODE-2 was a double-blind, placebo-controlled, European Phase IIb trial that enrolled 109 patients aged 12-24 years with new-onset T1D and diagnosed within 6 months of therapeutic intervention. These patients were given Diamyd® (or placebo) directly into a lymph node, following ultrasound guidance, on three occasions at one-

month intervals. The patients were followed for 15 months in order to evaluate their endogenous insulin production, as measured by C-peptide. Of 103 evaluable patients, 46 patients were positive for the HLA DR3-DQ2 haplotype. Out of the 46 patients, 29 received active treatment and 17 received placebo. Further study details can be found here.

Data also provided support of intranodal injection of Diamyd®, with a treatment effect of more than 50 percent greater preservation of endogenous insulin production after 3 injections compared to placebo in HLA DR3-DQ2 positive individuals post 15 months. This supports a higher dose-dependent treatment effect than what subcutaneous administration produces according to large-scale meta-analysis, approximately 44% in the corresponding patient group based on three or four doses. An improved effect of intranodal injection is consistent with previous results from the DIAGNODE-1 trial and observations in the allergen-specific immunotherapy field where trials have shown the potential to enhance the clinical and immunological response through intranodal injections, enabling the potential for long-term efficacy and superior patient adherence. Importantly, in support of the clinical findings, the immune response after 15 months in DIAGNODE1 is characterized by tolerance to the antigen GAD65.

Diamyd Medical reported positive trends in patients positive for HLA DR3-DQ2 on all the important secondary endpoints; change in blood glucose levels as determined by HbA1c (an important blood glucose marker of in diabetes management), insulin dose and insulin-adjusted HbA1c compared to placebo-treated patients. We look forward to reviewing data further when available, and we believe that a consistent trend across all these endpoints is important to reinforce the scientific rationale additionally. As always with drug development companies, disclosure of data is initially quite restrictive to not disturb potential patent and publication processes.

Diamyd® on track for Phase III with 50% LOA, targeting a multibillion-dollar market as a precision medicine game changer

Based on accumulated clinical data and the recent prospective Phase IIb results, Diamyd Medical will pursue the genetically defined patient group in an upcoming pivotal Phase III program that is currently under design. The company will also evaluate the potential for early, conditional market approval. We expect the company to set up End of Phase 2 meetings with the regulatory agencies FDA and EMA to receive guidance on the Phase 3 program and information needed to successfully support a marketing application. The outcome of these meetings will be key inflection points, providing insights into the agencies' view of Diamyd® and validating the road ahead to market. We look forward to following the regulatory agencies' feedback and getting more visibility into the pivotal program ahead.

A T1D disease-modifying therapy must primarily demonstrate effect on preservation of beta cell function, i.e. endogenous insulin production. C-peptide is the established marker for beta-cell function, and the FDA and EMA are aligned in that this marker forms the primary endpoint for Phase 3 trials. Other important endpoints will presumably include insulin use, HbA1c, hypoglycemic episodes and naturally safety.

Importantly, Diamyd® is one of very few treatments ever evaluated that has shown effects on both preserving endogenous insulin production, reducing the need for external insulin as compared to other treatments, while at the same time lowering HbA1c thus preserving normal blood glucose level.

As there are no disease-modifying therapies against T1D to delay or halt disease progression, and a pressing need for it, the approval hurdle for the primary endpoint will very likely be below the significant and highly clinically relevant 50% treatment effect demonstrated in the recent Phase IIb study post 15 months. The group initially targeted by Diamyd Medical is new onset patients aged 12-24 years, where the highest clinical and public health impact can be achieved as the disease otherwise progresses to inflict a major burden throughout life. Scientific advice therefore rather suggests that a treatment effect, without specifying the magnitude of it, that is shown to be clinically relevant is sufficient to support regulatory approval.

As always with drug development companies, the risk is notably above the average equity risk. The main risk in this case pertains to biological and clinical trial aspects of drug development. We set a 50% LOA for Diamyd® to advance through Phase III and reach the market, in line with the average LOA for a novel Phase III therapeutic against autoimmune disorders[1]. We believe this is motivated by the fact that the company will pursue a genetically well-defined patient group, confirmed as responders, thus reducing heterogeneity and variation considerably, addressing a significant reason why previous late-stage clinical trials have failed. Furthermore, the comprehensive dataset including in particular recent analyses and prospective results, corroborating a robust scientific rationale translatable into clinical effects, positions Diamyd® for successful progress through clinical development. The fact that Diamyd® has Orphan Drug Designation in the US and has demonstrated effects on important primary and secondary endpoints likely to be applied in the pivotal study substantiates our argumentation further. A higher LOA could actually be motivated given the ODD status.

A magnitude of documentation demonstrates multiple clinical short- and long-term benefits of preserving beta cells and endogenous insulin secretion, reducing the incidence of disease related complications, such as neuropathy, hypoglycemia and cardiovascular disease. With cumulative clinical data to date, combined with enhanced treatment effect of intranodal administration and attractive safety profile enabling patient adherence, there is convincing support for Diamyd®'s long- as well as short-term clinical benefit and potential to become first-line treatment of new-onset T1D, targeting a very large portion of disease suffers. Broadening of Diamyd® to include T1D prevention, treatment of long-term T1D and Latent Autoimmune Diabetes in Adults (LADA) are under planning and investigation.

Diamyd® benefits from several distinct advantages and there is no viable competition in late stage clinical development that would directly compete with Diamyd® upon market entry and onwards for the foreseeable future. The non-existent direct competition certainly renders the financial prospect favorable while reducing commercial risk. That being said, it is important to emphasize that a future treatment

[1] Hay et al. Nature Biotechnology 32.1 (2014): 40-51, Wong et al. Biostatistics 20.2 (2019):273-286

paradigm in such a severe and undertreated chronic disease as T1D will include a combination of various therapies, symptomatic and preventative.

Key competitive advantages:

1) Immunomodulatory mode of action, Safety

Compared to other late-stage, disease-modifying T1D therapies such as Diamyd® has a very favorable safety profile, modulating the immune system rather than suppressing it. This is an important factor making Diamyd® a commercially viable and sustainable treatment alternative for the intended patient population, particularly in a COVID-19 era. T1D patients are commonly risk groups of infectious diseases, and the disease burden is greatest among children and adolescents, thus highlighting the need for safe treatments that do not suppress the immune system and are viable for the long term.
Most of the disease-modifying treatments in clinical development within the T1D space aim at downregulating the autoimmune response by targeting the immune system on a systematic level. These treatments are associated with insufficient safety profiles and long hospital stays due to the unpredictable side effects and an increased risk of developing cancer in the long-term. Additionally, it is required to boost the immunomodulatory antibody injections regularly - meaning that the troublesome procedure must be repeated often.

2) Ease of delivery

Inguinal lymph nodes are readily accessible in patients and the pain associated with the injection is rated as below that of venous puncture. This administration procedure is becoming increasingly common in the field of allergen-specific immunotherapy due to the support for achieving long-term efficacy. Although the clinical workflow for administration of Diamyd® needs to be established, i.e. administration by radiologists, endocrinologists or non—specialist depending on the healthcare system, the procedure has several benefits over intravenous administration through which immunosuppressant therapies are commonly delivered, requiring hospitalization. After intralymphatic injection of Diamyd®, the patient can leave the hospital after one hour of monitoring. After three initial injections, and a potential fourth booster which may be evaluated going forward, one annual injection of Diamyd® is expected to maintain the effect over time. This treatment frequency combined with the administration procedure is far more convenient for patients and resource-efficient for healthcare systems, which is of particular importance due to the financial challenges posed by the ongoing pandemic.

3) Scalability

Furthermore, contrasting Diamyd® against the immunosuppressant monoclonal antibody candidates, the scalability aspect deserves some attention. Although the manufacturing of biologics has undergone significant improvements in the past years, it is not even comparable with the scalability opportunities with the recombinant protein formulation of Diamyd®, thus marking another important value driver to reach a competitive cost advantage in a future commercial position.

The area of cell and gene therapies is still at early stages for T1D due to the heterogeneous and complex pathophysiology of the disease and Diamyd® among other immunotherapies are likely to hit the market much sooner. However, we do not foresee that cell and gene therapies will pose any competition concerns, primarily due to the fact that the different treatment technologies cater to different parts of

healthcare systems, at varying costs. Cell and gene therapies are, and will probably for the foreseeable future be, comparatively limited in scale and accessible for a limited proportion of patients with the relevant financial means. Nevertheless, it is important to stress that a future treatment paradigm in such a severe and undertreated chronic disease as T1D will include a combination of various therapies, symptomatic and preventative.

Putting the opportunities of Diamyd® into a broader context, the economic impact of a disease-modifying therapy for T1D is outstanding. The annual economic burden of T1D is estimated to exceed USD 30bn in the US alone and USD 90bn globally[2]. While today's standard insulin treatments are symptomatic, Diamyd® has the potential to delay disease progression of T1D, and thus postpone the initiation of complete insulin treatment - including the escalating complications with glycemic control. This would indicate an exceptional gain as 10% of global health expenditure was spent on diabetes 2019, corresponding to USD 760bn and health costs arising from treatment diabetes complications account for over 50% of the direct health costs of diabetes[3]. According to the American Diabetes Association, diabetes is today the most expensive chronic disease in the U.S. and preserving the body's own ability to produce insulin may decrease the risk of complications among T1D patients by 60 – 80%[4].

Distinguished Team and BoD including leading T1D researchers and a commercially oriented focus with international reach

The fact that Diamyd Medical is backed by two of the world's leading T1D researchers[5] - Dr. Mark Atkinson and Dr. Johnny Ludvigsson - lend credibility to the company's scientific progress and should give the market confidence in the clinical development pursued. It is fairly rare for a small Scandinavian biotech company to attract such international recognition, which should emphasize the actuality and relevance of Diamyd®'s development progress among the international diabetes community.

Furthermore, Diamyd Medical's holdings in the stem cell therapy company NextCell Pharma (Sweden, NXTCL) and recently divested medical device company Companion Medical Inc (San Diego, USA) highlights its commercial capabilities in the field of T1D, creating additional shareholder value outside of the company's core operational focus. The holdings in Companion Medical were recently divested in connection with Medtronic's acquisition, yielding approximately SEK 120m to Diamyd Medical.

[2] Modelling the total economic value of novel type 1 diabetes (T1D) therapeutic concepts, January 2020, Health Advances

[3] IDF Diabetes Atlas 2019

[4] Economic costs of diabetes in the U.S. in 2017, May 2018, American Diabetes Association: Diabetes Care

[5] Expertscape 2020

Pipeline

The company's pipeline also includes Remygen®, an oral regenerative and immunomodulatory therapy targeting type 1 and type 2 diabetes (T2D) in a clinical Phase I/IIa trial (ReGenerate-1). Preliminary results from the first stage of the clinical trial, released in May 2020, suggest that Remygen® protects against hypoglycemia (acute low blood sugar) and improves blood sugar control.

Remygen® is based on the active compound GABA (gamma-aminobutyric acid), best known for its role as a neurotransmitter in the central nervous system. GABA has been shown to affect the secretion of insulin and glucagon both in healthy volunteers and in patients. Preclinical data indicate GABA's potential to stimulate the formation and function of glucagon and insulin-producing cells in the pancreas. Through this mode of action, without passing the blood-brain barrier, Remygen® has the potential to reverse the progression of T1D and T2D. As the GAD molecule is included in the same signaling pathway between beta cells, the GABA boost supported by Remygen® has the potential to also introduce a synergistic effect on beta-cell survival and renewal together with Diamyd® or alone.

The Phase I/IIa ReGenerate-1 trial is an open, investigator initiated clinical trial conducted at Uppsala University, involving a total of 36 patients aged 18-50 who have had T1D for longer than five years with low to non-existing residual insulin production. The trial consists of two parts; an initial safety and dose escalation part comprising six patients, and the main trial, which comprises 36 patients who will be followed up to nine months depending on the dose group to which they belong. The trial will examine whether Remygen® alone and in combination with Alprazolam can have a positive effect on the hormonal counter-regulatory response to low blood sugar and on the restoration of beta cell function, potentially allowing in the long run a patient to regain insulin-producing capacity. The trial is expected to be completed in 2022 and we look forward to following the interim analyses that will be performed during the study. The outcome of the study will also define the first indication for Remygen® that will be advanced onwards.

Preliminary results from the first part of Regenerate-1 showed that GABA decreased the otherwise elevated glucagon levels in type 1 diabetes, and increased the levels of glucagon and other counter regulatory hormones in hypoglycemia, supporting that Remygen® improves the hormonal protection mechanisms that counteract hypoglycemia. The therapy also indicated a good safety profile, and the findings are now patent pending. Based on satisfactory Phase I data, Remygen® has now advanced into the Phase IIa part of the combined trial.

We set an 18% LOA for Remygen®, in line with the LOA for a novel Phase II therapeutic developed for autoimmune disorders[6]. The 505(b)(2) regulatory pathway is potentially applicable for Remygen®, offering a faster road to market. This is currently under investigation.

[6] Hay et al. Nature Biotechnology 32.1 (2014): 40-51, Wong et al. Biostatistics 20.2 (2019):273-286

Outlook

Diamyd Medical expects to have the pivotal Phase III study with Diamyd® set up, ready to begin enrolment, within 12 months. Prior to that milestone, we see a string of potential catalysts that – if positive – should be de-risking and have a positive impact on the stock: further presentation of data from Phase II study, feedback from EMA and FDA on Phase III program, interim analysis from Regenerate-1 with Remygen®. We also anticipate that the company needs to raise capital to fund a Phase III study with Diamyd®.

Risk Analysis

This section provides an overview of the company's risk profile and how we deem the company positioned with regard to key risks pertaining to drug development companies. Primary focus is on Diamyd® as it is the lead asset and main short-term value driver. Successful progress provides, in our view, positive read-across to the development of Remygen®. We look forward too following updates from Regenerate-1, on the regulatory path ahead and initial indication.

Risks	Risk mitigation identified
Team and BoD	Retained KOLs and backing by internationally recognized experts in the field ensures adequate scientific and clinical development competence. Commercial focus and capabilities demonstrated through various commercial activities.
Clinical risk	Main risk in this case. Mitigation motivating a 50% LOA: 1) a genetically well-defined subgroup mitigates risk considerably, addressing disease heterogeneity – a significant reason why previous late-stage trials have failed; 2) primary and secondary endpoints highly likely to be applied in the pivotal study have already been implemented in clinical development program thus far; 3) robust scientific rationale and ODD status, retained KOLs, international experts lend credibility to the development program.
Regulatory risk	End of Phase II meetings will confirm Phase III readiness and provide details on the route to market. Extensive data package including favourable safety positions Diamyd® for positive feedback. Retained KOLs and internationally recognized experts provide confidence in competent development on par with standard.
Commercial risk	Diamyd® benefits from several distinct advantages (immunomodulatory MoA and safety, ease of delivery, scalability etc) and there is no viable competition in late stage development that would directly compete with Diamyd®, thus reducing commercial risk. Substantial health economic potential emphasizes commercial prospects. A future treatment paradigm in such a severe and undertreated chronic disease as T1D will include a combination of various therapies. Signing a commercial partner for key territories such as Europe and the US is a significant de-risking factor. While this would be a positive catalyst at the current stage, the highest shareholder value is likely to come from a deal post-positive Phase III results.
IP risk	Broad IP portfolio, continuously expanded to extend IP protection. Many companies in the field have a combination of indication, formulation, dosage

	patents etc. Diamyd Medical holds patent rights through exclusive licenses inter alia to: GAD65 (the active compound in Diamyd®) and the GAD gene, patent expiry excl extension 2032; The use of GABA for treating diabetes and other inflammatory diseases, patent expiry 2031 excl extension; Increase GABA's positive effects using GABA receptor modulating substances. Several patent applications filed to reinforce IP protection for its two assets, including formulation and administration. Patent applications covering intralymphatic administration (Diamyd®) have been granted in key European countries and are pending RoW, providing protection for Diamyd® until at least 2036. Patent applications covering oral formulation of Remygen® are pending worldwide and would upon approval extend protection beyond 2038. Diamyd Medical has also filed patent application for the treatment of patient groups defined by HLA genotypes and for various biomarkers.

Source: Vator Securities

Valuation

Outperform rating and target price SEK 100

Our target price is based on a project-based, risk-adjusted DCF valuation of future proceeds from Diamyd® and Remygen®, combined with comparison to a peer group. Since Diamyd Medical is presently a project-driven company using its resources to develop its candidates to generate future revenue streams, we argue that a project-based, risk-adjusted DCF analysis is the most appropriate valuation method. It is inherently difficult to apply the peer valuation approach on companies such as Diamyd Medical since relevant peers are showing a loss, resulting in inconclusive key ratios. Moreover, fundamental company specific circumstances differ between the peer companies. Therefore, we mainly use peer group comparison to put the project-based, risk-adjusted DCF-derived value into context.

Project-based, risk-adjusted DCF valuation

We assume that Diamyd Medical will enter partnerships for commercialization of Diamyd® and Remygen® and receive royalties on sales generated by respective asset. We forecast Diamyd Medical to generate risk-adjusted peak proceeds of SEK 1 842m from Diamyd® and SEK 1 209m from Remygen® in 2031. The following key parameters are applied as basis to our forecast:

Diamyd®

- Our sales forecast of Diamyd® is based on epidemiology data of T1D[7], selected to generate the initial target population of new onset patients aged 12-24 defined by relevant HLA and GAD autoantibodies. The forecast does not consider label expansion. We estimate launch in 2025, and only include the US and top-5 markets in Europe.
- 50% LOA in line with the average LOA for a novel Phase III therapeutic against autoimmune disorders[8].

[7] Global Data 2020, IDF Diabetes Atlas 2019

[8] Hay et al. Nature Biotechnology 32.1 (2014): 40-51, Wong et al. Biostatistics 20.2 (2019):273-286

- We have assumed a price of USD 35 000 per patient and year in the US and USD 21 000 in Europe, corresponding to 60% of US prices. As there are no disease-modifying therapies for T1D, we have benchmarked the price against other biological therapies with disease-modifying properties such as Humira (Abbvie, autoimmune diseases), Nucala (GSK, severe asthma), Ocrevus (Roche, multiple sclerosis) and Tysabri (Biogen, multiple sclerosis). We have also assumed that the price reflects the prevalence of the disease, i.e. a more prevalent disease has a lower price. Consequently, we have assumed a lower price for Diamyd® than Humira, Ocrevus and Tysabri since T1D is more prevalent. The price will ultimately be affected by the risk/benefit ratio of the product and what the health economic benefits of drug treatment can achieve. Diamyd®'s favorable safety profile seen thus far in trials encompassing >1000 individuals combined with the substantial health economic benefit potential of a disease modifying treatment render the commercial prospects exceptionally favorable.
- Peak penetration rate of 20% in the US and 15% in EU5 by 2030, 6 years post launch. We expect slower sales uptake in Europe due to the heterogeneity of European markets. Penetration will ultimately, like price, depend on efficacy and safety, and the competitive landscape. Provided a successful outcome of the upcoming pivotal trial, Diamyd® has several key competitive advantages (detailed above) that position it over other late-stage therapies under development. Therefore, we currently deem the estimated peak penetration rates as fully reasonable. In our forecast, however, we make a slightly conservative estimate and take into consideration the influence of other treatment alternatives by 2030, reflected in the years onwards.
- Commercial partner secured on the back of pivotal Phase III data. At this later stage, a partner licensing marketing and commercial rights usually comes with higher royalty rates and more modest milestone payments as the partnership usually involves less risk-sharing. As such, the partnership is usually structured similarly to a joint venture with a royalty rate of 50/50 and modest milestone payments. This is therefore reflected in our sales forecast and valuation of Diamyd®. We assume a modest total of SEK 100m in milestone payment triggered by regulatory filing and approval.
- Gradual sales decline of 10% y/y upon expiration of key patent. The composition of matter patent on GAD65 expires in 2032 in the US, and the patent on intralymphatic administration expires in 2036 in Europe. In addition to patent protection until 2032 in the US, the FDA has granted orphan drug designation for Diamyd®, which provides seven-year market exclusivity in an independent patent situation following FDA approval. We have not considered potential patent extensions. Patent applications covering intralymphatic administration have been granted in key European countries and are pending RoW. Upon approval, the IP protection is strengthened until at least 2036, excluding the potential for extension.

Remygen®

- Remygen® can potentially cater to both T1D and T2D patients. The outcome of the ongoing Phase I/IIa Regenerate-1 trial will be used as a basis to define the first indication. For now, we limit the scope to the patient population

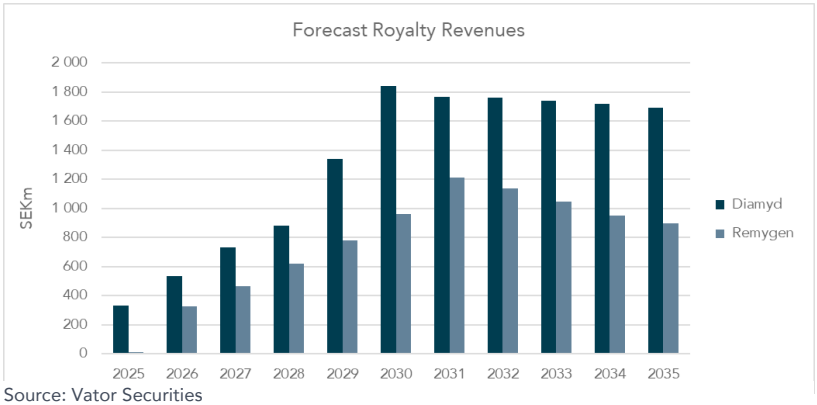
included in the study, i.e. patients aged 18-50 who have had T1D for longer than five years. The assumptions are subject to change as further details are disclosed and as the therapy progresses through the ongoing study. We estimate launch in 2026, and only include the US and top-5 markets in Europe.

- 18% LOA in line with the average LOA for a novel Phase II therapeutic against autoimmune disorders[9].
- To reflect the relatively higher prevalence compared to Diamyd®'s initial target market, we have assumed a price of USD 15 000 per patient and year in the US and USD 9 000 in Europe, corresponding to 60% of US prices.
- We have assumed peak penetration rates of 7% in the US and 5% in EU5 by 2031, 6 years post launch – again, reflecting the size of the patient population in question.
- License partner, granted marketing and commercial rights, secured on the back of Phase II data, ahead of Phase III. We have assumed a royalty rate of 15%, on par with industry standard at this stage, and total milestone payments of SEK 125m prior to launch.
- Gradual sales decline of 10% y/y upon expiration of key patent in 2031, excluding the potential for patent extension. Key patents on GABA expires in 2031 in the US. The company has filed international patent applications, covering oral formulation, that is pending approval. If granted, the drug is protected until at least 2038.

Other

- Research and development costs driven by clinical trials of Diamyd® and Remygen®.
- Diamyd Medical has a lean operation of seven full-time equivalent employees as of end May 2020. The cost increase is reflected by the partner strategy for both drug candidates, with an organizational build up driven by ramp up of commercial manufacturing.
- COGS at 90%
- We model two equity issues of SEK 300m in 2021 and SEK 300m in 2023

The graph below depicts forecast revenue streams (risk-adjusted) from Diamyd® and Remygen®.



Source: Vator Securities

[9] Hay et al. Nature Biotechnology 32.1 (2014): 40-51, Wong et al. Biostatistics 20.2 (2019):273-286

Risk-adjusted P&L

The table below summarizes Diamyd Medical's forecast financial development based on aforementioned assumptions.

Financials (SEKm)	FY20E	FY21E	FY22E	FY23E	FY24E	FY25E	FY26E	FY27E	FY28E	FY29E	FY30E	FY31E	FY32E	FY33E	FY34E	FY35E
Probability Adjusted Royalty Revenues	0	0	0	8	50	342	858	1 196	1 499	2 124	2 803	2 974	2 899	2 784	2 667	2 587
Gross Profit	**0**	**0**	**0**	**8**	**50**	**308**	**772**	**1076**	**1349**	**1911**	**2522**	**2676**	**2609**	**2506**	**2400**	**2328**
Sales and marketing costs	-10	-10	-10	-10	-10	-10	-10	-10	-10	-10	-10	-10	-5	-5	-5	-5
Personnel costs	-9	-10	-11	-12	-13	-19	-29	-34	-38	-42	-44	-46	-48	-50	-53	-56
R&D expenses	-15	-100	-125	-175	-125	-75	-50	-25	-25	-25	-25	-20	-20	-20	-20	-20
Other operating costs	-11	-13												-41	-43	-41
Total operating costs	**-45**	**-133**	**-161**	**-214**	**-167**	**-125**	**-112**	**-95**	**-101**	**-107**	**-112**	**-113**	**-112**	**-116**	**-121**	**-122**
EBITDA	**(45)**	**(133)**	**(161)**	**(206)**	**(117)**	**183**	**661**	**982**	**1 248**	**1 804**	**2 410**	**2 564**	**2 497**	**2 389**	**2 279**	**2 207**
Net income	**(45)**	**(135)**	**(163)**	**(208)**	**(118)**	**182**	**659**	**845**	**978**	**1 414**	**1 889**	**2 009**	**1 958**	**1 873**	**1 786**	**1 730**

Source: Vator Securities. Probability adjusted proceeds, including milestone payments. Includes proceeds from divestment of holdings in Companion Medical SEK 120m

Discounted Cashflow

We use a discount rate (WACC) of 12.1%, as well as 2.0% terminal growth rate (in line with GDP growth) with no adjustment to terminal value given the LOA assumption underpinning the entire forecast period. The risk-free rate is 0%, based on the Swedish government ten-year bond, and the risk premium is 8.5%, based on a size and market risk premium of 1.3% and 7.2% respectively. We use an equity beta value of 1.50 reflecting underlying volatility with a 100% equity ratio resulting in a 12.1% discount rate. We have also included a net present value of the cumulative tax shield. With our estimates and DCF input variables, our DCF model indicates an equity value for Diamyd Medical of approximately SEK 6 600m, equivalent to SEK 100 per share (based on approximately 66.6m outstanding shares).

DCF (SEKm)	FY20E	FY21E	FY22E	FY23E	FY24E	FY25E	FY26E	FY27E	FY28E	FY29E	FY30E	FY31E	FY32E	FY33E	FY34E	FY35E
EBIT	(45)	(135)	(163)	(208)	(118)	182	659	981	1 247	1 803	2 409	2 563	2 497	2 389	2 279	2 206
Paid tax	0	0	0	0	0	0	0	136	269	389	520	554	539	516	492	477
NOPLAT	(45)	(135)	(163)	(208)	(118)	182	659	845	978	1 414	1 889	2 009	1 958	1 873	1 786	1 730
Adj. for non-cash items	0	2	2	2	1	1	1	1	1	1	1	1	1	1	1	0
Changes in NWC	0	0	0	0	0	60	208	0	0	317	0	0	79	0	0	0
Capex	20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Free cash flow	**(65)**	**(133)**	**(161)**	**(206)**	**(117)**	**123**	**453**	**846**	**979**	**1 098**	**1 890**	**2 010**	**1 879**	**1 873**	**1 787**	**17 131**
Discount factor (formula based)	1.06	1.19	1.33	1.49	1.67	1.87	2.10	2.36	2.64	2.96	3.32	3.72	4.17	4.67	5.24	5.24
Net Present Value - Free Cash Flows	**(61)**	**(112)**	**(121)**	**(138)**	**(70)**	**66**	**216**	**359**	**371**	**371**	**570**	**540**	**451**	**401**	**341**	**3 270**

	SEK million
Terminal value	**17 131**
Life cycle adjustment TV	100%
Adjusted Terminal value	**17 131**
Net Present Terminal Value	**3 270**
Net Present Value FCF	**3 182**
NPV of FCF incl. TV	**6 452**
Tax shield, NPV	121
Interest bearing net debt	(57)
Equity Value	**6 630**
Number of shares, non-diluted, million	66.6
SEK/Share	**100**
Key metrics	
Terminal value/DCF	**51%**

Source: Vator Securities.

Valuation parameters

The stock should reach our target price in twelve months ahead assuming a data consistent trend across the Phase IIb secondary endpoints and pivotal Phase III trial set up to begin enrolment.

There are several upsides to our valuation, which currently are not factored in:

- Sales from RoW
- Label expansion of Diamyd® to include T1D prevention, treatment of long-term T1D and Latent Autoimmune Diabetes in Adults (LADA).
- Launch of Diamyd® earlier than 2025, as a result of conditional market approval in Europe and/or product designations speeding up the regulatory process in the US.
- Launch of Remygen® expected earlier than what we have assumed, due to 505(b)(2) pathway.
- Patent application approvals reinforcing the IP portfolio, providing longer protection.
- Commercial gains from holdings in NextCell Pharma or sales from GAD (preclinical research).

Peer group comparison

Diamyd Medical has no direct relevant listed local peer companies. Furthermore, there are fundamental circumstances differing between comparable companies in terms of disease area, competitive landscape, innovation level, safety and level of clinical validation, product designations etc. It is also difficult in this case to use the peer group valuation approach and draw any conclusions from it since applied multiples are non-conclusive.

However, the following table showing Nordic and US companies, comparable in terms of development stage, is a reference point for the value of Diamyd Medical, putting the current value into context.

Diamyd Medical's stock should reach our target price in twelve months ahead assuming a data consistent trend across the Phase IIb secondary endpoints and pivotal Phase III trial set up to begin enrolment. Given Diamyd®'s distinct competitive advantages with no direct viable competition, targeting a multibillion-dollar market as a disease-modifying precision medicine game changer with substantial health economic benefit potential, we argue that a technology value on par with BioArctic's, mainly driven by BAN2401, is highly reasonable. The opportunity with Remygen® underpins our argumentation further.

Even though Provention Bio is in registration phase with Teplizumab targeting initially at-risk patients, we argue that Diamyd Medical's technology value is higher. This is primarily due to Diamyd®'s immunomodulatory mode of action which, in contrast to Teplizumab, does not weaken the immune system and has a favorable safety profile, making it a commercially viable and sustainable treatment alternative for T1D patients,

independent of target indication. Remygen® provides another shot at goal, broadening the commercial potential in diabetes.

Hansa Biopharma received recently conditional approval in Europe for Idefirix[TM] on the back of phase II data, and are setting up a Phase III study to support US approval. While the company is targeting rare diseases, the stock's growth trajectory (primarily driven by one asset) provides a reference point for the future value of Diamyd Medical if Diamyd® is granted conditional approval in Europe.

Peer valuation comparison (SEKm)

Company	Market cap	Cash	Technology Value (EV)	Most mature project	Partner	Beta
Oncopeptides	8 946	938	8 008	Regulatory/Phase III	No	0.52
Provention Bio	6 257	1 529	4 728	Regulatory	No	3.56
Bioarctic	7 371	1 050	6 321	Ph III	Yes	3.00
Hansa Biopharma	10 256	400	9 856	Ph III US, CA Europe	No	1.22
Calliditas	5 153	1 460	3 693	Ph III	No	1.19
Average	*7 596*	*1 075*	*6 521*			1.90
Median	*7 371*	*1 050*	*6 321*			1.22

Market cap: as per close 2020-09-25
Cash: as per 2020-06-30
Source: S&P Global Market Intelligence. CA: Conditional approval

Key personnel

Ulf Hannelius, CEO. Ulf holds a PhD in Molecular Biology from Karolinska Institutet in Stockholm and Executive MBA from Stockholm School of Economics. Prior experience from business development in the biotech and medtech industries as well as from academic research in the fields of genetics and molecular biology. Ulf joined Diamyd Medical in 2015, CEO since 2016.

Martina Widman, Director Clinical Development. Martina holds a M.Sc. in Mechanical Engineering from the Royal Institute of Technology in Stockholm, with a specialization in Biomedical Engineering. Prior experience of clinical operation from the pharmaceutical industry. Joined Diamyd Medical in 2008.

Anna Styrud, CFO. Anna holds a B.Sc. in Business Administration from Uppsala University. Prior experience includes Treasurer of Vasakronan AB and various positions in finance and control within real estate and engineering industry. Joined Diamyd Medical in 2010.

Anton Lindqvist, Anton holds a M.Sc. in Molecular Biotechnology Engineering from Uppsala University. Research experience from University of Pittsburgh, Uppsala University, the Royal Institute of Technology and Karolinska Institutet. Prior experience in managing technical development at several biotech companies. Joined Diamyd Medical in 2013.

Board of Directors

Erik Nerpin, Chairman of the Board. Lawyer. Self-employed with Advokatfirman Nerpin AB. Independent of the Company and its principal owners. Board member since 2012. Chairman of Kancera AB and Blasieholmen Investment Group AB and Board member in among others Effnetplattformen AB.

Anders Essen-Möller, Board Member. M.Sc. Founder of and CEO during 1996-2007 of Diamyd Medical and Chairman 2007 –2015. Independent of the Company, principal owner. Founder of Synectics Medical AB, sold to Medtronic, Inc. in 1996. Chairman of NextCell Pharma AB.

Maria-Teresa Essen-Möller, Board Member. M.Sc. in Business Administration. CEO of Health Solutions AB. Independent to the Company, not independent to its principal owners. Previous experience includes Digital Marketing Manager at Sanofi and Account Director at Creuna. Board member since 2009.

Torbjörn Bäckström, Board Member. MD, PhD. CEO of Umecrine AB. Independent of the Company and its principal owners. Board member since April 2017. Head of Neurosteroid Research Centre in Umeå and Senior Professor in the Department of Clinical Science, Obstetrics and Gynecology at Umeå University.

Mark Atkinson, Board Member. PhD. Professor of Diabetes Research, Department of Pathology, Immunology and Laboratory Medicine, University of Florida, USA. American

Diabetes Association Eminent Scholar for Diabetes Research. Director, UF Diabetes Institute, University of Florida. Independent of the Company and its principal owners. Board member since November 2018.

Disclaimer

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I, Felicia Rittemar, the author of this report, certify that notwithstanding the existence of any such potential conflicts of interests referred to below, the views expressed in this report accurately reflect my personal view about the companies and securities covered in this report.

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