Active Biotech

Sector: Biotech

Advancing Three Active Projects

Redeye revisits its valuation of early-stage biotech company Active after significant progress across its three candidates, but also delays due to Covid-19. At the same time, we believe that the risk has increased slightly in tasquinimod.

Clinical progress

Active Biotech made progress across its pipeline during 2021 . Tasquinimod successfully completed the monotherapy arm in multiple myeloma (MM) with a good safety profile and early signs of meaningful pharmacological activity. A new eye-drop formulation was successfully developed for laquinimod, which entered a clinical phase I trial at the end of the year. Finally, naptumomab entered phase IIa in NSCLC.

The share may have been sold off due to lack of decisive catalysts

That no conclusive evidence about tasquinimod's treatment efficacy in MM could be drawn from the phase I results of the monotherapy arm last October, leading to the cancellation of the expansion cohort, may have hurt expectations. The next catalyst from this trial will be the safety read-out from the combination arm this year, which should have better potential. The bear market also appears to affect the share price.

Share price upside

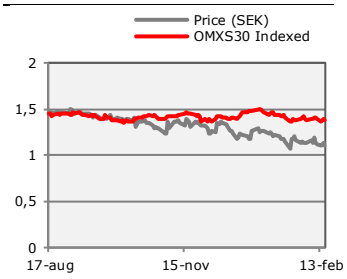
We have remodeled the approval pathway for tasquinimod, removing the accelerated approval as monotherapy. We still assume a licensing deal after phase IIb but now assume a partner sponsored phase III before approval. We lower the LOA for tasquinimod but have raised it for laquinimod and naptumomab. In the more difficult market situation, we raise our WACC to 14 percent (13), which leads to us to a valuation of SEK 2.5. This implies a considerable upside from the current price.

Key Financials (SEKm)	2019	2020	2021E	2022E	2023E
Revenues	8	7	0	0	0
Revenue growth	-58%	-20%	-100%	NA	NA
EBITDA	-32	-32	-46	-55	-76
EBIT	-32	-32	-46	-55	-76
EBIT Margin (%)	-383%	-482%	NA	NA	NA
Net Income	-30	-32	-46	-55	-76
EV/Revenue	13,0	37,4	NA	NA	NA

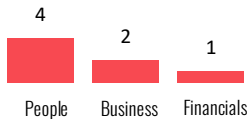
FAIR VALUE RANGE

BEAR	BASE	BULL
1.4	2.5	4.2

ACTI VERSUS OMXSPI



REDEYE RATING



KEY STATS

Ticker	ACTI.ST
Market	Small Cap
Share Price (SEK)	1,1
Market Cap (SEKm)	240
Net Debt (SEKm)	NA
Free Float (%)	70
Avg. daily volume ('000)	250

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Key Catalysts

Tasquinimod

The combination arm of tasquinimod (with ixazomib, lenalidomide, and dexamethasone) in multiple myeloma (MM) is ongoing. We should expect to see results from the dose-escalation part of the trial during 2022, while results from the expansion arm might be available in 2023. Positive results would be a clear value trigger. Our bull case of SEK 4.2 is based on the assumption of a clearly positive interim efficacy readout leading us to increase the probability of success in phase II (to 40 percent up from 24 percent).

Laquinimod

The first patient was dosed with laquinimod in December 2021. The phase I part of the trial should be comparatively quick. A single dose with up to four dose levels will first be tested as eye drops. Next, it will be administered daily for 14 days at a dose defined in the single-dose part. The trial should be finished by H2 2022. We assume a positive read-out in our bull-case.

Naptumomab

We hope to see more phase Ib data for naptumomab from the ongoing clinical trial in solid tumors in combination with durvalumab and obinutuzumab, showing the effect on anti-drug antibodies (ADA) through the addition of obinutuzumab. We hope to see an MTD readout in 2022. Results so far imply that it should have been successful, as does the initiation of the phase IIa trial in NSCLC in combination with docetaxel and obinutuzumab.

- Phase IIa data from the trial in NSCLC in combination with docetaxel is expected in 2023.
- We could see the initiation of the phase IIa part with naptumomab and durvalumab in solid tumours in 2022. A phase II readout might then be possible later in 2023.

Raising of capital

Cash at hand (SEK 53.1m at 31-12-2021) will likely fund Active Biotech through 2022 (or at least into Q4 2022). A rights issue could take place towards H2 2022.

Investment Thesis

Repurposed, well-studied compounds reduce risks. While Active Biotech's projects have a checkered history, all have demonstrated some level of clinical efficacy. Its internal projects are first-in-class, have well-documented safety profiles, and generally allow for easy administration. Data from previous trials come from several hundred to more than a thousand patients (depending on the drug), which can be referenced in the upcoming clinical trials, reducing the clinical risk and potentially cutting costs. Laquinimod's chosen area, ophthalmology, has, furthermore, a historically high likelihood of approval compared to many other disease areas.

Three shots on goal. If Active Biotech can bring just one drug to market, an investment in the share will likely be a success. Furthermore, Active Biotech only has to finance two shots, as naptumomab is outlicensed to NeoTX, which is paying for the compound's development (in two clinical trials). The deal involves total payments of up to USD 71m to Active Biotech, as well as progressive royalties. NeoTX has a strategic collaboration with AstraZeneca, who provide durvalumab free of charge, which provides some external validation of naptumamb.

Drug development credentials. The Active Biotech organization has more than 20 years of history in developing drugs that modulate the immune system. Alone and together with partners, it has conducted some 30 clinical trials. Historically, Active Biotech has been

successful in striking partnerships with larger partners, including Teva and Ipsen. The name "Active Biotech" could still be a door-opener among potential partners.

Counter-Thesis

Early-stage projects. Active Biotech's project portfolio is still at an early stage of development. Consequently, there is a high risk of attrition, and timelines are still uncertain. Moreover, Active Biotech and its partner NeoTX are targeting competitive markets in cancer treatment.

No significant tumor shrinking in phase I monotherapy. Tasquinimod was tested up to 1 mg in MM in the monotherapy arm in the ongoing clinical phase I/IIa trial. There was some activity in the form of stable disease, but no tumor shrinking in the admittedly very sick late-stage patients. The question is whether combination with ixazomib, lenalidomide, and dexamethasone will offer a powerful enough synergy in somewhat healthier patients. Furthermore, the attractive accelerated approval path after a phase II trial is closed. Now a phase III trial in combination therapy will have to be performed. This increases the risk and timeline in the project. We believe it is likely that a partner will want to see proof-of-concept from a phase IIb trial before a significant licensing deal can be made.

Diluation risk. Additional funds will be needed to fund the company through 2023. Assuming success in the ongoing trials, Active Biotech will likely need to raise more money to finance a potential phase II with laquinimod, and then then a phase IIb trial with tasquinimod. This could lead to dilution for investors who are unwilling or unable to defend their position. At the same time, positive results with laquinimod and tasquinimod could be strong share catalysts.

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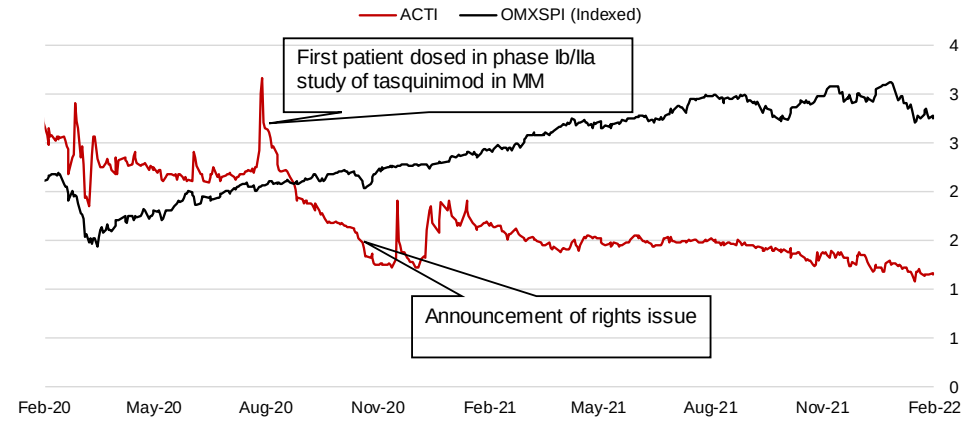
Share Performance and Ownership

The Active Biotech share has underperformed the Stockholm All-Share Index (OMXSPI) over the past two years. In fact, the share has had a steep decline since the most recent peak in 2010-2011. The share price declined following the announcement of a rights issue in November 2020, but it recovered after the issue was fully subscribed. Since the beginning of 2021, there has been a gradual decline in the share price again though. The clinical trial with tasquinimod in MM has taken slightly longer than expected. No conclusive evidence of a tumor shrinking effect was presented in the monotherapy arm during 2021, leading to the discontinuation of the monotherapy expansion cohort. This means that the accelerated approval pathway as a monotherapy has to be abandoned. A favorable safety profile was confirmed, however. The successful development of a new eye-drop formulation of tasquinimod and the initiation of a phase I trial with this in December 2021 had no impact on the share price, nor has the continued development of naptumomab by Active Biotech's partner NeoTX. It seems that more substantive news, such as a new licensing deal or efficacy data, might be needed to move the share.

Active Biotech's share price



Source: Redeye Research

The shareholder list is dominated by Mats Arnhög, who has held shares in Active Biotech for more than 20 years. Peter Thelin, who is a board member, owns two percent of the shares. Otherwise, only institutional investors have an ownership surpassing one percent. Active Biotech has an unusually large proportion of institutional and professional ownership for its market capitalization, a fact attributable to its history.

Active Biotech's shareholders

Rank	Shareholder	Total Shares	Share Capital
1	Mats Arnhög & bolag	57 002 107	26%
2	Handelsbanken Liv Försäkring AB	14 574 607	6,7%
3	Avanza Pension	14 508 563	6,7%
4	Fjärde AP-fonden	5 863 086	2,7%
5	Tredje AP-fonden	5 840 583	2,7%
6	Peter Thelin	4 452 783	2,0%
7	SEB-Stiftelsen	2 757 690	1,3%
8	Vidarstiftelsen	2 618 538	1,2%
9	Jacob Rajendram	2 000 000	0,9%
10	Carl Rosvall	1 962 690	0,9%
11	Stävie Förvaltnings AB	1 928 000	0,9%
12	Madeleine Lennhammer	1 739 801	0,8%
13	Nordnet Pensionsförsäkring	1 480 286	0,7%
14	T-Bolaget AB	1 352 074	0,6%
15	Ann-Louise Olander	1 293 200	0,6%
	Total 15 Largest Shareholders	**119 374 008**	**55%**
	Others	98 597 712	45%
	Total Number of Shares	**217 971 720**	**100%**

Source: Holdings.com

Events Since Initiation of Coverage

Active Biotech completed a rights issue of SEK 76m on January 26, 2021. The issue was oversubscribed, and the company did not utilize any guarantee undertakings. According to holdings.se, Nordstjernan, a significant seller during the fall of 2020, had almost divested all of its Active Biotech ownership by December 31, 2020.

During Q1 2021, Active Biotech's partner NeoTX had an IND approved for naptumomab, allowing it to initiate a phase IIa trial in the US. NeoTX plans a combination trial with chemotherapy (docetaxel) in lung cancer patients who have progressed after previous treatment with checkpoint inhibitors. We believe this indication is a promising add-on/backup opportunity for naptumomab because it represents a large and growing (albeit hard to treat) population owing to the success of the Keytruda+chemotherapy regimen in first-line treatment. Naptumomab is also being tested by NeoTX in combination with a checkpoint inhibitor in solid tumors in the phase I part of a phase I/II trial.

At a KOL seminar in July 2021, NeoTX commented that it had observed early indications of anti-tumoral activity in the phase Ib trial investigating naptumomab in combination with the checkpoint inhibitor durvalumab in pre-treated solid tumor cancer patients. NeoTX also commented that it had been able to control unwanted anti-drug antibody effects through pre-treatment with anti-CD20 antibodies. We consider the comments from NeoTX to be encouraging.

The development plan for laquinimod changed during 2021; Active Biotech no longer plans for a separate proof of concept phase II monotherapy trial for the oral formulation in uveitis that had previously been communicated. Instead, Active Biotech is eyeing a phase II trial including oral and topical administration and the combination of both. It is seeking an academic partner for the phase II trial, planned to start in 2023. While we see a clear rationale for combination therapy, the new plan suggests a delay to the start of efficacy studies and, consequently, to value-driving news flow for the project.

On October 3, 2021, Active Biotech announced results from the phase I trial in multiple myeloma (MM). A treatment of 1 mg per day was reached after a one-week run-in of 0.5 mg daily, which is in line with earlier clinical trials with tasquinimod. That two out of ten patients achieved significant periods of stable disease indicates that the drug affects the disease, though we had hoped for formal objective responses. All patients were resistant to existing modes of therapy as they had had, in median, eight prior treatments. Due to the somewhat lackluster results from the phase I part, the company will not initiate a monotherapy expansion cohort but will instead proceed directly to the dose-escalation combination treatment part with IRd in nine to 12 patients. IRd is a triplet combination of proteasome inhibitor ixazomib, lenalidomide, and dexamethasone.

On October 20, 2021, NeoTX initiated a phase IIa trial in non-small cell lung cancer (NSCLC) in combination with the chemotherapy treatment docetaxel in the second-line setting. Initial results indicate that the issue with anti-drug antibodies (a type of drug resistance) can be handled (through B-cell suppression).

On November 9, 2021, NeoTX presented new results with naptumomab at SITC 2021 and published an abstract. CAR-T cells have shown limited effect against solid tumors. In a preclinical in-vitro study, NAP was combined with Her2-CART-T cells. CAR-T cells grown in the presence of naptumomab became more potent. The combination of CAR-T and naptumomab resulted in a synergistic killing effect on the tumor cell line. This could be of interest to pharmaceutical companies looking to potentiate their CAR-T products.

The phase I trial with laquinimod eye drops was initiated in early December 2021. It will include 42 patients in a single-dose and multiple-dose ascending study. Endpoints relate to safety and pharmacokinetics, including eye toxicity.

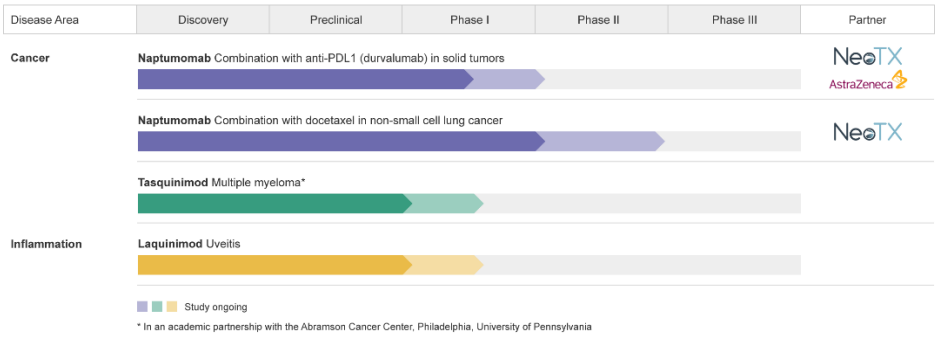
On February 7, the inclusion of the first patient in the combination part of the phase I/IIa trial with tasquinimod and IRd (ixazomib, lenalidomide, and dexamethasone) in MM was announced. The patients that will be recruited to the phase IIa part should also had fewer prior lines of treatment and, we believe, be less refractory compared to the monotherapy part. This should give tasquinimod a better opportunity to prove itself compared to the monotherapy part.

On February 9, Active Biotech enters into a global patent license agreement with Oncode Institute for tasquinimod in myelofibrosis.

Projects

Active Biotech has a long history, having been founded in 1998 as a spin-off from Pharmacia. Both tasquinimod and laquinimod have previously been out-licensed and returned – tasquinimod to Ipsen in prostate cancer and laquinimod to Teva in multiple sclerosis and Huntington's disease. Both substances have undergone phase III trials and accumulated large amounts of data. Since the cancellation of these programs, Active Biotech has downsized and focused its resources in the wake of a strategic overview that led the company to change direction at the beginning of 2020. Its focus is now on three projects: tasquinimod in multiple myeloma, laquinimod in uveitis, and naptumomab – out-licensed to NeoTX, which has been developing it since 2016 – in solid cancers.

Project pipeline

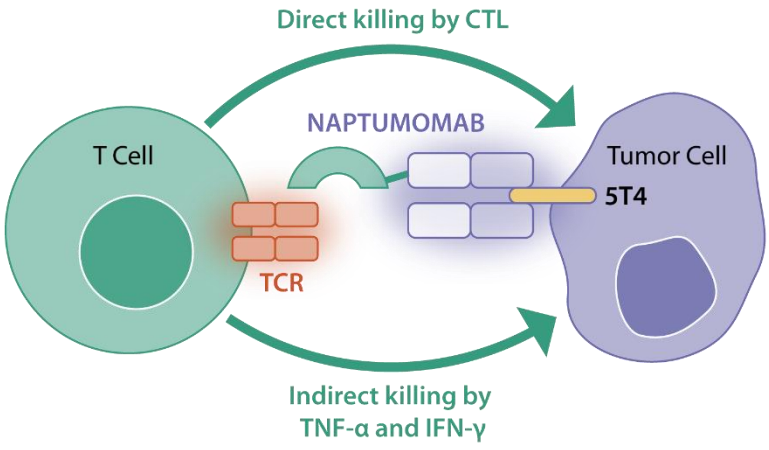


Source: Active Biotech

Naptumomab

Naptumomab estafenatox (naptumomab) is a therapeutic fusion protein that consists of the Fab fragment of a tumor-targeting antibody, combined with a modified bacterial superantigen (staphylococcal enterotoxin A, or SEA). The Fab fragment consists of binding sites that bind to 5T4, which is overexpressed on many tumors, while the superantigen binds to T-cell receptors, promoting direct killing by cytotoxic T lymphocytes (CTL or $CD8^+$ T-cells).

Mode of action of naptumomab



Source: Active Biotech

The activated T-cells also emit cytokines (TNF-α and IFNγ) that contribute to inflammation and the recruitment and activation of other immune cells to the environment, which should increase the immune response even further.

Active Biotech initiated a phase III trial with 513 patients in metastatic renal cell carcinoma in 2006, but this did not meet its primary endpoint of overall survival. Further investigation has shown that previous circulating antibodies against bacteria may have had a negative effect on the treatment and that pre-selection of individuals with low levels might show better results. Naptumomab has been under development by Israel's NeoTX since 2016. The total deal value amounts to USD 71m and is contingent upon achievement of clinical, regulatory, and commercial milestones. Active Biotech is also entitled to progressive, double-digit royalties on its net sales of naptumomab.

NeoTX is testing the candidate in two clinical trials:

- Phase Ib/II in advanced solid tumors in combination with PD-L1 inhibitor durvalumab (50 patients), now in the phase Ib part.
- Phase IIa in combination with docetaxel in patients with NSCLC (35 patients) – the primary endpoint is ORR.

Durvalumab is provided free of charge by AstraZeneca. A major issue with naptumomab has been anti-drug antibodies (ADA) – the antibodies that neutralize the drug itself. In the ongoing phase Ib/II trial in solid tumors, the protocol was changed so that a pre-treatment with obinutuzumab could be tested. This is an anti-CD20 monoclonal antibody. Its mode of action is B-cell depletion. B-cells develop into plasma cells that produce antibodies. The CD20 receptor is unique for B-cells (although not plasma cells). Directed targeting of B-cells will reduce antibody production. An obvious side effect is an increased risk for certain infections, plus potential reactivation of hepatitis B. The problem with ADA now seems to be under control, but the full phase Ib data have not yet been released. Obinutuzumab is also being given as a pre-treatment to the patients in the phase IIa trial in NSCLC.

CAR-T

According to the recently published preclinical data at SITC, there might also be potential to develop naptumomab for CAR-T therapy, with the aim of improving its efficacy in solid tumors. CAR-T cell therapy usually has limited effect on solid rather than hematological tumors because CAR-T cells circulate in the bloodstream and lymphatic system. CAR-T cells – short for chimeric antigen receptor T-cells – are T-cells that have had a receptor added to them (genetically) outside of the body. This is an interesting application that amounts to some positive optionality for the Active Biotech share, but it is too early and too uncertain for us to include it in our valuation at this stage.

Tasquinimod

Tasquinimod is being developed for multiple myeloma (MM), a cancer of antibody-producing plasma cells that enter the bone marrow and displace other white blood cells. Active MM is preferentially treated with stem cell transplantation, used in conjunction with high-dose chemotherapy that destroys the cells in the bone marrow before transplantation. Weaker, often older, patients are often not eligible for transplantation, however.

All patients receive induction therapy as first-line treatment (before a possible stem cell transplantation). In the US, the triplet combination VRd (Velcade + Revlimid + dexamethasone) is the preferred induction therapy. In the EU, the preferred induction therapy regimens are the Dara-VTD quadruplet (Darzalex + Velcade + Thalomide + dexamethasone) and the VRd triplet. Revlimid (an improved analogue of thalidomide) is the mainstay of most treatments from the first line onwards until resistance develops. In progressive or relapsed

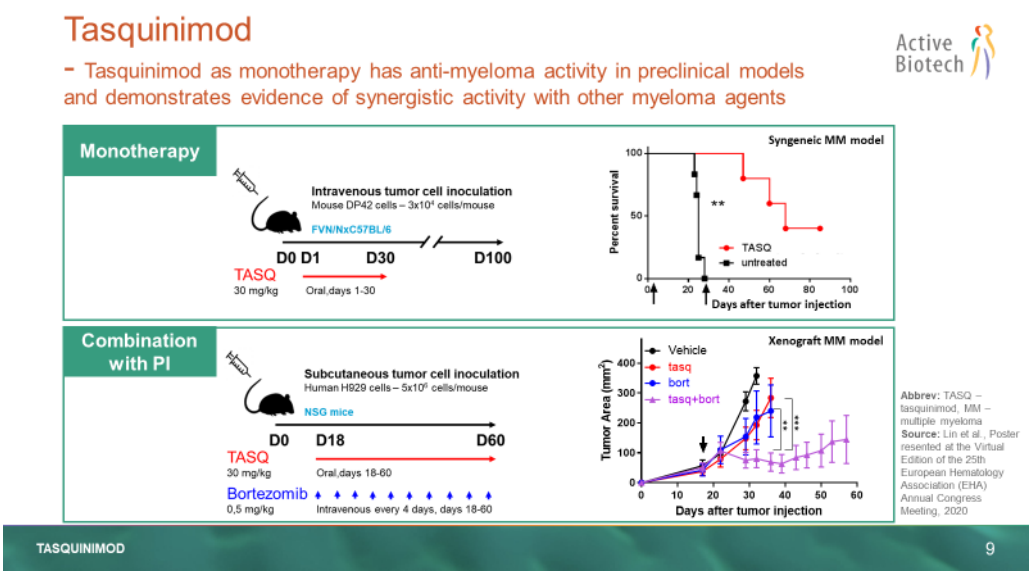
MM, there is a wide variety of regimens. Datamonitor lists seven preferred regimens in the US for the second to fourth lines and 12 for the second line or later in the EU. The all-oral therapy Ninlaro + Revlimid + dexamethasone (Ixa-Rd) is one of these preferred regimens. Tasquinimod is now being developed as an add-on to this treatment, making it an all-oral quadruplet therapy in the second to fourth lines (in the US).

Relapsed MM is a large indication. According to various estimates, the drug-treated population in the second-line treatment and beyond is between 40,000 and 80,000 in the US alone. Treatment is characterized by the development of resistance and the need to switch therapy due to repeated relapses – the patient tests various treatments until one is found that works and then switches when resistance to this sets in.

The results from the single agent dose-escalation arm were published in Q4 2021. They showed that two out of ten patients achieved significant periods of stable disease. Data from recently approved agents and pipeline projects show response rates exceeding 25 percent in advanced RRMM settings, although many of these drugs have severe side effects. We believe that the benchmark for tasquinimod as a single agent would have been a tumor response in 20-25 percent of patients. Stable disease is only equivalent to tumors not growing, and the response rate (defined as tumor shrinking) in the phase I arm of tasquinimod consequently had a response rate (ORR) of 0. It should be noted, however, that the patients enrolled had exhausted all other options, were resistant to all therapies and in bad physical shape, which may explain why the ORR was 0. A planned expansion cohort for the monotherapy arm was cancelled, which is logical considering the somewhat lackluster results.

Tasquinimod works as an immuno-modulator that inhibits S100A9 and has the ability to block tumor sustaining signals from the bone marrow microenvironment. It represents a new class of drugs in MM with a new mode of action. There four current main classes: immunomodulatory imides (IMiDs), proteasome inhibitors (PI), monoclonal antibodies and alkylating agents. Tasquinimod has shown preclinical synergies with Revlimid, Velcade and Ninlaro (ixazomib). The results from the pre-clinical study of tasquinimod with Velcade (bortezomib) is shown in the graph below. We note that the dose was comparatively high at 30 mg/kg. Both Velcade and Ninlaro are proteasome inhibitors. Ninlaro (ixazomib) is used in the ongoing clinical trial with tasquinimod, as is Revlimid. The combination of all three therapies (plus the corticosteroid dexamethasone) could be strongly synergetic.

Proof of Principle in Preclinical Models of Multiple Myeloma: tasquinimod monotherapy ("tasq") (top) and tasquinimod in combination with proteasome inhibitor Velcade / bortezomib ("tasq+bort")

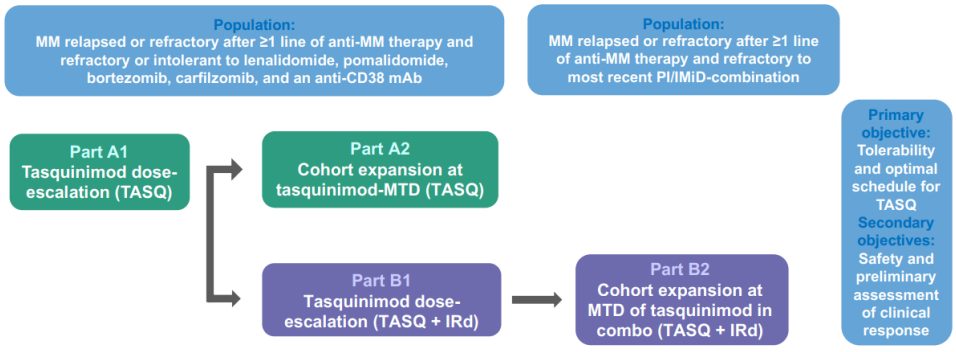


Source: Active Biotech

Furthermore, tasquinimod has previously demonstrated biological activity in human cancer patients. In a large phase III trial (NCT01234311) in metastatic castration-resistant prostate cancer with 1,245 patients, a statistically significant improvement in FPS was demonstrated at 7.0 months with tasquinimod versus 4.4 months with placebo. No improvement in overall survival was demonstrated, however.

The phase IIa combination trial that began in early 2022 will consist of two parts: a dose escalation of TASQ + Ixa-Rd-dex, and an expansion arm at the maximum tolerated dose (which could be up to 1 mg if the part I dose can be maintained). Results from this expansion arm will likely decide the future direction of this project. The patients that will be recruited to the phase IIa part should have had fewer prior lines of treatment and, we believe, be less refractory. This should give tasquinimod a better opportunity to prove itself compared to the phase Ia monotherapy part. There might be an advantage in treating patients with tasquinimod in earlier setting and as a combination treatment.

Tasquinimod phase I/II in MM (note that part A2 has been cancelled)



Source: Active Biotech

In our view, there seems to be good rationale and evidence for believing that tasquinimod has a synergetic effect in MM. At the same time, a good safety profile is very important in a combination treatment with four drugs. We believe this should be a strong point in tasquinimod's favor. Part B2 of the expansion arm should clarify the efficacy characteristics of the quad combination and hopefully some clues can be gathered from part B1, which is focused on safety. Triplet therapies generally have high ORRs in early lines. The results from VRd (Velcade + lenalidomide and dexamethasone) and KRd (Kyprolis + lenalidomide and dexamethasone) are shown below.

Clinical Results Proteasome Inhibitor Triplets

Proteaseome Inhibitors						
Treatment	Proteasome Inh.	Prior Lines of therapy	ORR	mPFS	mOS	SAE vs control
IRd	Ixazomib	1	78%	20.6	NR	-2%
KRd	Carfilzomib	2	87%	26.3	NR	3%

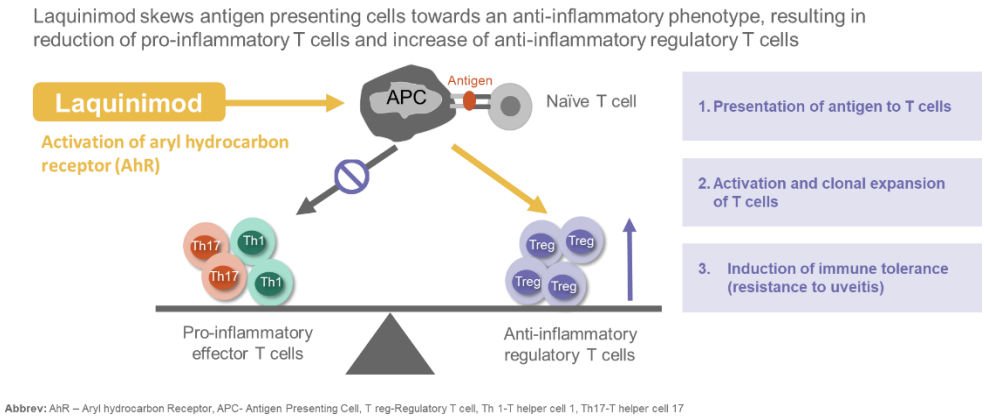
Source: Redeye. ORR: Objective Response Rate. mPFS: median Progression-Free Survival. mOS: median Overall Survival. SAE: Serious Adverse Events.

In our last update, we assumed a scenario in which tasquinimod enters the market as a monotherapy in later lines through an accelerated approval on the basis of a phase IIb trial. This way to the market is not open for tasquinimod as combination treatment. It will almost certainly have to go through a phase III trial. We expect Active Biotech to have to sponsor a phase IIb trial, with around 100 patients, before a partner can be found who will sponsor the phase III trial. We expect that the conditions for such a deal would be slightly less favorable to Active Biotech, with a smaller upfront payment and lower royalties, as it would be further from the market. From a cost perspective, however, little changes, as we still assume that Active Biotech will have to sponsor a phase IIb trial.

Laquinimod

Laquinimod was previously a candidate in multiple sclerosis (MS) and has been tested in more than 5,000 patients. It is a small molecule immuno-modulator that targets the aryl hydrocarbon receptor (AhR), which is present on antigen-presenting cells (APCs), the most important of which are dendritic cells. Laquinimod's mode of action is phenotypic regulation of APCs from pro-inflammatory into tolerogenic types – in other words, it makes the cells transform into types that induce regulatory T-cells. Regulatory T-cells dampen inflammation by inhibiting immune cells, such as cytotoxic T-cells. Pro-inflammatory APCs, on the other hand, activate the adaptive immune system (cytotoxic T- and B-cells) and directs it towards a target. Active Biotech has produced a new formulation of laquinimod with topical eye-drop administration rather than oral. It intends to test both the oral and the topical formulation in the potential upcoming phase II trial.

Laquinimod's mechanism of action

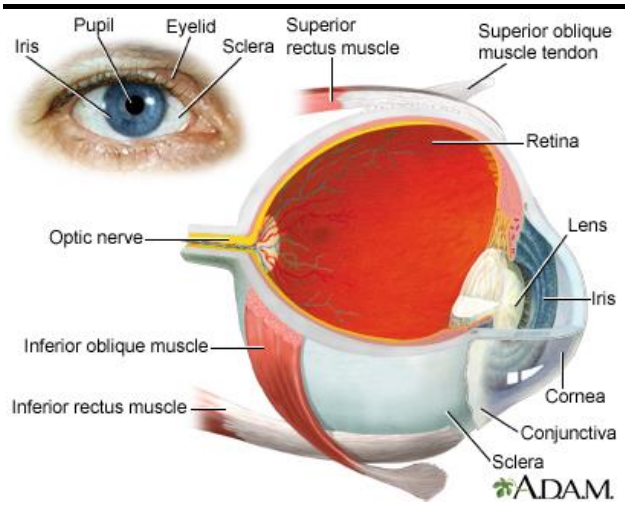


Source: Active Biotech

Laquinimod is being developed as a treatment for uveitis, a type of eye inflammation. The substance reduced brain atrophy in earlier MS trials, including through an effect on microglia. Furthermore, there is evidence for laquinimod's capacity to reduce inflammation in a preclinical model of autoimmune uveitis. As the eyes are an extension of the central nervous system, it appears, at first sight, logical to repurpose a drug for MS (an autoinflammatory disease) for inflammatory eye disease.

The eye is made up of three layers plus fluids. The fluids are contained in two spaces: the vitreous humour (the largest part of the eye) inside the three combined layers, and the aqueous humour between the cornea and the lens. The outer layer or tunic consists of the sclera (the white of the eye) and cornea, which are fibrous and tough. The uvea is the middle layer consisting of three parts (choroid, ciliary body, and the iris) and is vascular. The innermost layer is the retina, which registers light.

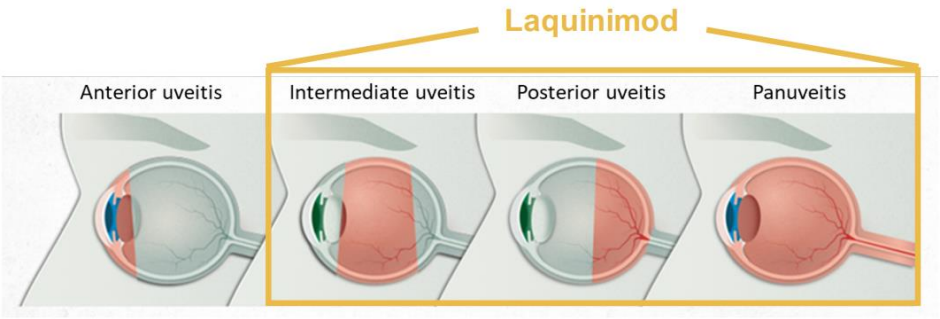
Overview of the eye



Source: National Library of Medicine

Uveitis is an inflammation of the uvea. Infections sometimes cause uveitis, but the non-infectious, or idiopathic, type is more common. Inflammation of the uvea is defined according to its location: in the front, middle, back, or in its entirety. Posterior uveitis is the most dangerous type as it can damage the retina or cause glaucoma (damage to the optic nerve). Uveitis in the front of the eye is the more common and milder form.

Uveitis diagnoses



Source: Active Biotech

Uveitis is the third most common cause of blindness worldwide. It is estimated by the Uveitis Foundation that 2.4 million people worldwide suffer from uveitis. Despite advances, the prevalence of blindness as a result of uveitis has not decreased in the last 30 years. Around 10 percent suffering from the condition are expected to eventually become blind. Blindness occurs due to glaucoma, retinal damage, or macular edema. Around 40 percent of non-anterior uveitis patients develop macular edema.

Initial treatment usually consists of high-dose oral anti-inflammatory corticosteroids. If these are not satisfactory, patients might require corticosteroid injections in or around the eye. Ozurdex is an extended-release biodegradable ocular implant containing dexamethasone (a potent corticosteroid) that can be used for difficult cases. However, long-term treatment of steroids in high doses is associated with severe side effects. For refractory patients, immuno-suppression or anti-TNF antibody therapy (such as Humira/adalimumab) are options.

According to Active Biotech, around 300,000 patients in the seven major markets receive treatment for non-infectious non-anterior uveitis. Laquinimod has the potential to be used as an add-on treatment to steroids for these patients in the first line. 125,000 of these patients do not respond to treatment with corticosteroids and are the target population for laquinimod in the second line.

Laquinimod has been reformulated as eye drops. The phase I trial of these started in December 2021. It will include 42 subjects (healthy volunteers) in a standard phase I single-dose and multiple-dose ascending study. Endpoints relate to safety and pharmacokinetics. The results from the trial are scheduled to be available by H2 2022. A phase II trial could likely start in 2023, assuming that financing is in place by then. The phase II trial could have three arms with a topical and an oral arm and a combination of the oral version and topical versions in a third arm.

IP and Market Protection

Patent protection is a significant consideration in drug repurposing. Often, as in the case with Active Biotech, the remaining original substance patent life is short or has expired. Applying for method-of-use patents in new indications is a common strategy. However, this requires that further medical use is indeed new and non-obvious (e.g., has not been described in scientific literature), which leaves the new indications more vulnerable to challenges. New formulation patents are another way to fight off potential generic competition.

Pursuing an orphan indication is a lucrative opportunity, if feasible, since it provides market protection for seven and ten years of marketing protection in the US and the EU, respectively, following approval.

Tasquinimod – clear orphan drug opportunity

The original substance patent for tasquinimod has expired. As MM is an orphan indication, Active Biotech will benefit from market exclusivity if no generic drug reaches the market first, which seems highly unlikely. Also, there are method-of-use-patents valid until 2035 and a recently filed patent application protecting the use of tasquinimod in combination with existing therapies, which has the potential to protect the use of tasquinimod until 2042 in multiple myeloma. The FDA has granted Orphan Drug Designation (ODD) to tasquinimod in MM. Active Biotech has not yet applied for an ODD in Europe, but we believe this could happen when the company has gathered clinical data from the ongoing clinical trial. In February 2022, Active Biotech licensed the patent rights for tasquinimod in myelofibrosis, a rare blood cancer, from Oncode Institute in Utrecht. This expands tasquinimod's potential in hematologic cancers.

Laquinimod – new formulation could play a crucial role

The original patent for laquinimod expired in 2019. Former partner Teva invested in several method-of-use patent applications, including ophthalmology and inflammatory bowel disease. If granted, the use in ophthalmology patent application expires in 2033. Active Biotech has developed a topical formulation for administration in the eyes. We assume that the company will be working on a new patent application for the formulation. ODD could be a possibility for the US market. However, we would argue that it is a borderline case.

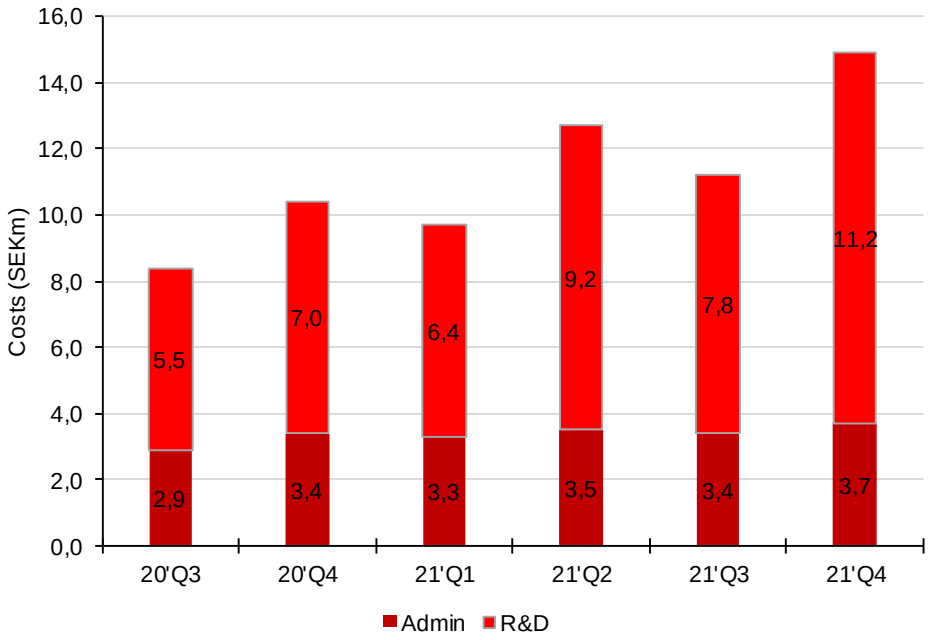
Naptumomab

The original patent for naptumomab expires in 2022. NeoTX manages the patent portfolio and has applied for a method-of-use patent for the combination with checkpoint inhibitors which is approved in the US and will expire in 2036.

Financial Overview

As of the end of Q4 2021, Active Biotech had a cash position of SEK 53m. As can be seen in the graph below, operating expenses (largely similar to the company's cash flow) have been around SEK 11m per quarter. We can see a rising trend, which correlates with the projects' advancement. If this trend continues, Active Biotech's cash position should last it through 2022 (or at least into Q4). An equity issue during 2022 is likely in order to finance the projects for 2023.

Active Biotech: Operating Costs



Source: Redeye Research

Valuation

Assumption adjustments for tasquinimod

We make some changes to the probability of success for tasquinimod based on reference probabilities from Pharmapremia following the results from the phase I monotherapy trial. We raise the probability of phase I to 90 percent (75). We adjust the probability of phase II down from 35 percent in our previous analysis to the average value of 24 percent. This represents an LOA of 12 percent (15). We no longer expect tasquinimod to be approved after a phase II trial based on an accelerated approval. We still assume that a phase IIb will be undertaken by the company, but that a phase III will have to be done by a partner. We adjust peak sales to USD 390m (450) and forecast a launch as combination therapy in 2028 (2026). We assume the same total deal value of USD 580m for tasquinimod, but we reduce the upfront by about half and reduce the royalty rate to 15 percent (20), as the stage when the assumed out-licensing can take place is earlier (phase III ready) compared to our initial assumptions (NDA ready).

Assumption adjustments for naptumomab and laquinimod

We make smaller adjustments to naptumomab and laquinimod. We raise the likelihood of approval for naptumomab to 10 percent (9) and laquinimod to 20 percent (15) thanks to clinical progress. The LOA of laquinimod is much higher compared to the other projects because ophthalmology projects are more likely to get approved. The LOA, based on statistics, in ophthalmology is almost twice that of oncology from phase I to market approval. We extended the development timeline of laquinimod and naptumomab by one year. We now assume a launch for both candidates in 2027 (2026). We assume the same total of USD 125m for laquinimod, while naptumomab is already out-licensed for up to USD 71m.

General

- We raise the WACC to 14 percent (13) mainly due to a more challenging market environment.
- Active Biotech has a substantial loss carryforward, which shields future royalty and milestones payments from taxes.

Valuation of Active Biotech

Sum-of-the-parts Valuation, Active Biotech						
Project	**Indication**	**Peak Sales (USDm)**	**LOA**	**Royalty**	**Launch**	**rNPV (SEKm)***
Tasquinimod	Multiple Myeloma	390	12%	15%	2028	247
Naptumomab	Solid tumors	560	10%	15%	2027	176
Laquinimod	Ophthalmology	230	20%	15%	2027	214
Total		1180				637
	Shared costs, incl. taxes					-136
	Net cash, Q1'22E					53
	Total					**554**
	Shares outstanding (mil.)					218
	Value Per Share					**2.5**

* Based on the assumption of an average SEK/USD of 9.0

Source: Redeye Research

Bear Case: SEK 1.4

- Development of tasquinimod is cancelled owing to unfavorable results in the phase I combination trial.

Base Case: SEK 2.5

- For laquinimod, we pencil in a partnering deal in 2024 following completion of a phase II trial in uveitis.
- For tasquinimod, we assume an LOA of 12 percent and peak sales of USD 390m in MM as combination therapy.

Bull Case: SEK 4.2

- Tasquinimod shows favorable results in the phase I/IIa combination trial. We raise the probability of success for the phase II trial to 40 percent.
- We assume that laquinimod completes phase I successfully.

Catalysts

Results from dose escalation with tasquinimod in combination cohort

During 2022, we expect the results from the dose escalation in the combination arm of tasquinimod (with ixazomib, lenalidomide and dexamethasone).

IMPACT				
Downside		Upside		Time Frame
Significance	Likelihood	Significance	Likelihood	
Moderate	Unlikely	Moderate	Likely	Short

Results from laquinimod's phase I

We expect results from laquinimod's phase I trial in the second half of 2022.

IMPACT				
Downside		Upside		Time Frame
Significance	Likelihood	Significance	Likelihood	
Moderate	Unlikely	Moderate	Likely	Short

Naptumomab

We might see a read-out from the MTD cohort of naptumomab with durvalumab during 2022.

IMPACT				
Downside		Upside		Time Frame
Significance	Likelihood	Significance	Likelihood	
Moderate	Possible	Moderate	Possible	Short

Summary Redeye Rating

The rating consists of three valuation keys, each constituting an overall assessment of several factors that are rated on a scale of 0 to 1 points. The maximum score for a valuation key is 5 points.

Rating changes in the report

People: 4

Management consists of a small, experienced team with extensive experience in clinical and business development. The CEO was previously Chief Scientific Officer at the company and led the research and clinical development of Active Biotech's projects in neurodegenerative diseases and cancer. The board's composition has changed significantly since 2018, having been extended by two members who bring extensive and relevant international bio-pharma experience. We view these steps as positive and believe an active and experienced board is instrumental in supporting the new strategic direction of Active Biotech.

Business: 2

Active Biotech is a clinical-stage biotech, developing first-in-class treatments in oncology and inflammatory eye disorders. Current commercial and academic partnerships enable low-cost development of tasquinimod (multiple myeloma) and naptumomab (solid tumors).

Financials: 1

Active Biotech has never generated any income from product sales and has not been profitable on an annual basis since 2001. The company raised SEK 75m before costs for January 2021 in a rights issue. We believe the capital raise will fund operations through 2022.

	2020	2021E	2022E	2023E
INCOME STATEMENT				
Revenues	7	0	0	0
Cost of Revenues	0	0	0	0
Gross Profit	7	0	0	0
Operating Expenses	39	46	55	76
EBITDA	-32	-46	-55	-76
Depreciation & Amortization	0	0	0	0
EBIT	-32	-46	-55	-76
Net Financial Items	0	0	0	0
EBT	-32	-46	-55	-76
Income Tax Expenses	0	0	0	0
Non-Controlling Interest	0	0	0	0
Net Income	-32	-46	-55	-76
BALANCE SHEET				
Assets				
Current assets				
Cash & Equivalents	26	60	5	-71
Inventories	0	0	0	0
Accounts Receivable	0	0	0	0
Other Current Assets	4	0	0	0
Total Current Assets	30	60	5	-71
Non-current assets				
Property, Plant & Equipment, Net	0	0	0	0
Goodwill	0	0	0	0
Intangible Assets	0	0	0	0
Right-of-Use Assets	2	1	1	1
Shares in Associates	0	0	0	0
Other Long-Term Assets	0	0	0	0
Total Non-Current Assets	2	1	1	1
Total Assets	32	61	5	-70
Liabilities				
Current liabilities				
Short-Term Debt	1	10	10	10
Short-Term Lease Liabilities	0	0	0	0
Accounts Payable	3	0	0	0
Other Current Liabilities	5	0	0	0
Total Current Liabilities	9	10	10	10
Non-current liabilities				
Long-Term Debt	1	0	0	0
Long-Term Lease Liabilities	0	0	0	0
Other Long-Term Liabilities	0	0	0	0
Total Non-current Liabilities	1	0	0	0
Non-Controlling Interest	0	0	0	0
Shareholder's Equity	22	51	-4	-80
Total Liabilities & Equity	32	61	5	-70
CASH FLOW				
NOPAT	-32	-46	-55	-76
Change in Working Capital	-2	-4	0	0
Operating Cash Flow	-32	-40	-55	-76
Capital Expenditures	0	0	0	0
Investment in Intangible Assets	0	0	0	0
Investing Cash Flow	0	0	0	0
Financing Cash Flow	0	73	0	0
Free Cash Flow	-32	-40	-55	-76

	2020	2021E	2022E	2023E
CAPITAL STRUCTURE				
Equity Ratio	0,7	0,8	-0,8	1,1
Debt to equity	0,1	0,2	-2,2	-0,1
Net Debt	-24	-50	5	81
Capital Employed	23	51	-4	-80
Working Capital Turnover	-1,7	NA	NA	NA
GROWTH				
Revenue Growth	-20%	-100%	NA	NA
Basic EPS Growth	NA	NA	NA	NA
Adjusted Basic EPS Growth	NA	NA	NA	NA
PROFITABILITY				
ROE	-85%	-125%	-238%	179%
ROCE	-142%	-90%	1275%	95%
ROIC	661%	2297%	NA	NA
EBITDA Margin (%)	-482%	NA	NA	NA
EBIT Margin (%)	-482%	NA	NA	NA
Net Income Margin (%)	-481%	NA	NA	NA
VALUATION				
Basic EPS	NA	NA	NA	NA
Adjusted Basic EPS	NA	NA	NA	NA
P/E	NA	NA	NA	NA
EV/Revenue	37,4	NA	NA	NA
EV/EBITDA	NA	NA	NA	NA
EV/EBIT	NA	NA	NA	NA
P/B	12,4	5,4	NA	NA

SHAREHOLDER STRUCTURE	**CAPITAL %**	**VOTES %**
Mats Arnhög & bolag	26,2%	26,2%
Avanza Pension	6,8%	6,8%
Handelsbanken Liv Försäkring AB	6,6%	6,6%
Fjärde AP-fonden	2,7%	2,7%
Tredje AP-fonden	2,7%	2,7%

SHARE INFORMATION	
Reuters code	ACTI.ST
List	First North
Share price	1,14
Total shares, million	217,972

MANAGEMENT & BOARD	
CEO	Helen Tuvesson
CFO	Hans Kolam
Chairman	Michael Shalmi

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Redeye Rating and Background Definitions

Company Quality

Company Quality is based on a set of quality checks across three categories; PEOPLE, BUSINESS, FINANCE. These are the building blocks that enable a company to deliver sustained operational outperformance and attractive long-term earnings growth.

Each category is grouped into multiple sub-categories assessed by five checks. These are based on widely accepted and tested investment criteria and used by demonstrably successful investors and investment firms. Each sub-category may also include a complementary check that provides additional information to assist with investment decision-making.

If a check is successful, it is assigned a score of one point; the total successful checks are added to give a score for each sub-category. The overall score for a category is the average of all sub-category scores, based on a scale that ranges from 0 to 5 rounded up to the nearest whole number. The overall score for each category is then used to generate the size of the bar in the Company Quality graphic.

People

At the end of the day, people drive profits. Not numbers. Understanding the motivations of people behind a business is a significant part of understanding the long-term drive of the company. It all comes down to doing business with people you trust, or at least avoiding dealing with people of questionable character.

The People rating is based on quantitative scores in seven categories:

- Passion, Execution, Capital Allocation, Communication, Compensation, Ownership, and Board.

Business

If you don't understand the competitive environment and don't have a clear sense of how the business will engage customers, create value and consistently deliver that value at a profit, you won't succeed as an investor. Knowing the business model inside out will provide you some level of certainty and reduce the risk when you buy a stock.

The Business rating is based on quantitative scores grouped into five sub-categories:

- Business Scalability, Market Structure, Value Proposition, Economic Moat, and Operational Risks.

Financials

Investing is part art, part science. Financial ratios make up most of the science. Ratios are used to evaluate the financial soundness of a business. Also, these ratios are key factors that will impact a company's financial performance and valuation. However, you only need a few to determine whether a company is financially strong or weak.

The Financial rating is based on quantitative scores that are grouped into five separate categories:

- Earnings Power, Profit Margin, Growth Rate, Financial Health, and Earnings Quality.

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Disclaimer

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Redeye Rating (2022-02-17)

Rating	People	Business	Financials
5	32	15	4
3-4	149	133	44
0-2	5	38	138
total	186	186	186

Duplication and distribution

CONFLICT OF INTERESTS

Richard Ramanius owns shares in the company : No
Redeye performs/have performed services for the Company and receives/have received compensation from the Company in connection with this.