EDISON

RhoVac

Initiation of coverage

Stopping metastasis in its tracks

Pharma & biotech

RhoVac is developing RV001, a cancer immunotherapy designed to prevent or limit metastasis by activating T-cells against cells with metastatic potential. The therapy contains fragments of the protein RhoC, which is overexpressed in cells with metastatic potential across a range of cancers. The recently announced rights issue (SEK154.2m net) is fully committed to by a group of investors, funds from which will be used for a Phase IIb study in prostate cancer (results in H221) and a potential Phase II combination study with a checkpoint inhibitor in a different solid tumour indication. RhoVac will require a partner following positive Phase IIb results. We value RhoVac at SEK708m or SEK37.2/share.

Year end	Revenue (SEKm)	PBT* (SEKm)	EPS* (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/17	0.0	(12.9)	(1.3)	0.0	N/A	N/A
12/18	0.0	(20.2)	(2.0)	0.0	N/A	N/A
12/19e	0.0	(36.6)	(2.6)	0.0	N/A	N/A
12/20e	0.0	(49.4)	(2.6)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles and exceptional items.

RV001: Potential for use in any metastatic cancer

There are currently no drugs that can effectively prevent metastasis. Inhibition of known metastatic pathways has so far proved unsuccessful. RV001 offers a new approach by priming the immune system to recognise and kill tumour cells with metastatic potential, before they can grow into new metastases. RV001 contains fragments of the protein RhoC, which is overexpressed in these cells in a range of cancers. Since it does not target primary tumours, RV001 should be given in combination with a different therapy treating the primary tumour.

Ph IIb in prostate cancer to start Q319, results H221

Following a positive Phase I/II safety study (unpublished) in patients with prostate cancer (n=22), RhoVac is planning a Phase IIb proof-of-concept study in the same indication (n=150) in Europe. The company has received a positive response from the EMA and FDA, and is awaiting clinical trial approval from the Danish authorities (CTA submitted). A few US sites might also be included in the study. The study will also be funded by proceeds from the rights issue. If all goes to plan, management expects to initiate the study in Q319. If a Phase III study is carried out, the primary endpoint will likely be metastasis-free survival (MFS), rather than overall survival (OS) since this is now accepted by the FDA and EMA in prostate cancer trials.

Valuation: SEK708m or SEK37.2/share

We value RhoVac at SEK708m or SEK37.2/share including estimated net cash of SEK170.3m (net cash from end-2018 + net proceeds from planned rights issue, to which we assign 100% probability since it is fully committed to by a group of investors). We currently only value RV001 in prostate cancer, with peak sales of $888m (SEK8.6bn). Near-term catalysts for the share price will be the initiation of the Phase IIb study and of the second potential Phase II combination study. According to our model, a successful Phase IIb outcome would result in an increase in RhoVac's rNPV to SEK2.0bn or SEK107.1/sh (see Valuation section).

28 May 2019

Price	**SEK18.15**
Market cap	**SEK172m**
	US$:SEK9.63
Net cash (SEKm) at end-2018 + planned rights issue	170.3
Shares in issue	9.5m
Free float	70%
Code	RHOVAC
Primary exchange	Spotlight Stockholm
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(48.0)	(49.2)	(35.0)
Rel (local)	(46.6)	(48.2)	(33.3)
52-week high/low	SEK52.4	SEK18.15	

Business description

RhoVac is an immunotherapy company listed on the Spotlight Stock Market in Sweden, with a 100%-owned subsidiary in Denmark. It is currently developing a peptide-based immunotherapy, RV001, which aims to train the immune system to specifically target cancer cells with metastatic potential. This is a novel approach that could have utility across a range of cancer settings.

Next events

Estimated publication of prospectus	3 June 2019
Estimated date for publication of the outcome of the rights issue	25 June 2019
Initiation of Phase IIb study	Q319
Initiation of Phase II combination study	H120

Analysts

Jonas Peciulis +44 (0)20 3077 5728

Alice Nettleton +44 (0)20 3077 5700

healthcare@edisongroup.com

RhoVac is a research client of Edison Investment Research Limited

Investment summary

Company description: Swedish biotech targeting metastasis

RhoVac is an immunotherapy company listed on the Spotlight exchange in Stockholm. RhoVac AB is the listed entity, however all company activities are carried out by its wholly owned subsidiary (and only holding) RhoVac ApS based in Hørsholm, Denmark. RhoVac ApS was founded in 2007 around the original technology (patent filed 2007), and RhoVac AB was created in 2015 in order to access capital from an IPO. Since the companies have the same ownership, we refer to both companies as 'RhoVac'. RhoVac operates as a virtual organisation supported by partnerships, with few full-time staff and a low fixed-asset base. Management is considering an uplisting to Stockholm First North after the rights issue, but no decision has been taken by the board yet.

Valuation: SEK708m or SEK37.2/share

We value RhoVac based on risk-adjusted NPV analysis using a 12.5% discount rate, including estimated net cash of SEK170.3m (net cash from end-2018 plus net proceeds from the planned rights issue, which we assign 100% probability since it is fully secured). This results in a value of SEK708m or SEK37.2/share. We include a single asset in a single indication in our valuation, which is RV001 in prostate cancer, specifically in patients with biochemical recurrence following radical prostatectomy or radiotherapy. Further additions are possible depending on a future strategic decision from RhoVac, for example with the initiation of its second Phase II study in combination with a checkpoint inhibitor in another cancer indication. According to our model, a successful Phase IIb outcome would result in an increase in RhoVac's rNPV to SEK2.0bn or SEK107.1/share.

Financials: Planned rights issue will fund RhoVac to 2022

RhoVac reports no income, while the operating spend was SEK20.2m in 2018, up from SEK12.9m in 2017, mainly to fund the Phase I/II study. The company had cash of SEK16.1m at the end of 2018 and no debt. On 29 April 2019, RhoVac announced a planned rights issue of approx. SEK180.9m gross (SEK154.2m net). In total, 9.5m shares should be issued (a 100% increase in the number of shares outstanding) at a price of SEK19/share (versus SEK34.9/share on the day before the announcement). A group of investors have agreed to make commitments in the share issue amounting to 100% of the full amount. The subscription period will run from 5–19 June 2019. According to RhoVac, current cash plus cash from the rights issue will fund activities until 2022.

Sensitivities: Single asset, early stage biotech

RhoVac is subject to typical biotech company development risks, including the unpredictable outcome of trials, regulatory decisions, success of competitors, financing and commercial risks. Our model assumes that RV001 will be out-licensed; therefore, our valuation is sensitive to potential licensing timing and actual deal terms. The near-term R&D sensitivities are tied to RV001 in prostate cancer, which is the only clinical-stage programme. Any setbacks with this asset will influence RhoVac's share price significantly. RhoVac has one family of patents protecting its immunotherapy, expected to expire in 2028 (Europe, Australia, Japan) and 2032 (US). This gives a limited patent life once on the market, but we expect the Biologic License Application (BLA) to provide protection. In our model, we assume a four-year Phase III trial in prostate cancer. However, there is a risk that the trial could take longer than expected. It is also possible that a future partner carries out a second Phase II study before starting a Phase III. Our valuation is sensitive to such delays. Finally, although a group of investors have agreed to make commitments in the share issue amounting to 100% of the full amount, there may be some risk that it does not receive the full amount, which could delay plans. A single investor, M2 Asset Management, is responsible for the majority of the new commitments.

RhoVac: Developing immunotherapy for metastasis

An early clinical-stage biotech built around a single technology

RhoVac is a development-stage company, and is built around a single technology and corresponding family of patents. RhoVac's technology involves the use of immunotherapy to activate T-cells against the protein RhoC, for the treatment or prevention of metastasis. Currently, it has one product in development: RV001, which contains RhoC protein fragments plus the adjuvant Montanide ISA 51.

The treatment of metastatic cancer remains a significant unmet need; most patients who reach this advanced stage are terminal, and yet the treatment of metastasis is challenging and far behind the treatment of primary tumours. The metastatic cascade is generally believed to be 'undruggable' using traditional small molecule drugs or antibodies.[1] Therefore, the idea of preventing or limiting metastasis through T-cell activation is an attractive one. RhoVac's chosen target RhoC is a promising target since it is overexpressed in cancer cells with metastatic potential compared with healthy cells across multiple cancer types.

Currently RhoVac has just one clinical programme, which is in localised prostate cancer, but it intends to explore further indications. The recently announced rights issue (fully secured) will provide sufficient capital for RhoVac to conduct two Phase II studies with RV001:

- The first study will be a double-blind, placebo-controlled Phase IIb study (n=150) evaluating RV001 in patients (men) with biochemical recurrence following radical prostatectomy or radiotherapy. It is **due to start in Q319**.
- A second Phase II study (n=20–30) will evaluate RV001 in combination with a checkpoint inhibitor in metastatic solid tumours. It is an exploratory study and is **due to start in H120**.

Management's current strategy is to develop RV001 to proof-of-concept stage before securing a partnership agreement or sale, which could generate some returns for shareholders. Management therefore does not expect to take RV001 into Phase III itself, but aims to secure some kind of partnership for the asset around the time of Phase IIb trial completion. We do not expect a deal if the trial does not reach its primary endpoint, in which case RhoVac might have to raise more money or rely on its other programme, ie the combination trial.

Understanding metastasis

Metastatic cancer is the most advanced stage of cancer and is terminal. Unfortunately, a large proportion of patients who are diagnosed with cancer already have metastases. As a result, advanced cancer is a key focus area for pharmaceutical development. Recently there has been great success in this field with the introduction of immune therapies such as checkpoint inhibitors, which are able to reduce the size of primary and secondary tumours, and improve outcomes for patients such as overall survival or progression-free survival. However, these drugs do not always prevent disease progression. Metastases are difficult to treat because they are heterogeneous and can develop drug resistance. Preventing metastasis is also difficult; for example, even if a patient's cancer is caught early and they are 'cured' through the successful removal of the primary tumour, the cancer can still return in the form of a distant metastasis.

Despite the significance of metastasis, there is much less research in this area compared to the treatment of primary tumours. This could be due to the fact that the mechanisms of metastasis are

[1] Lin Y, Zheng Y. Approaches of targeting Rho GTPases in cancer drug discovery. *Expert Opin Drug Discov*. 2015;10(9):991–1010. doi:10.1517/17460441.2015.1058775

less known than the mechanisms of primary tumour development. This represents both a challenge and an opportunity for companies developing treatments targeting metastasis.

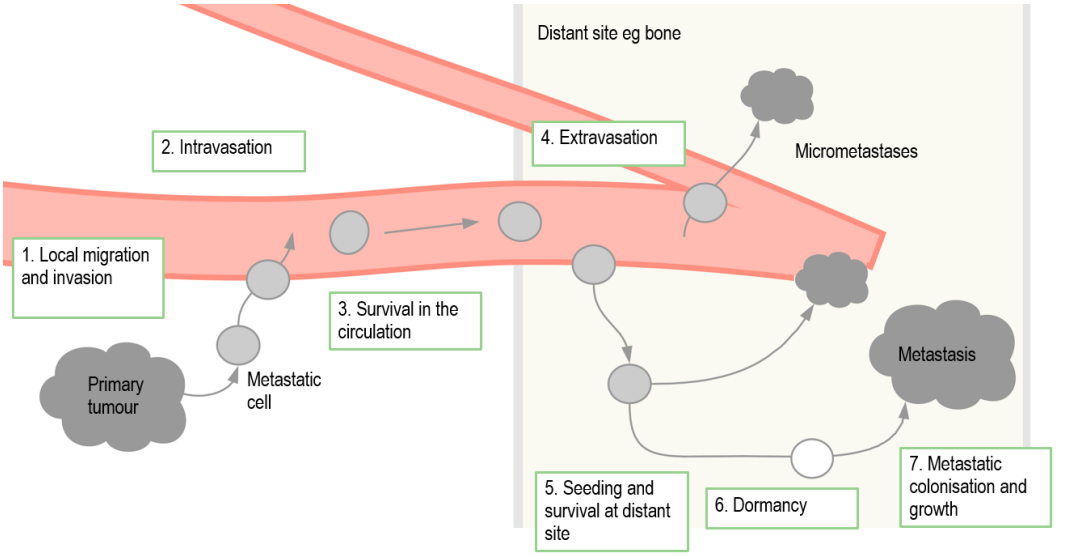
The metastatic cascade

Cancer metastasis is a complex process and still is not fully understood. However, it is generally accepted that metastases form via a 'metastatic cascade' with several steps that can occur over several years:

1. **Local migration and invasion.** Certain cancer cells from the primary tumour gain metastatic potential and start to migrate out of the primary tumour and invade local tissues. Some cancers have greater metastatic potential than others.
2. **Intravasation.** Tumour cells enter the blood or lymph from the local tissues through a process called epithelial mesenchymal transition (EMT), and become circulating tumour cells or 'CTCs'.
3. **Survival in the circulation.** Many CTCs die in the circulation, due to the harsh environment including attack by immune cells, and this is why metastasis is a very inefficient process.
4. **Extravasation.** Of the cells that entered the circulation, only a small portion survive and enter distant tissues.
5. **Seeding and survival at a distant site.** There is an important concept of 'seed and soil' first described by Stephen Paget.[2] The seed is the cancer cell, and the soil is the environment of the distant metastatic site in which the cancer cell is able to grow. If a suitable cell reaches a suitable environment, a metastasis can form. Different cancers favour different sites, for example the most common metastatic site in prostate cancer is the bone (84%) (Gandaglia et al 2013).
6. **Dormancy.** Cancer cells that are 'disseminated', ie that have left the primary tumour, can remain dormant. This could be because a tumour cell exits the cell cycle. For example, in prostate cancer, the majority of metastases form in the bone. Tumour cells can stay in the bone in 'disseminated tumour cell niches' for years. It is thought that these cells could be cancer stem cells, since they are able to initiate the growth of a new metastasis.
7. **Metastatic colonisation and growth.** The new metastasis then grows, supported by a changing tumour microenvironment.

[2] The distribution of secondary growths in cancer of the breast. 1889. Paget S *Cancer Metastasis Re*v. 1989 Aug; 8(2):98-101.

Exhibit 1: Metastatic cascade



Source: Edison Investment Research

Very few drugs developed specifically inhibit metastasis

Despite the significance of the metastatic cascade in cancer progression, there has been an apparent lack of interest in this area from the pharmaceutical industry. According to one review article published in *Nature*, "overt scepticism exists in the pharmaceutical industry and some academic quarters about the concept of drugging metastasis."[3]

There are a few notable drugs that have attempted to target specific stages of the metastatic cascade directly. Roche's bevacizumab (Avastin), an angiogenesis inhibitor, is the most successful commercially. However, this drug has been more successful at treating the primary tumour rather than metastasis. Denosumab, a RANKL inhibitor, has been the most successful at inhibiting metastasis so far, since it actually helps to delay the time to bone metastasis and bone metastasis-free survival in solid tumours. This drug is mainly used to treat bone diseases including osteoporosis. Suggested reasons for failure in this field so far include poor understanding of metastatic pathways, trial design and over interpretation of Phase II clinical data.[4]

[3] Steeg PS. Targeting metastasis. *Nature Reviews Cancer* volume 16, pages 201–218 (2016)

[4] Steeg PS. Targeting metastasis. *Nature Reviews Cancer* volume 16, pages 201–218 (2016)

Exhibit 2: Drugs targeting the metastatic cascade

Drug	Company	Stage of metastatic cascade	Mechanism of action	Indication	Status
Cilengitide	Merck	Local invasion, distant invasion, outgrowth	Angiogenesis and invasion inhibitor – inhibits αvβ3 and αvβ5 integrins, which mediate tumour cell adhesion	Various solid tumours	Various Phase II and Phase III studies (failed)
Denosumab (Xgeva)	Amgen, Daiichi Sankyo	Outgrowth (specifically in bone)	Monoclonal antibody targeting RANKL, prevents bone degradation and further activation of tumour cells	Bone metastases from solid tumours (prostate cancer, breast cancer, multiple myeloma other solid tumours)	Marketed
Bevacizumab (Avastin)	Roche	Survival in distant tissues, outgrowth	Angiogenesis inhibitor – prevents the metastasis from being able to grow a blood supply	Various solid tumours	Marketed
Dasatinib	Bristol-Myers Squibb	Growth, invasion, metastasis	Src tyrosine kinase inhibitor	Chronic Myeloid Leukaemia	Marketed
				Acute lymphoblastic leukaemia	Marketed
				Various solid tumours	Various Phase II and Phase III studies (failed)
Saracatinib	AstraZeneca	Growth, invasion, metastasis	Src tyrosine kinase inhibitor	Various solid tumours	Various Phase II and Phase III studies (failed)

Source: www.nature.com/articles/nrc.2016.25, clinicaltrials.gov, EvaluatePharma.

Key challenges for drug development in this area include:

- **A large proportion of patients diagnosed with cancer already have metastatic disease**. Therefore, drugs are unlikely to be able to prevent metastasis in these patients. Limiting or delaying further metastasis might be achievable, while treating established tumours with tumour shrinking therapies.
- **Disseminated tumour cells.** Even if a patient is 'cured' from early stage cancer by successfully removing the primary tumour, patients can still relapse, sometimes many years later. This is because cancer cells are constantly entering the circulation from the primary tumour. Even when the primary tumour is removed, these so called 'disseminated tumour cells' can still exist in the body. Most will die but some can stay dormant for many years, and eventually initiate new metastases. Therefore, even if there are no diagnosed metastases, several stages of the metastatic cascade might have taken place in a patient. A drug that is targeting the early stages of the cascade, eg migration and invasion, may not be able to target cells that have already entered the circulation. Some authors suggest that a better approach could be to target the later stages of metastasis, or to target so-called 'dormant stem cell niches'.[5]
- **Metastasis targets are not very 'druggable'.** It has been found that many potential proteins in metastasis pathways are not very druggable, including the Rho GTPases, which are involved in most stages of metastasis (such as RhoC).[6] RhoVac is using a different strategy and so might be able to avoid this issue. Rather than directly inhibiting a metastatic pathway, it is attempting to train the immune system to recognise and kill cells with metastatic potential. This avoids the requirement to understand the underlying pathways; it is not inhibiting RhoC, but using it as a marker to identify metastatic cells.
- **Multiple pathways**. There are many pathways involved in each stage of metastasis, and inhibition of one pathway might not be sufficient to inhibit that stage of metastasis due to alternative pathways.[7]
- **Clinical trial design, endpoints**. Many of these anti-metastasis therapies will be adjuvant therapies and will be preventative. Metastasis-free survival and distant metastases-free survival

[5] Ghajar CM. Metastasis prevention by targeting the dormant niche. *Nature Reviews Cancer* volume 15, pages 238–247 (2015)

[6] Lin Y, Zheng Y. Approaches of targeting Rho GTPases in cancer drug discovery. *Expert Opin Drug Discov*. 2015;10(9):991–1010. doi:10.1517/17460441.2015.1058775

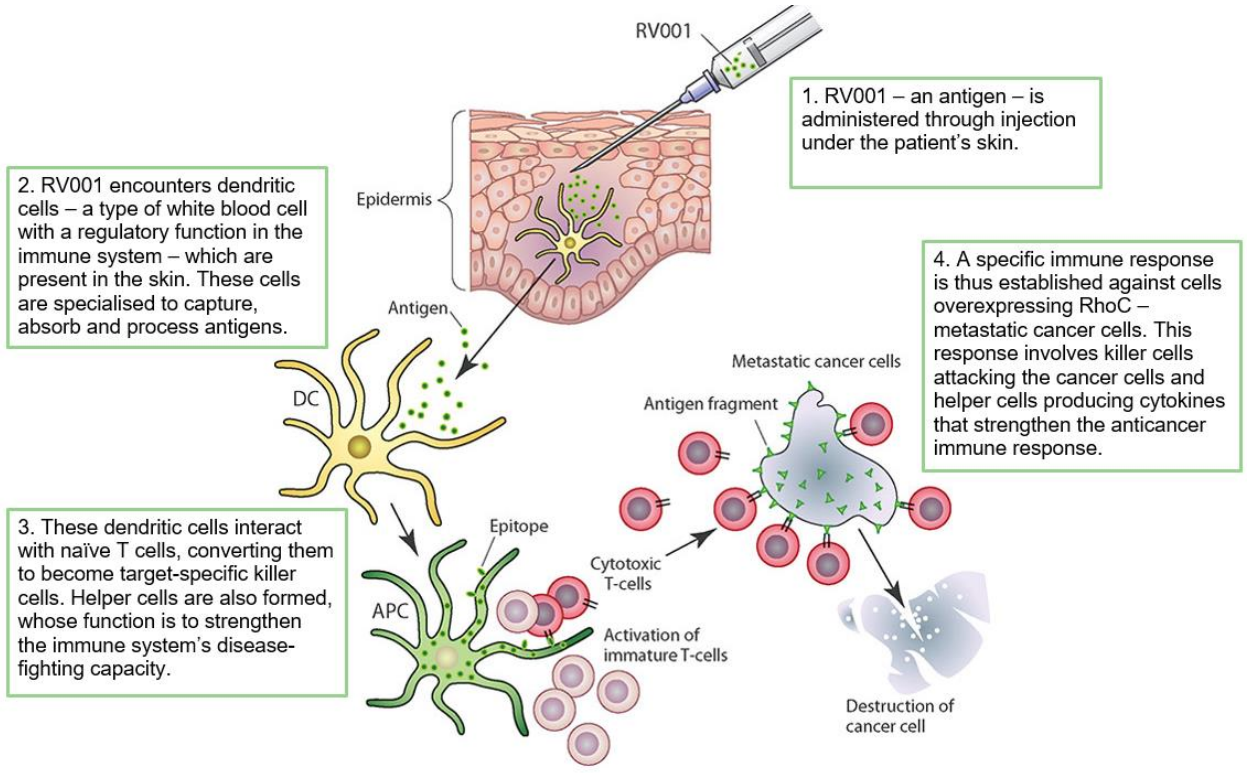
[7] Steeg PS. Targeting metastasis. *Nature Reviews Cancer* volume 16, pages 201–218 (2016)

are now accepted endpoints by the FDA and EMA respectively in prostate cancer patients at high risk of metastasis, and have been used as the basis for approval of new prostate cancer therapies apalutamide and enzalutamide in high-risk, non-metastatic, castrate-resistant prostate cancer. These endpoints make it possible for shorter trials compared with OS, but even so the time taken to reach these endpoints could still be very long (especially in slowly progressing cancers like prostate cancer). This could be a barrier to companies wishing to start trials evaluating anti-metastasis therapies.

RV001: A peptide-based immunotherapy

RV001 is a peptide-based immunotherapy that contains fragments of a protein called RhoC, which is overexpressed in cells with metastatic potential in a range of cancers (Karlsson et al 2009). It has been found to be essential for metastasis (Hakem et al 2005), and to cause metastasis in animal models (Clark et al 2000). The adjuvant Montanide ISA 51 is used together with the peptides to increase the immune response. The strategy that RhoVac is employing is similar to other peptide immunotherapies in that the aim is to elicit a T-cell response against a particular protein expressed by tumour cells. RhoVac expects RV001 to elicit a T-cell response against RhoC through MHC class I and II (Exhibit 3). RhoVac envisages that RV001 would be best administered as a combination/adjuvant therapy with a treatment targeting the primary tumour. This is not the case with its lead programme in prostate cancer, since here RV001 is used as an adjuvant to radical prostatectomy or radiotherapy, but future trials in other cancers will likely be combination trials.

Exhibit 3: RV001 proposed mechanism of action



Source: RhoVac

RhoC is an Rho GTPase. Rho GTPases have a role in important cellular processes such as migration and cell adhesion. Since metastasis employs these mechanisms, Rho GTPases are also associated with metastasis. Rho GTPases and their pathways have already been investigated as targets for cancer treatment, but so far unsuccessfully. RhoVac has IP around RhoC in cancer immunotherapy.

RhoC is on the National Cancer Institute list as a priority cancer antigen. RhoC regulates the cytoskeleton at the point of the cell that is infiltrating cellular matrix so it is directly associated with invasion. However, this is not a cancer-specific mechanism as any cell involved in tissue repair or angiogenesis will use the same mechanism. Therefore, although this protein is overexpressed in tumour cells, it is only tumour-associated. There is always a risk with tumour-associated antigens (ie. those that are also expressed by healthy cells), in that the body may have developed so-called 'immune tolerance' to this protein, so as not to cause a harmful autoimmune response. This occurs through elimination of T-cells that react to the self-protein.

An interesting finding is that RhoC overexpression is maintained in secondary tumours (Liu et al 2007). This observation led RhoVac to the idea that RV001 could be effective at preventing secondary metastases too, so it can theoretically be useful at any stage of cancer.

What are peptide-based immunotherapies?

In a malignant process, cancer cells die and proteins/antigens are released. These are then taken up by the patient's own antigen-presenting cells, or dendritic cells (DCs), and in lymph nodes they present these antigens to T-cells. This leads to an activation and production of populations of T-cells, which can now recognise and destroy cancerous cells that display the same antigens as those previously presented. However, this process is not perfect, which is why not every malignant process is stopped. Once a tumour develops, it often also has multiple ways to suppress the immune response and enable the tumour to 'hide' from the immune cells.

The goal of cancer immunotherapies is to expose the tumour cells as foreign to the patient's immune system so the tumour is recognised and immunologically attacked. It is generally accepted that the best way to utilise immunotherapies to treat tumours is to combine them with other strategies targeting different parts of the cancer immunity cycle (Schlom and Gulley, 2018). Peptide-based immunotherapies are one such cancer immunotherapy, and work by presenting peptides to the patient's immune system that are likely to be expressed by the patient's tumour so that T-cells will be able to target and kill these cells. As with other immunotherapies, it is ideal to combine peptide immunotherapies with other immunotherapy strategies.

Targeting an unmet need in prostate cancer

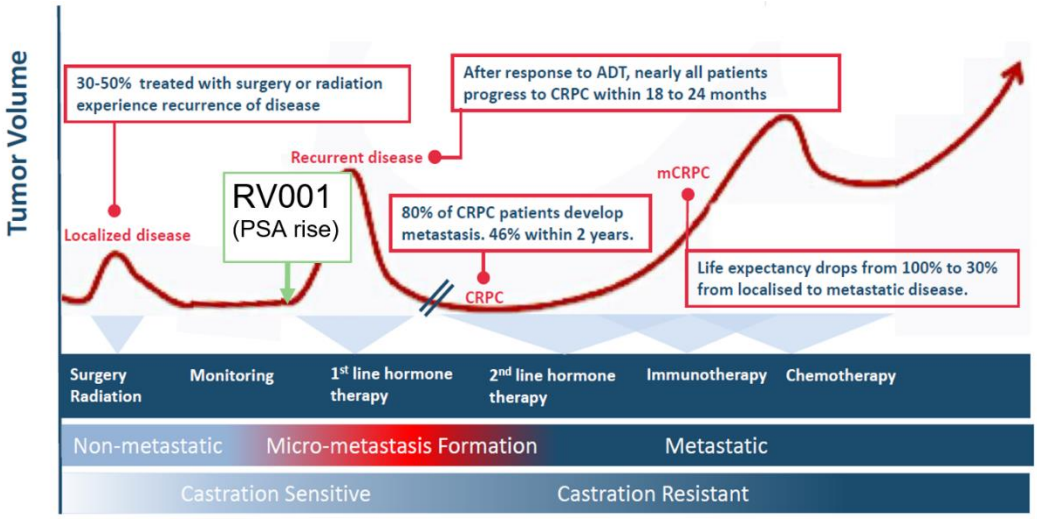
Prostate cancer is a common cancer in men over the age of 50. The National Cancer Institute estimates that 174,650 patients in the US will be diagnosed with prostate cancer in 2019 and there will be an estimated 31,620 deaths from the disease in the US during 2019. Prostate cancer is usually diagnosed by carrying out a mixture of prostate-specific antigen (PSA) blood test, digital rectal examination and biopsy. PSA is an important tool also to monitor patients for relapse. Guidelines can differ on recommendations for population-based screening; some recommend screening for men over the age of 50 with average risk, or over the age of 40 with increased risk, whereas others do not recommend it on the basis of unnecessary cost and overtreatment. The stage of prostate cancer at diagnosis is a significant contributor to survival as patients with early local disease have a five-year relative survival rate of 98%, while patients with advanced metastasis have a relative five-year survival of 28% (Tewari et al 2014). The stage of prostate cancer together with the risk level determines treatment options:

- **Localised prostate cancer with low risk or intermediate risk** is treated with active surveillance, or radical therapy (either radical prostatectomy or radiation therapy). Low-risk patients might get watchful waiting with delayed androgen deprivation therapy (or hormone therapy) as an alternative if they are very low risk. Intermediate-risk patients might also receive adjuvant hormone therapy with their radiation therapy. Many patients will relapse after radical

therapy, and will move on to hormone therapy or salvage radiotherapy. Most patients live for many years with localised disease, but most will eventually still progress.

- **Patients with high-risk localised or locally advanced prostate cancer** might receive a hormone therapy, radical prostatectomy, radiotherapy, and on relapse additional hormone therapy or radiotherapy. Many patients will progress to metastatic disease, which is most often bone metastases.
- **Metastatic disease can be either hormone naïve or castrate resistant**. Hormone naïve patients can receive androgen deprivation therapy, but castrate-resistant prostate cancer patients have to move on to other options. These include abiraterone and enzalutamide (other hormone drugs), sipuleucel-T (Provenge, dendritic cell vaccine), Radium-223 and docetaxel. Radium-223, denosumab and zoledronate can be used for patients with bone metastases.

Exhibit 4: Prostate cancer progression and RV001 positioning



Source: RhoVac

RhoVac is targeting patients with localised disease who have relapsed. A relapse in these patients is known as biochemical recurrence/biochemical failure and can be defined as a rise in PSA ≥0.2ng/mL (American Urological Association, European Association of Urology). Currently these patients will move on to hormone therapy or salvage radiotherapy, but RhoVac wants to delay disease progression by extending the effect of the radical therapy (ie radical prostatectomy or radiotherapy). RV001 will be given therefore as an 'adjuvant' treatment to the radical therapy. Discussions with the EMA and FDA highlight that this is an area of unmet medical need.

The best-selling drugs in 2018 have been the newer branded hormone drugs targeting advanced disease, ie Zytiga (abiraterone acetate, Janssen Biotech) with sales of $1.8bn, Xtandi (enzalutamide, Astellas) $1.5bn, and Leuplin (leuprolide acetate, Takeda) $400m (EvaluatePharma). EvaluatePharma estimates the revenues per patient per year from Zytiga to be around $30,000 and Xtandi to be around $45,000. RV001 is a peptide-based immunotherapy and these tend to come with a biologics price tag. However, RhoVac is targeting patients with earlier-stage disease so may not be able to command a price as high as Zytiga or Xtandi.

RV001 clinical development in prostate cancer

RV001 was studied in a Phase I/II study with 22 patients (Exhibit 5). The primary objective was to evaluate safety and tolerability, while the secondary objective was looking at immune response. Patients were given 11 subcutaneous injections over the course of 30 weeks. So far, the company has not published the full results of the study in any scientific journal, but top-line results were

published in August 2018 and on subsequent immune response follow-ups. According to the press release, RV001 was well tolerated in all patients, with no grade 3, 4 or 5 reactions. There were local injection site reactions, but these are common and usually a result of the adjuvant Montanide. Of the 21 evaluable patients, 18 (86%) had an immune response during or following treatment (measured by IFNγ ELIspot analysis). Based on these results, RhoVac now plans to evaluate the therapy in a larger Phase IIb study.

Exhibit 5: Phase I/II trial design (NCT03199872)

Summary design	A Phase I/II study to evaluate RV001 in patients with prostate cancer who have had a prostatectomy
Objective	To evaluate safety and tolerability of RV001, as well as immunological response before, during and after treatment
Number of patients	22
Treatment groups	Experimental treatment arm: RV001 (11 subcutaneous vaccinations over 30 weeks)
Endpoints	Primary endpoint: safety and tolerability Secondary endpoints: immunological response before, during and after treatment
Key inclusion criteria	Prostatectomised due to histologically verified adenocarcinoma of the prostate gland who are not currently being treated or expected to be treated within the next 8 months with any anti-cancer treatment EGOG PS 0-1
Key exclusion criteria	Not receiving androgen-deprivation therapy
Clinical trial sites	Denmark
Sponsor	RhoVac
Timelines	Study start: March 2017 Study end: August 2018

Source: RhoVac

RhoVac has also carried out preclinical studies with RV001. These were *ex vivo* studies with human cancer cells in breast cancer, bowel cancer and melanoma. These studies are not published, but according to RhoVac, they demonstrate that a T-cell response can be elicited from RV001, and that the T-cells attack and kill metastatic cells.

Phase IIb controlled trial to initiate in Europe in Q319

Following the positive Phase I/II study, RhoVac has designed a larger Phase IIb study to explore efficacy in the same patient group (Exhibit 6). RhoVac received a positive response from the EMA and submitted a clinical trial application to the Danish authorities in April 2019. The trial is expected to initiate in Q319, following clinical trial approval and once funds have been secured from the rights issue. The study will enrol patients in Europe. The therapy will be administered as 12 subcutaneous injections, over several months.

In terms of endpoints, RhoVac plans to use time to PSA progression as the primary endpoint. Patients will be included in the study who have had biochemical recurrence where their PSA level reaches ≥0.2ng/mL, and who have PSA doubling time of between three months and 12 months. During the study their PSA will be measured, in terms of PSA doubling time. RhoVac is aiming to reduce the PSA increase by 50% compared with the placebo group, which is an outcome that would be interesting to urologists.

In our view, PSA progression is a good endpoint for this group of patients (biochemically recurrent prostate cancer following radical therapy) in a Phase II trial, mainly because it allows RhoVac to perform a relatively small, fast and cheap study. Feedback from both the EMA and FDA was positive on the endpoints, and other studies in the same group of patients are also using PSA endpoints in Phase II, eg nivolumab (Bristol-Myers Squibb) and olaparib (AstraZeneca). PSA is known to be a reliable measure of disease progression/metastasis in prostate cancer. However, it is not clear whether a more substantial endpoint such as metastasis-free survival (MFS), OS or PFS would be required at Phase III. RhoVac plans to include MFS as an exploratory endpoint in the Phase IIb study, but it should be noted that the study is not large or long enough to be able to conclude anything about MFS. A good outcome from the trial would be if the study meets its primary endpoint, ie showing that RV001 can delay PSA progression in these patients.

Exhibit 6: Planned Phase IIb trial design (trial not yet approved)	
Summary design	A Phase II, double-blind, placebo-controlled study of RV001V in adult males with biochemically relapsed prostate cancer following definitive local therapy (eg prostatectomy, radiotherapy)
Objective	To investigate whether a vaccination regimen with multiple subcutaneous administrations of RV001 0.1mg/mL (RV001V) can reduce prostate-specific antigen (PSA) progression compared to the control group
Number of patients	150 (will enrol 180 in order to have 150 evaluable patients)
Treatment groups	Experimental treatment arm: RV001 (12 subcutaneous vaccinations: priming period of 6 vaccinations – one every 2 weeks, then a boosting period of 5 vaccinations – one vaccination every 4 weeks, then final vaccination given 6 months after the 11th vaccination) Control: placebo (same dosing as RV001)
Endpoints	Primary endpoint: time to documented PSA progression or clinical recurrence, death of any cause Secondary endpoints: safety and tolerability, time to subsequent antineoplastic therapy, disease-free survival Exploratory endpoints: relationship between immune-response and antitumour efficacy, identification of predictive biomarkers, metastasis free survival
Key inclusion criteria	Biochemical recurrence within 3 years of radical prostatectomy (PSA ≥0.2ng/mL, PSA doubling time >3 months and <12 months, history of Gleason 7 (4+3) or higher) or definitive radiotherapy (same definitions except PSA >nadir + 2ng/mL)
Key exclusion criteria	No distant metastasis or locoregional recurrence No castration-resistant prostate cancer Not receiving androgen-deprivation therapy PSA>10ng/mL
Clinical trial sites	Denmark and other European countries
Sponsor	RhoVac
Timelines	Study start: Q319 Study duration (approximate): 2 years (1-year enrolment, 1-year follow-up) Expected data readout: H221

Source: RhoVac

Strategic options for late-stage development

If the Phase IIb study is positive, at least one successful Phase III study will likely be required for regulatory approval. RhoVac's current strategy is to partner following the Phase IIb outcome, as it does not have the financial firepower to carry out a large Phase III study, but management is open to options including selling the company. Management currently envisages a single Phase III study (Exhibit 7). In our model we also assume a licensing deal in 2022 following the Phase IIb readout followed by a single Phase III study, which we assume will be a global study including both European and US sites, and will take approximately four years to complete. However, it is also plausible that an additional Phase II or Phase III study would be required, or that the Phase III study will take longer. This would increase time to market.

Pre-IND meetings with the FDA went well; RhoVac received a positive response from the FDA in April 2019. RhoVac expects to receive clinical trial approval from the Danish authorities and start the trial in Denmark in Q319 and plans to resume discussions with the FDA at this time. For the moment, we do not include a separate Phase IIb study in the US but assume the FDA will allow the European study (possibly including some US sites) as the basis for approval, together with the global Phase III study (which should include US sites).

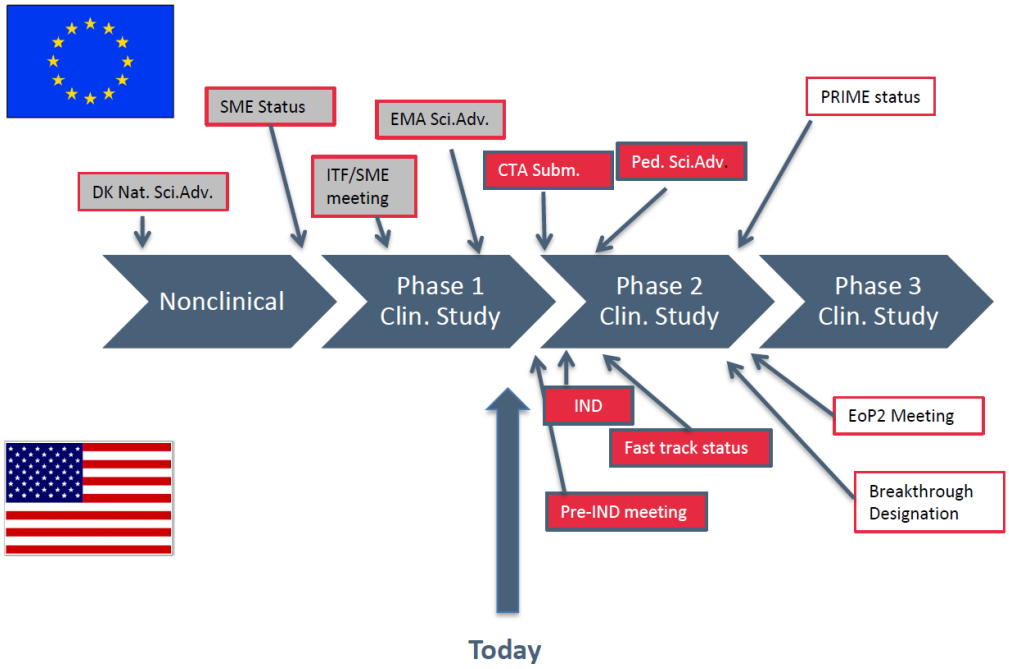
Likely endpoint for a Phase III study: Metastasis-free survival

So far, the only endpoints that have been the basis for FDA approval in prostate cancer are OS, PFS and MFS. Based on discussions with the FDA and EMA, RhoVac expects metastasis-free survival (MFS) to be accepted as the primary endpoint. Both the FDA and EMA now accept this endpoint in non-metastatic, castrate-resistant prostate cancer patients at high risk of developing metastases, demonstrated by recent apalutamide and enzalutamide approvals in this patient population using the same endpoint. RhoVac is targeting a slightly earlier patient population, but expects MFS to be acceptable based on discussions with the regulators. Studies with MFS as the primary endpoint can take many years to complete; for example, this study in high-risk localised or locally advanced prostate cancer is recruiting 1,500 patients and is expected to take seven years (NCT02531516). There is a call for other surrogate endpoints in prostate cancer trials, including

PSA endpoints, which could shorten trials.[8,9] Time to biochemical failure has been proposed as a surrogate endpoint, as demonstrated in a Phase III study in localised disease, but no products have been approved on PSA. According to RhoVac, the EMA and FDA are open to discussing the use of such endpoints, because they recognise the problem of designing trials in this group of patients, where there is a significant unmet need. However, until the Phase IIb outcome and further discussions with the regulators, the Phase III endpoints remain uncertain.

Based on feedback from the regulators, RhoVac does not need to carry out any further toxicology studies or Chemistry, Manufacturing, and Controls (CMC) development. In addition, any further studies in new indications can go directly into Phase IIb, since the safety data will also be sufficient for these new indications.

Exhibit 7: Development plan



Source: RhoVac

Competitive landscape

Two approved anti-metastatic therapies for prostate cancer, but without survival benefit

There have been several studies carried out in prostate cancer with drugs targeting metastasis:

- Denosumab is approved for the prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumours, including prostate cancer (Phase III study). Studies have demonstrated that denosumab is able to delay the time to bone metastasis and bone metastasis-free survival in castrate-resistant prostate cancer patients at high risk for bone metastasis, but this does not correspond with an improvement in overall survival.

[8] Kyriakopoulos CE, Antonarakis ES. Surrogate end points in early prostate cancer clinical states: ready for implementation?. *Ann Transl Med*. 2017;5(24):502. doi:10.21037/atm.2017.10.25

[9] Williams S. Surrogate endpoints in early prostate cancer research. *Transl Androl Urol*. 2018;7(3):472–482. doi:10.21037/tau.2018.05.10

- Zoledronic acid is a bisphosphonate, and has also been shown to delay time to first skeletal-related event. When compared with denosumab in prostate cancer in a Phase III study, denosumab was superior in delaying skeletal-related events, but neither improve overall survival. The ESMO clinical practice guidelines (2015) recommend either denosumab or zoledronate for patients with castrate-resistant prostate cancer at high risk for clinically significant skeletal-related events (SRE), but state that the added value for SRE prevention is unclear.
- Cilengitide (developed by Merck) inhibits αvβ3 and αvβ5 integrins, which regulate cell adhesion, migration, invasion, motility and angiogenesis. Cilengitide was evaluated in a Phase II study in bone metastatic prostate cancer (n=106). This study enrolled patients who already had a diagnosis of metastatic disease and had progressed following hormone therapy, where progression is defined as PSA rise. The primary endpoint was clinical progression by bone scan or CT scan. The suggested reasons for trial failure include suboptimal dosing, incomplete understanding of integrins in prostate cancer, and tumour resistance.
- Dasatinib (Bristol-Myers Squibb) inhibits Src tyrosine kinase, which is involved in cell division, motility, adhesion and survival. A Phase II study with dasatinib was positive with a PSA endpoint but the following Phase III study where OS was used (n=1930) was not successful. A potential reason for failure is that Src is mainly involved in the earlier stages of metastasis and the trial was treating patients with more advanced disease. Dasatinib is approved as Sprycel for CML and ALL. Saracatinib (AstraZeneca) is also an Src tyrosine kinase inhibitor. It was unsuccessful in all indications, including in a Phase II head-to-head trial against zoledronic acid in prostate cancer and breast cancer.

Prostate cancer is ‘cold tumour’, many immunotherapy failures

So far, immunotherapies have not been successful in prostate cancer, but extremely successful in many other cancers. Several checkpoint inhibitors and other immunotherapies have been evaluated as monotherapies in prostate cancer trials but without much success. The only immunotherapy approved for prostate cancer is Provenge (Sipuleucel-T) developed by Dendreon. As a result, it has been suggested that prostate cancer is a ‘cold tumour’ that resists T-cell infiltration.[10] Immunotherapies are now being studied in combination for prostate cancer, which could improve T-cell infiltration. RV001 might be able to avoid this issue, since it is designed to target cells with metastatic potential rather than primary tumours.

Provenge/Sipuleucel-T (Dendreon) is an autologous cellular immunotherapy, which involves leukapheresis, treatment of the patient’s peripheral blood mononuclear cells with prostatic acid phosphatase (PAP) and GM-CSF followed by reinfusion into the patient. It was approved by the FDA in 2010 and is still the only approved immunotherapy for prostate cancer, specifically asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer (mCRPC). It has been withdrawn from the market in Europe for commercial reasons. Despite adding four months of survival benefit in Phase III, it has not been very successful commercially. This is likely due to the high cost ($93,000 per patient), lack of efficacy, complexity of the procedure (the patient must undergo three procedures) and concerns about reimbursement.

Prostvac (Bavarian Nordic) is another high-profile example of an immunotherapy developed for prostate cancer, but so far has not been approved. It encodes transgenes for PSA (prostate specific antigen) as the targeted tumour associated antigen, and three co-stimulatory proteins known as TRICOM (B7-1, ICAM-1 and LFA-3) that further activate cytotoxic T lymphocytes that may recognise and kill PSA-expressing cancer cells. It was evaluated in asymptomatic or minimally

[10] Jansen CS., Prokhnevska N., Kissick HT. The requirement for immune infiltration and organization in the tumor microenvironment for successful immunotherapy in prostate cancer. *Urol Oncol.* 2018 Nov 13. pii: S1078-1439(18)30393-4. doi: 10.1016/j.urolonc.2018.10.011

symptomatic mCRPC. Although it showed an 8.5-month improvement in OS vs placebo in a Phase II study, this was not replicated in a Phase III study. Bristol-Myers Squibb took an option to Prostvac in 2015 prior to the Phase III results, and started to evaluate it in combination with ipilimumab. It is still being evaluated in several other studies, including by the National Cancer Institute in biochemical recurrence (Exhibit 8).

Clinical studies in biochemical failure

The majority of clinical development in prostate cancer is for mCRPC. However, there are a few ongoing studies with immunotherapeutics being conducted in patients with biochemical recurrence – the same population as RhoVac's planned Phase IIb study (Exhibit 8). To our knowledge, there have not been any Phase III studies carried out in this group of patients. Results from these studies could provide insights for RhoVac, and if any Phase III studies are initiated it will also be helpful for RhoVac when discussing endpoints with the regulators.

Exhibit 8: Drugs in development for biochemical recurrence in localised prostate cancer

Product	Pharmacological class	Company	Phase of development	No. patients	Primary endpoint(s)	Estimated primary completion date
RV001	Peptide-based immunotherapy (RhoC)	RhoVac	Phase IIb-ready	150	Time to documented PSA progression or clinical recurrence, death of any cause	H221
ProscaVax	PSA/IL-2/GM-CSF vaccine	OncBioMune Pharmaceuticals Inc	Phase II [NCT03579654]	120	Prostate cancer progression measured by PSA test, digital rectal examination and prostate biopsy	February 2021
Prostvac	Vector-based vaccine (PSA)	National Cancer Institute	Phase II [NCT02649439]	110	Time to progression	October 2020
Enzalutamide	Anti-androgen	Astellas	Phase II [NCT02203695] (marketed in other prostate cancer populations)	122	Rate of Freedom-from-PSA-progression (FFPP) at 2-years	March 2020
Nivolumab	PD-1 inhibitor	Bristol-Myers Squibb	Phase II [NCT03637543]	34	Disease control (proportion of patients that experiences decline or stabilisation of PSA)	March 2022
Olaparib	PARP inhibitor	AstraZeneca	Phase II [NCT03047135]	50	Response rate (decline in PSA to 50% of baseline level)	March 2021
Rucaparib	PARP inhibitor	Clovis Oncology	Phase II [NCT03533946]	29	50% Reduction in PSA levels	July 2023

Source: Evaluate Pharma, Clinicaltrials.gov.

Patent protection to 2028/2032, plus BLA exclusivity

RhoVac has a single patent family based on the PCT application WO2009076966 and priority date of December 2008. It has patents in Europe, Australia and Japan (EP2234635B1, AU2008338063B2, JP5813801B2) expected expiry December 2028), and the US (US9163077B2, expected expiry March 2032), and patents pending in Canada. This patent family covers RV001 and any other immunotherapies that RhoVac may develop relating to RhoC. According to our model, if RV001 reaches the market in prostate cancer, this will likely be in 2027 (assuming a four-year Phase III study that includes a longer endpoint such as MFS or PFS), which does not leave much room for patent protection (and it would take even longer to reach the market in other indications). Patent protection could be extended, but we expect that RhoVac or a potential partner would have to rely on market exclusivity resulting from the Biologic License Application (BLA). Since RV001 is an immunotherapy, we expect it will go down the BLA pathway, which would secure 12 years' exclusivity in the US and at least 10 years in Europe (upon market authorisation). To achieve patent extension in the US, RhoVac would benefit from including clinical trial centres in the US as early as possible, ie in the Phase IIb study.

In the pipeline

Exploratory Phase II study will evaluate RV001 in late-stage metastasis in combination with checkpoint inhibitor

A second Phase II study (n=20–30) is planned to evaluate RV001 in combination with a checkpoint inhibitor. This will be more of an 'exploratory' study and will be carried out with the planned funds from the rights issue. The study is still in the early planning stages. For the moment, this trial plan demonstrates the fact that RhoVac is looking to evaluate RV001 in multiple stages of cancer and in combinations. RhoVac is trying to evaluate the immunotherapy in combination with a therapy that can tackle the established tumours, while RV001 aims to prevent further metastasis/disease progression in these patients.

Stem cell collaboration could add support to treatment concept

Cancer stem cells have been heavily implicated in metastasis, but their existence is still debated. There are different theories about their involvement in metastasis; for example, one theory suggests that only cancer stem cells can establish metastasis, another that both cancer cells and cancer stem cells can metastasise.[11]

RhoVac has entered into a collaboration with Lund University in order to understand whether its immunotherapy can also target cancer stem cells to treat metastasis. The aim of the collaboration is to firstly confirm that RhoC is expressed in prostate cancer stem cells, and then, if so, work out whether RV001 is active against these cells. Since metastasis is a relatively unknown area of science, and there is no consensus on the involvement or requirement of cancer stem cells in this process, it would add significantly to RhoVac's scientific rationale if RhoC was overexpressed in all types of metastasising cell. If cancer stem cells do contribute to metastasis and overexpress RhoC, they would represent a target for RhoVac's immunotherapy.

Sensitivities

RhoVac is subject to typical biotech company development risks, including the unpredictable outcome of trials, regulatory decisions, success of competitors, financing and commercial risks. Our model assumes that RV001 will be out-licensed; therefore, our valuation is sensitive to potential licensing timing and actual deal terms.

RhoVac is an early-stage drug developer, therefore in the foreseeable future the value creation will depend on successful R&D progress and any potential partnering activities, although typically the timing of licensing deals is difficult to forecast. The near-term R&D sensitivities are tied to RV001 in prostate cancer, which is the only clinical-stage programme. Any setbacks with this asset will influence RhoVac's share price significantly. As additional indications reach clinical development, this risk will be diversified.

Currently, RhoVac is a single technology company, which is high risk since if the technology is not successful in treating metastasis the company cannot fall back on any alternatives. RhoVac has one family of patents protecting its technology, which are expected to expire in 2028 and 2032. This gives a short patent life once on the market (if successfully commercialised). We expect the BLA to provide protection, but there could be some risks relating to this short patent life such as reduced interest from potential partners.

[11] Shiozawa Y, Nie B, Pienta KJ, Morgan TM, Taichman RS. Cancer stem cells and their role in metastasis. *Pharmacol Ther*. 2013;138(2):285–293. doi:10.1016/j.pharmthera.2013.01.014

A significant unknown is the design of the Phase III study in prostate cancer including the cost and length of the study. In our model, we assume a four-year Phase III trial in prostate cancer. However, there is a risk the trial could take much longer if a different endpoint is required, which could affect the valuation, or that a partner carries out a second Phase II study before starting a Phase III. Such delays would delay any licensing revenues to RhoVac, thus significantly lowering our valuation.

Finally, although a group of investors have agreed to make commitments in the share issue amounting to 100% of the full amount, there may be some risk that it does not receive the full amount, which could delay plans. Importantly, a single investor, M2 Asset Management, is responsible for the majority of the new commitments (49.2%).

Valuation

We value RhoVac based on risk-adjusted NPV analysis using a 12.5% discount rate, including estimated net cash of SEK170.3m (net cash from end-2018 plus net proceeds from the planned rights issue, which we assign 100% probability since it is fully secured) (Exhibit 9). This results in a value of SEK708m or SEK37.2/share. We assume a 10% probability of success, reflecting the fact that the Phase IIb study has not yet initiated.

Exhibit 9: Sum-of-the-parts RhoVac valuation

Product	Launch	Peak sales (US$m)	Unrisked NPV (SEKm)	Technology probability (%)	rNPV (SEKm)	rNPV/share (SEK)
RV001 – prostate cancer	2027	888	3,140.9	10%	537.5	28.2
Net cash at end-2018 + guaranteed rights issue			170.3	100%	170.3	8.9
Valuation			**3,311.2**		**707.8**	**37.2**

Source: Edison Investment Research. Note: WACC = 12.5% for product valuations.

We include a single asset in a single indication in our valuation, which is RV001 in prostate cancer, specifically in patients with biochemical recurrence following radical prostatectomy or radiotherapy. Exhibit 10 summarises our detailed assumptions for the risk-adjusted NPV valuation, while licensing deals used for benchmarking are shown in Exhibit 11. We use these deal terms but apply a 30% discount due to the differences between these deals and RhoVac's asset. The key difference is the stage of development – these deals are for Phase III assets, whereas RV001 is Phase IIb-ready. Additionally, in our view, if a partner were to license RV001, it may want to conduct another Phase II study before starting a Phase III study. Finally, these deals were made a few years ago and the products were not successful, which will likely influence the deal negotiations. We use the following deal terms: upfront payment of $30m, development and regulatory milestones totalling $150m, sales milestones of $250m and tiered double digit royalties starting from 10%.

Exhibit 10: Assumptions for RV001 valuation

Product/indication	Comments
RV001 – prostate cancer	■ Target population: c 22k prostate cancer patients in US who have biochemical recurrence annually, and c 41k in EU14. This is reached by taking the incidence of prostate cancer in each region (175k US and 324k in EU14) x proportion that are diagnosed with local disease (approx. 66%) x proportion treated with radical prostatectomy or radiotherapy (approx. 55%) x proportion having biochemical recurrence per year (approx. 35%). 20% peak penetration. ■ Pricing*: $50k per patient per year in the US, 30% discount in Europe. Peak sales in five years. ■ R&D cost: SEK122.6m to complete Phase IIb, then out-licensed. ■ Licensing deal terms: upfront of $30m, $150m development and regulatory milestones, $250m in sales milestones. Out-licensed in 2022. Tiered 10–13% royalty rates used. ■ IP rights: proprietary technology; patent protection until 2028 (Europe, Australia, Japan) and 2032 (US). Biologicals market exclusivity 12 years in the US and 10 years in Europe.

Source: Edison Investment Research. Note: Target geographies used in the model are the US, and top 14 European countries (EU5 + Netherlands, Belgium, Luxembourg, Denmark, Finland, Norway, Sweden, Austria and Switzerland).

Exhibit 11: Comparable deals for immunotherapy assets in late stage development for prostate cancer

Date	Licensor	Licensee	Product	Pharmacological class / Target	Indications included in the deal	Upfront ($m)	Development and regulatory milestones	Sales milestones	Royalties
04/03/2015	Bavarian Nordic	Bristol-Myers Squibb	PROSTVAC	Prostate-specific antigen targeting cancer immunotherapy	Asymptomatic or minimally symptomatic (mCRPC)	60 (+ 80 if option exercised)	340	495	Tiered double-digit royalties on sales
31/03/2008	Takeda	Cell Genesys	GVAX	GM-CSF gene-transfected tumour cell vaccine	Prostate cancer	50	270	N/A	Tiered, double-digit royalties based on net sales
29/05/2014	Janssen Biotech	Aduro BioTech	GVAX/LADD	GM-CSF gene-transfected tumour cell vaccine	Prostate cancer	365 (upfront and milestones)			Tiered royalties on worldwide net sales.

Source: Edison Investment Research, EvaluatePharma, company press releases. Note: GM-CSF = granulocyte macrophage colony stimulating factor, mCRPC = metastatic castration-resistant prostate cancer

Sensitivity analysis

We decided to perform a sensitivity analysis on two key inputs, **peak penetration** and **pricing**. This is because there are no comparable treatments in this specific patient population. For our pricing assumption we have used Zytiga (abiraterone) and Xtandi (enzalutamide) as the closest benchmarks, which have a list price of $45–70k per patient per year (EvaluatePharma). However, these hormone therapies are used in more advanced patient populations, so are not directly comparable. We have assumed 20% peak penetration, since there are a few other treatments in development for this patient population, but penetration will ultimately depend on the strength of RVV001's clinical data and pricing vs other available treatments.

Exhibit 12: Sensitivity analysis on pricing and market penetration to value per share

Pricing/market penetration	$30,000	$50,000	$70,000
10%	29.2	31.0	33.6
20%	32.3	**37.2**	39.9
30%	36.0	40.8	45.5

Source: Edison Investment Research

According to our model, a **successful Phase IIb outcome** would result in a significant increase in RhoVac's rNPV to SEK2.0bn or SEK107.1/share (not including the net cash estimate). For this scenario, we increased the probability of success to 40% as a Phase III-ready asset and changed the date of the valuation to the start of 2022, but left all other inputs unchanged.

Financials

RhoVac reports no income, while the operating spend was SEK20.2m in 2018, up from SEK12.9m in 2017, mainly to fund the Phase I/II study. RhoVac received SEK2.9m in tax credits in 2018. The company had cash of SEK16.1m at the end of 2018 and no debt. In April 2019, RhoVac announced a rights issue of SEK180.9m gross (SEK154.2m net). In total 9,523,551 shares should be issued (a 100% increase in number of shares outstanding) at a price of SEK19/share (versus SEK34.9 per share the day before the announcement). The rights issue is guaranteed by commitments from a group of investors. The subscription period is planned to last from 5 June to 19 June 2019.

RhoVac reported SEK6.2m in loss before tax in Q119. The Phase IIb study is expected to start in Q319 after the rights issue. The fresh capital will support RhoVac's Phase IIb study and the potential exploratory study with a checkpoint inhibitor. According to the company, and our model the cash will be sufficient to fund the budgeted activities until 2022. We therefore forecast operating expenses to pick up in H219 through to H221 (Phase IIb completion). Our current operating spend estimates for 2019 and 2020 are SEK37.0m and SEK50.0m, respectively.

Exhibit 13: Financial summary

SEK000s	2017	2018	2019e	2020e
Year end 31 December	K3	K3	K3	K3
PROFIT & LOSS				
Revenue	0	0	0	0
Cost of Sales	0	0	0	0
Gross Profit	0	0	0	0
Research and development	(12,243)	(19,154)	(37,000)	(50,000)
EBITDA	(12,857)	(20,148)	(37,000)	(50,000)
Operating Profit (before amort. and except.)	(12,857)	(20,148)	(37,000)	(50,000)
Intangible Amortisation	0	0	0	0
Exceptionals	0	0	0	0
Other	0	0	0	0
Operating Profit	(12,857)	(20,148)	(37,000)	(50,000)
Net Interest	(5)	(64)	382	577
Profit Before Tax (norm)	(12,861)	(20,212)	(36,618)	(49,423)
Profit Before Tax (reported)	(12,861)	(20,212)	(36,618)	(49,423)
Tax	1,911	2,936	0	0
Profit After Tax (norm)	(10,950)	(17,276)	(36,618)	(49,423)
Profit After Tax (reported)	(10,950)	(17,276)	(36,618)	(49,423)
Average Number of Shares Outstanding (m)	8.2	8.9	14.3	19.0
EPS - normalised (SEK)	(1.34)	(1.95)	(2.56)	(2.59)
EPS - normalised and fully diluted (SEK)	(1.34)	(1.95)	(2.56)	(2.59)
EPS - (reported) (SEK)	(1.34)	(1.95)	(2.56)	(2.59)
Dividend per share (SEK)	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	2,342	2,848	2,848	2,848
Intangible Assets	2,342	2,848	2,848	2,848
Tangible Assets	0	0	0	0
Investments	0	0	0	0
Current Assets	13,598	20,372	137,954	88,531
Stocks	0	0	0	0
Debtors	1,141	240	240	240
Cash	9,428	16,060	133,643	84,220
Other	3,029	4,071	4,071	4,071
Current Liabilities	(2,177)	(4,380)	(4,380)	(4,380)
Creditors	(2,177)	(4,380)	(4,380)	(4,380)
Short term borrowings	0	0	0	0
Long Term Liabilities	(505)	(596)	(596)	(596)
Long term borrowings	0	0	0	0
Other long term liabilities	(505)	(596)	(596)	(596)
Net Assets	13,258	18,245	135,827	86,404
CASH FLOW				
Operating Cash Flow	(13,853)	(17,097)	(37,000)	(50,000)
Net Interest	(6)	(64)	382	577
Tax	1,945	2,229	0	0
Capex	0	0	0	0
Acquisitions/disposals	0	0	0	0
Financing	1,182	21,756	154,200	0
Other	(241)	(191)	0	0
Dividends	0	0	0	0
Net Cash Flow	(10,973)	6,632	117,582	(49,423)
Opening net debt/(cash)	(20,401)	(9,428)	(16,060)	(133,643)
HP finance leases initiated	0	0	0	0
Other	0	(0)	0	(0)
Closing net debt/(cash)	(9,428)	(16,060)	(133,643)	(84,220)

Source: RhoVac accounts, Edison Investment Research

Contact details	Revenue by geography
Medicon Village Scheelevägen 2 Lund Sweden +46 73-751 72 78 www.rhovac.com/	N/A

Management team

CEO, CSO, Co-founder: Anders Ljungqvist	CFO: Henrik Stage
Anders Ljungqvist is a co-founder, CEO and board member of RhoVac. Mr Ljungqvist has been a board member of RhoVac ApS since 2008 and RhoVac AB since its establishment in 2015. He has an MSc in pharmacy and more than 35 years' experience in the pharmaceutical industry. Mr Ljungqvist has extensive expertise in fields such as project management, product formulation and regulatory issues. As board chair, he was involved in the successful exit of SurVac ApS.	Henrik Stage has an MSc in finance and more than 25 years' experience in leading biotechnology and finance sectors positions. Mr Stage's background includes several pharmaceutical deals and he was involved in the successful exit of Santaris Pharma, which was sold to Roche for US$450m in 2014. Mr Stage is a part-owner of Ventac Holdings (Cyprus) Ltd., which owns shares in RhoVac.
CBO, Deputy CEO: Anders Månsson	
Anders Månsson has extensive experience from the pharmaceutical world both internationally and locally. He has worked in senior positions in major pharmaceutical companies in Sweden, Denmark, the UK and Switzerland. The focus was on sales and the market, as well as on business development including distribution and licence agreements, divestments and acquisition agreements worth over several billion SEK. In recent years, he has also held a number of board positions in biotech/life science in southern Sweden. He has also held a CEO position in a stem cell company in Lund.	

Principal shareholders	(%)
RQ Solutions ApS	14.07
Ventac Holdings (Cyprus) Limited	12.49
Avanza Pension	6.49
Nordnet Pensionsförsäkring	3.73
Nils Berntsson	2.10
Ola Forsman	1.41
Anders Bremer	1.31

Companies named in this report

Aduro BioTech, Amgen, AstraZeneca, Bavarian Nordic, Bristol-Myers Squibb, Cell Genesys, Daiichi Sankyo, Dendreon, Janssen Biotech, Merck KGaA, OncBioMune Pharmaceuticals Inc, Roche, Takeda

General disclaimer and copyright

This report has been commissioned by RhoVac and prepared and issued by Edison, in consideration of a fee payable by RhoVac. Edison Investment Research standard fees are £49,500 pa for the production and broad dissemination of a detailed note (Outlook) following by regular (typically quarterly) update notes. Fees are paid upfront in cash without recourse. Edison may seek additional fees for the provision of roadshows and related IR services for the client but does not get remunerated for any investment banking services. We never take payment in stock, options or warrants for any of our services.

Accuracy of content: All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report and have not sought for this information to be independently verified. Opinions contained in this report represent those of the Edison analyst at the time of publication. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations.

Exclusion of Liability: To the fullest extent allowed by law, Edison shall not be liable for any direct, indirect or consequential losses, loss of profits, damages, costs or expenses incurred or suffered by you arising out or in connection with the access to, use of or reliance on any information contained on this note.

No personalised advice: The information that we provide should not be construed in any manner whatsoever as, personalised advice. Also, the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The securities described in the report may not be eligible for sale in all jurisdictions or to certain categories of investors.

Investment in securities mentioned: Edison has a restrictive policy relating to personal dealing and conflicts of interest. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report, subject to Edison's policies on personal dealing and conflicts of interest.

Australia

Edison Investment Research Pty Ltd (Edison AU) is the Australian subsidiary of Edison. Edison AU is a Corporate Authorised Representative (1252501) of Myonlineadvisers Pty Ltd who holds an Australian Financial Services Licence (Number: 427484). This research is issued in Australia by Edison AU and any access to it, is intended only for "wholesale clients" within the meaning of the Corporations Act 2001 of Australia. Any advice given by Edison AU is general advice only and does not take into account your personal circumstances, needs or objectives. You should, before acting on this advice, consider the appropriateness of the advice, having regard to your objectives, financial situation and needs. If our advice relates to the acquisition, or possible acquisition, of a particular financial product you should read any relevant Product Disclosure Statement or like instrument.

New Zealand

The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (i.e. without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision.

United Kingdom

This document is prepared and provided by Edison for information purposes only and should not be construed as an offer or solicitation for investment in any securities mentioned or in the topic of this document. A marketing communication under FCA Rules, this document has not been prepared in accordance with the legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research.

This Communication is being distributed in the United Kingdom and is directed only at (i) persons having professional experience in matters relating to investments, i.e. investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "FPO") (ii) high net-worth companies, unincorporated associations or other bodies within the meaning of Article 49 of the FPO and (iii) persons to whom it is otherwise lawful to distribute it. The investment or investment activity to which this document relates is available only to such persons. It is not intended that this document be distributed or passed on, directly or indirectly, to any other class of persons and in any event and under no circumstances should persons of any other description rely on or act upon the contents of this document.

This Communication is being supplied to you solely for your information and may not be reproduced by, further distributed to or published in whole or in part by, any other person

United States

The Investment Research is a publication distributed in the United States by Edison Investment Research, Inc. Edison Investment Research, Inc. is registered as an investment adviser with the Securities and Exchange Commission. Edison relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a) (11) of the Investment Advisers Act of 1940 and corresponding state securities laws. This report is a bona fide publication of general and regular circulation offering impersonal investment-related advice, not tailored to a specific investment portfolio or the needs of current and/or prospective subscribers. As such, Edison does not offer or provide personal advice and the research provided is for informational purposes only. No mention of a particular security in this report constitutes a recommendation to buy, sell or hold that or any security, or that any particular security, portfolio of securities, transaction or investment strategy is suitable for any specific person.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1,185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia