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ERIK PENSER BANK

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Spago Nanomedical

Standing out from the crowd

All eyes on Tumorad

After years of development, it is now time for the evaluation of Tumorad in patients. The project stands out from the majority of cancer treatments under development thanks to its unique profile and approach. What makes the current situation especially interesting is that we see the possibility for an indication of safety and efficacy in patients relatively early on in the upcoming clinical trial. In this, the study programme differs from other cancer treatments, and positive results could prompt considerable risk reduction within six to 12 months.

Market dynamics moving in right direction

We note that the pharmaceutical industry's interest in the field of cancer in recent years has moved in a direction that well suits the company's main project, Tumorad. This is reflected in renewed interest by investors and the industry in projects with an intrinsic toxic effect on cancer cells but with minimal adverse effects on normal tissue. Early clinical data showing positive signs that Tumorad can have an effect at an acceptable level of safety should motivate industry stakeholders and support the company's future financing.

Short-termism driving the share

Based on our valuation and how similar companies are valued, we see Spago's actual stock market valuation as uncoupled from the fundamentals. In our view, the share is currently hindered by uncertainty about the company's financing, but for those investors prepared to take a closer look and see beyond this, we consider this an interesting case potentially offering rich rewards if developments remain positive. The risk level is very high, but so is the potential for returns that live up to good sector risk/reward.

Change in estimates

	23e	24e	25e
Total revenue	0.0%	0.0%	0.0%
EBITDA, adj.	0.0%	0.0%	0.0%
EPS, adj.	0.0%	0.0%	0.0%

Upcoming events

Q3 - report	08 November 2023

Company facts (SEK m)

Number of shares	91m
Market capitalization	39
Net debt	-31
EV	7
Free float	80%
Daily trading volume, average	132k
Bloomberg Ticker	SPAGO SS EQUITY

Analyst

Klas Palin
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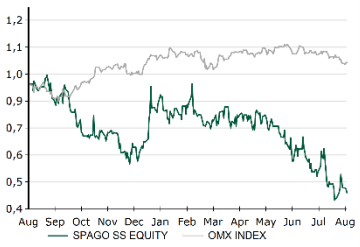
Forecast (SEK m)

	2022	2023e	2024e	2025e
Total revenue	6	11	14	16
Revenue growth	-1%	67%	32%	11%
EBITDA, adj.	-39	-41	-48	-62
EBIT, adj.	-39	-41	-48	-63
EPS, adj.	-0.4	-0.4	-0.5	-0.7
EPS growth, adj.	N.m.	N.m.	N.m.	N.m.
BV/share	2.2	2.0	1.9	1.8
EBIT margin	Neg.	Neg.	Neg.	Neg.
ROE, adj.	Neg.	Neg.	Neg.	Neg.
ROCE, adj.	Neg.	Neg.	Neg.	Neg.
EV/Sales	-	0.7x	0.5x	0.5x
EV/EBITDA	0.1x	-	-	-
EV/EBIT	0.1x	-	-	-
P/BV	0.3x	0.2x	0.2x	0.2x
Net debt / EBITDA	1.6x	1.0x	0.6x	0.3x

Value and risk

Fair value	SEK 1.9 – 2.0
Share price	SEK 0.5
Risk level	High

Price Performance 12 months



Conflicts of interest

	Yes	No
Liquidity provider		✓
Certified adviser		✓
Transactions 12m		✓

Investment case

Spago stands out as a specialist in the development of targeted nanoparticles for the diagnosis and treatment of cancer and carcinogenic diseases. It has seen positive developments in recent years, but this positivity has not transferred to investors or the stock, which is steered by short-termism and concerns about financing. The share price is under pressure, the market cap just surpassing the cash position. We believe investors are overlooking the potential of Tumorad in particular. The company is an interesting case, especially now the project portfolio is moving ahead, and we see potential for major value-driving news in the next six to 12 months. Positive results could prompt a doubling of the valuation.

We expect Tumorad in particular to spur interest and drive the valuation in the coming year. A ph 1/2a study is soon due to be initiated and conducted at clinics in Australia. Ph 1 studies can be relatively protracted, with limited value potential for investors. Here, however, the Tumorad study is markedly different, with the potential for relatively early results on how the Tumorad nanoparticles being distributed in the body, making it possible to gauge efficacy and side effects.

We see considerable interest in the pharmaceutical industry in targeted toxic cancer treatments, particularly radioactive treatments. Spago is on its own path, based on the EPR (enhanced permeability and retention) effect. We know from the other projects and pre-clinical studies that the radioactive isotope lutetium-177 is effective against cancer. The question is whether Tumorad accumulates in tumours to a high degree and with a manageable side-effect profile. Support for the EPR effect and the platform stems from pre-clinical studies, largely the positive results from the ph 1 SpagoPix study.

We highlight that drug development is one of the riskiest areas and any setbacks in clinical studies can induce termination of a project, in turn making it challenging for the company to continue operating.

Company profile

Spago Nanomedical specialises in the development and optimisation of nanoparticles. The company has two ongoing projects: SpagoPix (a contrast agent for MRI (magnetic resonance imaging) scans) and Tumorad (cancer treatment).

Project portfolio – Spago

Project	Indication	Development stage				
		Preclin	Phase 1	Phase 2	Phase 3	Market
SpagoPix (SN132D)	Breast cancer					
	Endometriosis					
Tumorad (SN201)	Solid tomours					
Completed						
Ongoing						

Source: EPB, Company

SpagoPix has the potential to replace established gadolinium-based contrast agents on the market, thanks to its better contrast properties and safety profile. We see the greatest potential in Tumorad (SN201), which could be used as a complement to established cancer treatments. SN201 is a nanoparticle loaded with radioactive lutetium (^{177}LU) optimised for selective absorption by cancer cells. SN201 has shown promising results in pre-clinical models of aggressive and metastatic cancers.

Central to both projects is the EPR effect. This is a well-documented effect in cancer in which cavities in the rapidly growing blood vessels for tumours are used to provoke nanoparticles to leak and accumulate. Moreover, the lymphatic system is often dysfunctional in cancer, meaning that molecules attached to tumour tissue often remain there for longer and can thus be used advantageously.

Valuation

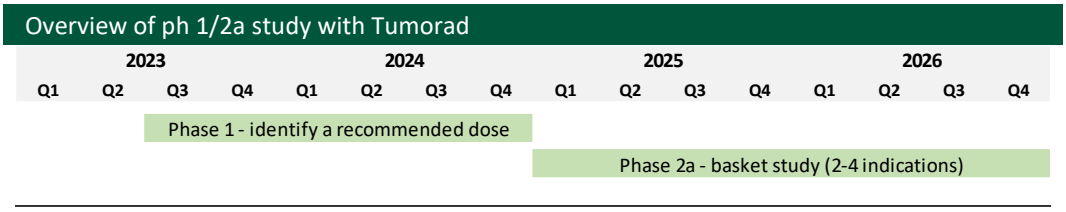
Our valuation of Spago is based on a probability-adjusted cash flow model in which we value each project individually before applying them to a sum-of-the-parts (SOTP) model. Our NPV SOTP model suggests a fundamental value of SEK 1.97 per share, with a WACC of 20%. We thus arrive at a fundamental fair value range of SEK 1.9–2.0.

Tumorad takes to the stage

After several years' development work, it is now time for Tumorad (^{177}Lu-SN201) to move to human studies, and the dosing of first patients in the coming ph 1/2a study is expected during Q3 2023. That Tumorad will now be tested in human studies means we are drawing closer to key data points that can provide the first indications of its safety and efficacy.

The ph 1/2a study will be carried out at clinics in Australia, allowing Spago to utilise the country's innovation support. Spago has established operations there and the first clinics are ready. A further benefit of a study in Australia is that local production of lutetium-177 (^{177}LU) makes logistics easier, since deliveries of the radioactive isotopes to clinics are time critical. Agreements with manufacturers of ^{177}LU and the production of nanoparticles are in place.

As usual, the main objective of a ph 1 trial is to evaluate safety/tolerability with escalating doses to identify the safe dose level to proceed to the next stage. The ph 1 will include up to 30 patients with late critical-stage solid tumours. The ph 1 trial is expected to take around 1.5 years – as shown below.



Source: Company

When a dose has been selected, the study will be expanded to ph 2a, aiming to evaluate the effect in 2–4 different cancer indications (basket trial). The company has highlighted ovarian cancer and triple-negative breast cancer as being of interest. Pre-clinical studies have also been conducted in colorectal cancer models – another potential indication for the ph 2a trial.

Prominent news flow on ph 1 study

The equity market sees ph 1 studies in cancer as essential but less likely to propel stock values. They take quite some time, are costly, and are the stage at which the risk of unwanted side effects is most probable. One advantage is the possibility of an indication of efficacy since cancer trials are conducted on patients. But demonstrating a clear effect is challenging. Usually, these trials include very seriously ill and frail cancer patients who have undergone many previous treatments. Moreover, a sub-optimal dose is typically used. Overall, it is now rare to see a convincing anti-tumour response in ph 1 studies. Ph 2 trials are thus the main value drivers, since the dose is at a recommended level and given to patients judged to have the greatest potential of responding to treatment.

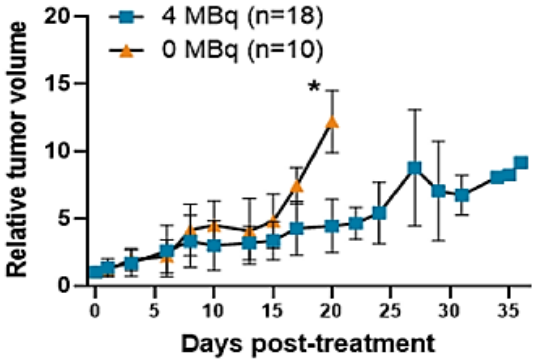
Here, the profile of the coming ph 1/2a study with Tumorad differs significantly, and we see potential for an indication of safety and tolerability within six to 12 months. We know from the pre-clinical trials and established therapies (Lutathera and Pluvicto from Novartis) that ^{177}LU has an effect on cancer. The question is whether a sufficient quantity of Tumorad accumulates at the tumour and whether side effects on vital organs, such as bone marrow and the liver, remain manageable. As ^{177}LU also emits gamma radiation (in addition to beta radiation) during its decay, it might be possible via imaging systems like SPECT (single-photon emission computed tomography) to trace how Tumorad is distributed in the body, even at low doses. This could make it possible to get an indication of uptake in vital organs and tumours from just a couple of patients. Important data thus has the potential to reduce the risks relatively quickly, which would spur interest among both pharma companies and investors.

Tumorad – background

Tumorad comprises nanoparticles charged with ^{177}LU, optimised to prolong circulation in the bloodstream to ensure a sufficient amount leaks out and accumulates at the tumours, but with limited uptake in the vital organs. As it is prompted by physiological properties in the tumours (EPR effect), Tumorad's targeting is not limited to cancer-specific target proteins. The EPR effect thus has broader potential and is relevant for more or less all malignant tumours.

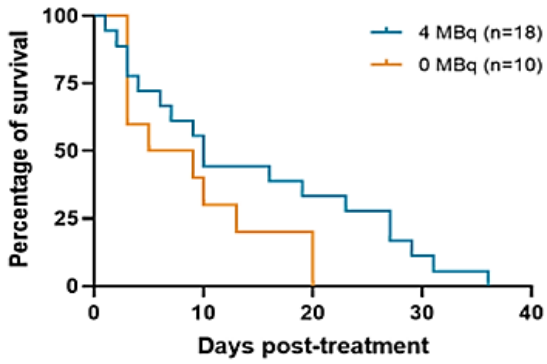
Prior to clinical development, Spago had undertaken pre-clinical studies with Tumorad, and earlier this year, an article was published in which Tumorad was shown to slow tumour growth and have a positive effect on survival (37% longer survival time compared with the control group in a pre-clinical colon cancer model). No unwanted reactions were noted with proteins in the blood or complement system, and the side-effect profile appeared manageable.

Pre-clinical results with Tumorad



Source: Mattisson et al. 2023

Pre-clinical results with Tumorad



Source: Mattisson et al. 2023

These results, together with earlier pre-clinical data from regulatory studies, showed a good safety profile for SN201 at doses surpassing the calculated clinical dose.

Lutetium confirmed as anti-cancer

Radioactive isotopes are unstable and can change to a more stable form through radioactive decay and the emission of different types of radiation. The radiation emitted has been shown to be useful against cancer and thus used as part of treatments like brachytherapy (placing radioactive sources close to tumours) or radiotherapy (radiation from an external source targeting the disease site). Radioactive substances are also used directly in the bloodstream for diagnosis and treatment of cancer. Drugs based on radioactive isotopes have historically proven a relatively lacklustre area, fraught with production, logistics, and handling challenges at clinics, while side effects have also limited their use.

In recent years, major advances have revitalised this field, driven largely by regulatory approval of Lutathera and Pluvicto from Novartis. These two treatments are based on ^{177}LU as an active anti-cancer substance. ^{177}LU induces cancer cell death directly via radiation to DNA, as well as indirectly via the reactive substances formed. It uses relatively limited tissue penetration of around 2mm, reducing the risk of irradiation of healthy surrounding tissue. The half-life is just over six days, which provides a window of transportation from the reactor production facilities to the clinics, while remaining radioactive when dosed, and allowing time for the substance to circulate the body and act on tumours.

Pluvicto (lutetium Lu 177 vipivotide tetraxetan) comprises ^{177}LU linked to a ligand, vipivotide tetraxetan, which is targeted at and binds strongly with PSMA (prostate-specific membrane antigen). PSMA is over-expressed in 85% of patients with metastasised castration-resistant prostate cancer (mCRPC), which is the indication being treated. Pluvicto was approved by the US's FDA during 2022 and by Europe's EMA in October of the same year.

The approval of Pluvicto stems mainly from a ph 3 study (VISION) in which the treatment was added to the standard of care (SOC), the result being compared with patients receiving only SOC. The Pluvicto arm showed tumour shrinkage in 30% of patients, compared with 2% among those receiving only SOC. The tumour effect also brought longer survival times and Pluvicto reached a median survival rate of 15.3 months compared with 11.3 months.

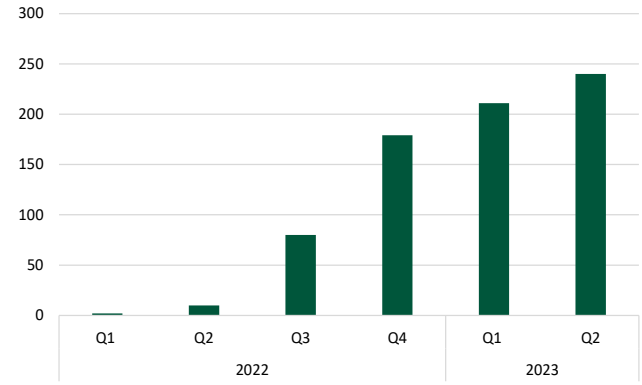
Lutathera (lutetium Lu 177 dotatate) was the first ^{177}LU-based drug to receive regulatory approval from the EMA (September 2017) and FDA (January 2018). Here, ^{177}Lu is linked to a somatostatin analogue (octreotate) that binds strongly with somatostatin receptor subtype 2 (SST2). Lutathera has been approved for treatment of somatostatin receptor positive patients with advanced gastroenteropancreatic neuroendocrine tumours (GEP-NET). SST2 is expressed on tumour cells in this patient group.

The NETTER-1 study was significant for the approval of Lutathera, with patients given the treatment alongside somatostatin analogues (SSA) compared with those receiving just SSA. Patients in the Lutathera arm demonstrated an 18% tumour response versus 3% in the control group. Treatment with Lutathera brought a median survival of 48.0 months compared with 30.9 months (adjusted for patients who switched to Lutathera treatment).

We believe that data for Lutathera and Pluvicto clearly supports an effect on cancer tumours with ^{177}LU, as seen in several pre-clinical models. They are associated with certain side effects, the most serious noted among patients being haematological changes, also affecting the liver and kidneys.

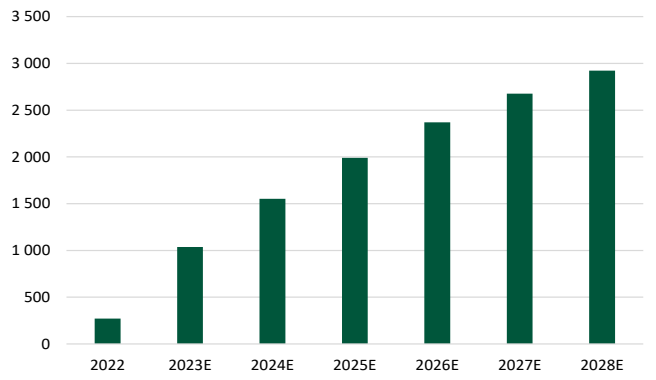
A challenge for Novartis since launch has been production, an area where it has faced scrutiny by the authorities. Production setbacks have delayed patient treatment, and it has struggled to match supply with demand. Novartis has invested in expanding its delivery capacity, though. Sales of Pluvicto have been strong regardless and just over a year after launch were at a 12-month rolling level of USD 1bn. Market forecasts suggest sales will close in on USD 3bn during 2028. The treatment price in the US is around USD 250,000.

Quarterly sales of Pluvicto (USDm)



Source: EPB, Novartis

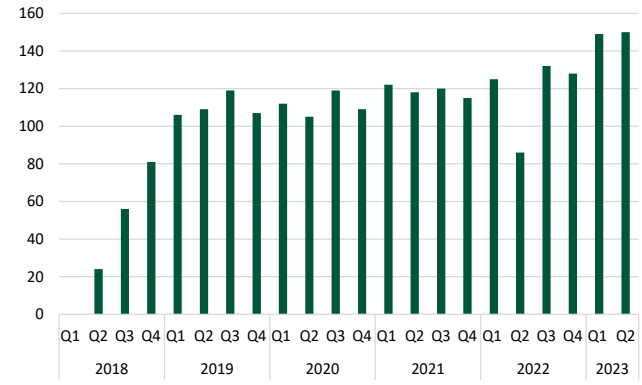
Sales forecasts for Pluvicto (USDm)



Source: EPB, Evaluate Pharma 2023

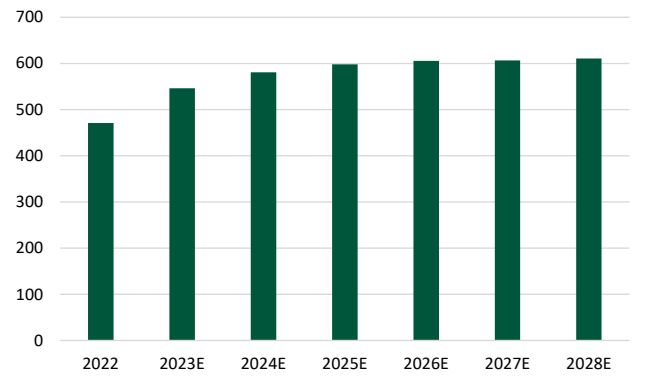
GEP-NET is a less prevalent cancer and we see other competing treatments clearly challenging Lutathera, which can partly explain the lower sales expectations.

Quarterly sales of Lutathera (USDm)



Source: EPB, Novartis

Sales forecasts for Lutathera (USDm)



Source: EPB, Evaluate Pharma 2023

The success of Lutathera and Pluvicto has shed new light on treatment with radioactive substances (radionuclide therapy). The positive results with ^{177}Lu have led several companies to use isotopes in development projects, although we cannot identify any other projects targeting tumours using the EPR effect. Lutathera and Pluvicto might have experienced production issues, but we believe they are prompting the expansion and improvement of production facilities along with essential experience for clinics in handling lutetium, and this will make it easier for Spago in its more comprehensive studies in the future.

Breast cancer study reduces the risks

For some years now, Spago has focused on developing nanoparticles that are selective to tumours. The company's final report for its first clinical studies with SpagoPix was released in December 2022 at the San Antonio Breast Cancer Symposium (SABCS). The study results are relevant to Tumorad, owing to the many similarities and as the nanoparticle is built on the same foundations.

A total of 12 breast cancer patients were included and divided into two dosing groups with SpagoPix – one lower (10 micromole Mn/kg) and one higher dose (20 micromole Mn/kg). Reported side effects in the study were mild and transient, not requiring additional treatment. Clinically relevant imaging improvements were reported in all patients on the highest dose, while even the six patients on the lower dose saw an imaging improvement. The most important factor was accumulation at the tumour, which we believe the study supported.

EPR effect central to Tumorad and SpagoPix

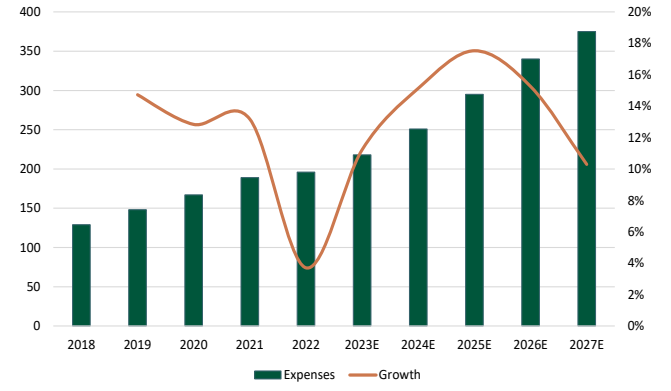
Both projects benefit from the EPR effect (**E**nhanced **P**ermeability and **R**etention effect). When tumours grow, new blood vessels are formed to supply the increased need for nutrients and oxygen. The blood vessels grow rapidly and as they mature, they are more porous owing to their cavities. Another effect of cancer is the lymph system's inability to drain around the tumours, which creates the conditions for nanoparticles that have seeped out around the tumour to remain and have an effect for longer. Researchers identified the EPR effect forty years ago, and it has since been scientifically accepted. Even at a tumour size of around 2 mm, new blood vessel formation is considered to take place, which is why it is possible to utilise the EPR effect even in smaller metastases. There are a number of drugs on the market that utilise the EPR effect, but none are designed and optimised to capitalise on its benefits. Abraxane (nab-paklitaxel) from Bristol Myers Squibb and Doxil (doxorubicin liposomal) from Johnson & Johnson are examples of nano-drugs for which the EPR effect plays a role.

The design similarities between Tumorad and SpagoPix are numerous, which is why we set great store by the positive results shown in the ph 1 study with SpagoPix in breast cancer patients, providing the first proof-of-concept for the platform.

Trends suggest early partner interest

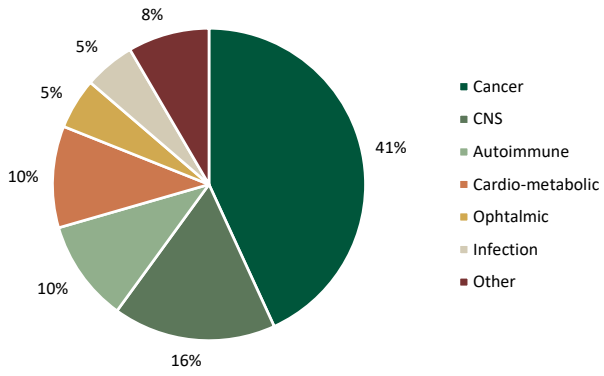
Cancer is by far the largest therapeutic area measured in annual drugs sales, accounting for just over 25% of the total drugs market. The largest pharmaceutical companies are today active in the field and devote a large part of their R&D budgets to this area. The field also attracts smaller companies, whose market share has risen in recent years. Cancer drugs are often priced high, making it appealing to build sales themselves, even in limited cancer indications. We have seen a marked shift in recent years, with the large pharma companies' dominance diminishing from 36% to 21% between 2017 and 2022. On the business side, cancer is the largest field, representing more than 40–50% of all licensing deals.

Global expenditure on cancer drugs, USDbn



Source: Iqvia Global Oncology Trends 2023

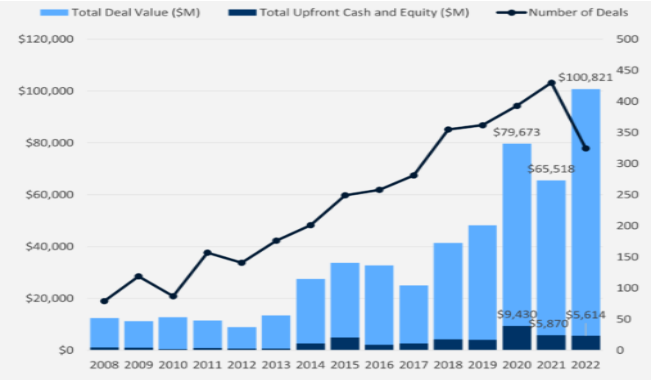
Split of licensing agreements across different therapeutic areas



Source: EPB, DealForma 2023

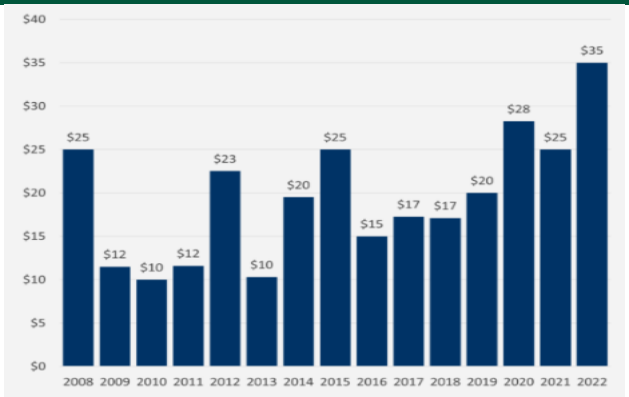
The number of transactions and deal values in the cancer field has steadily increased over the past 15 years, but we note a general decline in activity in H1 2023 that started last year – see below.

Licensing activity in the cancer field, 2008-2023 (USDm)



Source: DealForma.com, March 2023

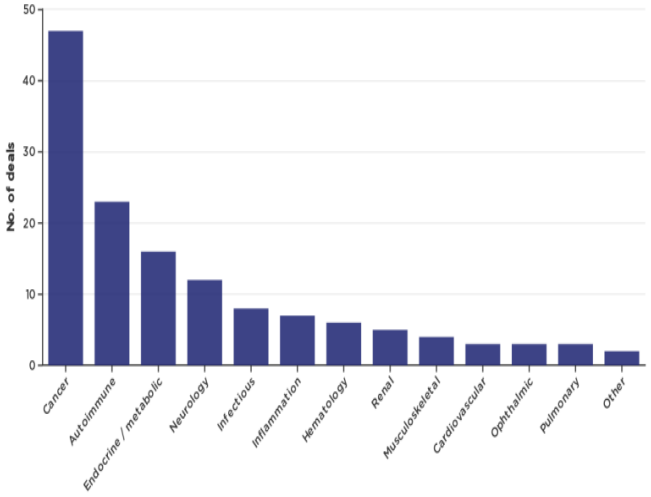
Median cash compensation for licensing deals (USDm)



Source: DealForma.com, March 2023

New figures compiled by Biocentury confirm a continued high level of activity in recent years among Big Pharma to license or acquire cancer projects. The decline is mainly among the smaller companies. It is notable that most transactions are made up to and including ph 2, when the most promising projects are snapped up. We believe the coming clinical trials will be when a partner for Spago could materialise.

Big Pharma deals, Q3 2022–Q2 2023 (indications)



Source: Biocentury, August 2023

Big Pharma deals, Q3 2022–Q2 2023 (development stage)

Source: Biocentury, August 2023

An area moving in the right direction

Some of the greatest progress in cancer in recent decades has been within immunotherapies, and much R&D focus has thus been on this area. We note a broadening of interest in recent years, however, as well as a return of interest in toxic anti-cancer treatments – the difference being that instead of chemotherapy, targeted drugs are now being sought to limit the side effects and optimise the dosage. Two examples are antibody conjugates (ADC) and radionuclide therapies, in both of which we note a significant increase in activity. This suits Spago and its position well, as the EPR effect can provide tumour selectivity with a cancer-killing effect.

We perceive the appeal in ADC to be the combination of a treatment with toxic properties (like chemotherapy) and the targeting precession of antibodies. The challenge in developing ADC has been the link between the toxic substance and the antibody, as it is important to keep the molecules together long enough for them to be taken up by the cancer cells but then released so they separate in the tumour cell. We do not anticipate this challenge for Tumorad, as the radioactive substance remains in the particles until activity ends or the nanoparticle is excreted. Tumorad does not need to be taken up by the cells, since it works by attaching itself to the tumour.

Activity in the radionuclide area is similar to that within ADC, with more or less all projects based on the same principles but instead with a radioactive isotope linked to a targeting molecule, which is directed at target structures overexpressed on the tumour. This is where the EPR effect, which is cancer-specific but not indication-specific, differs. Even though radionuclide therapies have long existed as a pharmaceutical field, activity in this area only started to take off in the past couple of years. The majority of companies active here are thus relatively newly started and only about to enter the clinical phase. We note significant interest among venture capital firms and list a selection of transactions below.

None of those listed have chosen the same path as Spago, instead using a radioactive isotope linked to a molecule that searches for target structures on tumours. Given Spago's unique path, there are considerable uncertainties associated with Tumorad, but should Spago prove the concept works in humans, it can point to a clear differentiation that should appeal to both pharma companies and investors.

Selection of funding activities in radionuclide therapy, 2020–2023

Company	Date	Last transaction	Total	Radionuclide and target of main program	Development stage
ITM Isotope	Jun-23	USD 273m	USD 470m	^{177}LU linked to a peptide (edotreotid)	Phase 3
Artbio	Jun-23	USD 23m	USD 23m	^{212}Pb ligand (alfa particle) - tumours specific ligands	Phase 0
Convergent Therapeutics	May-23	USD 90m	USD 90m	^{225}AC linked to antibody targeting PSMA (alfa particle)	Phase 1
Ariceum Therapeutics	Apr-23	USD 48m	USD 75m	^{177}LU linked to peptide	Phase 2
Abdera Therapeutics	Apr-23	USD 142m	USD 175m	Radionuclide linked to antibody (DLL3)	Preclin
Ratio Therapeutics	Feb-23	USD 20m	USD 40m	^{225}AC (alfa particle)	Preclin
Alpha-9 Theranostics	Dec-22	USD 75m	USD 86m	Peptides and small molecules linked to lutetium os actinium	Preclin
Rayzebio	Sep-22	USD 160	USD 418m	^{225}AC linked to antibody	Phase 1
Full-Life Technologies	May-22	USD 37m	USD 47m	Rodio active isotpoes linked to peptide	Preclin
Precirix	Mar-22	USD 88m	USD 132m	225AC linked to antibody	Preclin
Plus Therapeutics	Jan-22	USD 5m	USD 142,8m	^{186}Re (beta particle) encapsulated in liposome	Phase 2
Radionetics	Oct-21	USD 30m	USD 30m	Small molecule, G protein linked receptor	Preclin
POINT Biopharma	Jul-21	USD 287m (IPO)	USD 307m	^{177}LU linked to peptide (edotreotid)	Phase 3
Aktis Oncology	Mar-21	USD 72m	USD 161m	^{225}AC (alfa particle)	Preclin
Clarity Pharmaceuticals	Dec-20	USD 25m	USD 97m	^{67}Cu, peptid-link	Phase 2
PentixaPharm	Feb-20	USD 17m	USD 17m	^{90}Y peptide ligand targeting tumours	Phase 1

Källa: EPB, Company data

Examples of other companies active in radionuclide therapies are Fusion Pharma (ph 2), Telix Pharma (ph 2), Radiopharm Theranostics (pre-clinical), and Qsam Bioscience (ph 1). Below, we list a selection of the largest transactions in the radionuclide field in recent years.

Selection of acquisitions and licensing agreements in the radionuclide field, 2020–2023

Buyer	Seller	Development stage	Upfront	Total deal value	Date
Ariceum Therapeutics	Theragnostics	Preclinic	2,5 MUSD	44 MUSD	june 23
Bayer	Bicycle Therapeutics	R&D stage	45 MUSD	1.700 MUSD + 5-10% royalty	may 23
Novartis	3B Pharmaceuticals	Phase 1 (FAP-2286)	40 MUSD	425 MUSD + royalty	apr-23
Novartis	Bicycle Therapeutics	R&D deal	50 MUSD	1.700 MUSD + royalty	mar-23
Novartis	Clovis Oncology	Phase 1 (FAP-2286)	50 MUSD	680 MUSD, 297 MUSD sales related	dec-22
Lantheus	Point Biopharma	Phase 3	260 MUSD	2.000 MUSD + royalty	nov-22
Grand Pharmaceuticals	ITM Isotope	Phase 3	ND	588 MUSD + royalty	dec-21
Bayer	Noria Therapeutics	Preclinic	ND	ND	june 21
Novartis	Artios Pharma	Preclinic	20 MUSD	1.300 MUSD + royalty	apr-21
Novartis	iTheranostics	Preclinic	20 MUSD	1.300 MUSD + royalty	mar-21
Astrazeneca	Fusion Pharmaceuticals	Preclinic	ND	ND	nov-20
Genentech	Bicycle Therapeutics	R&D deal	30 MUSD	1.700 MUSD + royalty	feb-20

Source: EPB, Company data

Bayer and Novartis have been the most active, while AstraZeneca and Genentech/Roche are also present in the field. Bayer and Novartis have had a positive view of this area for many years. For example, Bayer bought Norway's Algeta back in 2013 to get its hands on Xofigo through a USD 2.9bn deal. During 2018, Novartis bought Endocyte for USD 2.1bn in a deal carried out primarily for access to Pluvicto. The year before, it had acquired Advanced Accelerator Applications for USD 3.9bn, the

main asset being Lutathera, which was approved in the EU. We believe that as this field matures, we will see more Big Pharma firms making deals, largely since radionuclide therapies are well suited for combination with other cancer treatments.

Prognosis for Tumorad

Thanks to its use of physiological targeting (the EPR effect), Tumorad has broad potential against solid tumours. The fierce competition in the cancer field is why we limit our forecasts for Tumorad to only a few cancer indications. In our assessment of the potential, we have chosen to stick to three cancer indications: breast, colorectal, and ovarian cancer. We use what the company has communicated and the pre-clinical data generated so far. We believe these three indications are likely to be included in the ph 2a part of the studies. Our forecasts for these indications are based on data for Europe and the US, while we consider the rest of the world as upside.

Developing a cancer treatment is one of the most challenging pharmaceutical areas and the probability of achieving market approval is low. In our view, the development risk at every stage is based on statistical evidence from a variety of studies that are weighted by industry standards. The pre-clinical data and results for SpagoPix are the reason why we adjust from the industry standards and assume a slightly lower development risk than for the average project.

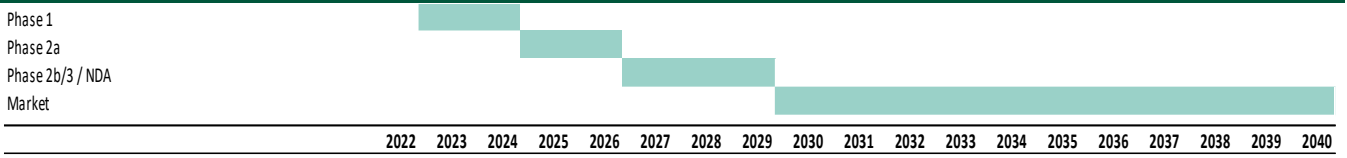
Probability assessment for each stage of Tumorad's development

		Phase I	Phase II	Phase III	NDA	Total
Tumorad	Solid tumours	50%	40%	50%	85%	**8.5%**
Industry standard	Solid tumours	40%	30%	50%	85%	**5.1%**

Source: EPB, Various reports

Below, we show an estimated timeline for Tumorad's development in these markets. For colorectal cancer, we have added one extra year to account for the potential need for larger pivotal studies.

Estimated timeline for Tumorad towards market approval



Source: EPB, Company

Our modelling of the potential in each indication is patient-based, assuming Tumorad is used in later-stage treatment lines when other options are no longer available. We have based the price on other cancer drugs, using the launched radioactive therapies as a reference, and thus arrive at USD 150,000 in the US and USD 75,000 in Europe.

Tumorad forecasts by region and indication (USDm)

	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
Ovarian																		
Europe	0	0	0	0	0	0	0	14	36	60	86	108	120	115	110	105	100	95
USA	0	0	0	0	0	0	0	28	80	150	229	288	322	308	295	282	269	258
TNBC																		
Europe	0	0	0	0	0	0	0	9	31	57	86	107	120	114	109	103	99	94
USA	0	0	0	0	0	0	0	18	54	99	148	186	209	202	194	188	181	175
Colonrectal																		
Europe	0	0	0	0	0	0	0	42	106	178	258	326	366	351	337	324	245	149
USA	0	0	0	0	0	0	0	44	112	188	272	345	388	372	357	342	259	157
Total																		
Europe	0	0	0	0	0	0	0	65	172	295	430	542	606	580	555	532	444	338
USA	0	0	0	0	0	0	0	89	245	438	649	819	918	882	845	812	710	590
Sum	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**155**	**417**	**733**	**1079**	**1361**	**1525**	**1462**	**1401**	**1343**	**1153**	**928**

Source: EPB

A new path for SpagoPix

After achieving positive results in a ph1 study in breast cancer, the company saw the potential to build added value in SpagoPix by broadening the clinical evidence and evaluating the image-enhancing properties in patients with suspected endometriosis. As with cancer, here blood vessels form to provide nutrition to the tissue and these exhibit porous properties that SpagoPix can use to leak out at the disease sites. Taking the next step towards endometriosis increases the potential in an area with limited competition from established players. This made a study programme cost-effective for Spago, as research grants account for the bulk of the funding.

The study was initiated at the end of 2022 at Skåne University Hospital in Malmö, with the aim of evaluating the safety profile and whether SpagoPix can contribute to imaging improvements shown via MRT. For most patients with suspected endometriosis, there is still no alternative method to reliably make a diagnosis. MRT is used to some extent with cases like deep-seated endometriosis, but with varying results.

In May, the principal investigator, Dr Ligita Jokubkiene, presented their first observations – which were described as promising – at the 15th World Congress on Endometriosis. The following month, the first clinical results were released after eight of the 18 patients were examined with SpagoPix. This was prompted by the study's data monitoring committee considering the patient number sufficient to implement a full analysis of tolerance and efficacy, and so recruitment of further patients was halted. As expected, the preliminary results showed that treatment with SpagoPix was tolerated, without any material side effects, and confirming the results previously reported in breast cancer. However, it was not possible to draw direct conclusions on its impact, although further analysis is ongoing. The analysis is delayed since it relates to patients with deep endometriosis, complicating the interpretation of the data.

We look forward to a more detailed analysis of the data, but our expectations on SpagoPix are tempered while we wait. We believe it not being able to draw direct conclusions could pose a risk that the final analysis does not provide clear enough signals of efficacy to justify further development in this indication.

Major female disease in need of better diagnosis

Endometriosis is a chronic inflammatory disease that affects up to one in ten women of childbearing age. In endometriosis, tissue similar to the endometrium grows outside the uterus, causing inflammation and scarring. This can lead to severe pain and, in the worst case, infertility. There is no curative treatment, simply a focus on alleviating the symptoms. Typical treatment is with hormones or surgical removal of the tissue in some cases. The disease is hard to diagnose, often confused with other, similar conditions, and it can thus take seven to ten years to gain a correct diagnosis. Diagnosis is based on patient symptoms and gynaecological examination, but suspected endometriosis is investigated using keyhole instruments (laparoscopy), ultrasound, and, in some cases, MRT. There is demand for additional diagnostic methods – most of all, non-invasive – to identify deep endometriosis, for example.

Prognosis for SpagoPix

Estimates for SpagoPix are hampered by the lack of a clear path ahead. The breast cancer study certainly offered promising results, but the industry currently seems to have limited interest in new, more efficient and environmentally friendly alternatives. We believe the company's decision to take its next step outside of breast cancer supports this view.

Given the uncertainty regarding further development in breast cancer, we have built our forecasts on the endometriosis path. We see considerable uncertainty about future developments here, though, and hope that the final analysis can provide data that convinces us of the potential. Based on what we know today – or sooner, what we do not know – we assign a low likelihood to the project.

Probability assessment per development step for SpagoPix

		Phase I	Phase II	Phase III	NDA	Total
SpagoPix	Breast cancer	100%	0%	0%	0%	**0.0%**
	Endometriosis	100%	15%	40%	90%	**5.4%**

Source: EPB

The potential we pencil in for SpagoPix is based on some 20–30% of the patients having suspected deep endometriosis. Of these, we calculate around 20% will undergo an MRT scan, with half of these being given SpagoPix to facilitate diagnosis. We estimate the potential at USD 190m using these assumptions and a price of USD 800 in the US and half that in Europe. We have included a deal in 2026 for a total USD 100m – with USD 10m in upfront and royalties of 12%, but appropriately risk-adjusted.

Forecasts for SpagoPix in endometriosis (USDm)

	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
Endometriosis																		
Europe	0	0	0	0	10	24	35	41	41	41	39	37	36	32	29	26	23	20
USA	0	0	0	0	30	76	113	138	143	148	145	142	140	130	120	111	101	93
Sum	**0**	**0**	**0**	**0**	**39**	**100**	**148**	**179**	**184**	**189**	**184**	**180**	**176**	**162**	**149**	**136**	**124**	**113**

Source: EPB

It is difficult to judge the appeal to partners from the outside, but that none have yet wanted to license SpagoPix implies that they need more data to be convinced. Hopefully, the endometriosis study can provide that.

One challenge for finding a licensing partner for SpagoPix is the status of the diagnostic imaging field, with its limited number of players and oligopolistic market structure. Moreover, not all these companies have the same type of organisation that can adopt innovations in this area as the pharmaceutical industry, where the survival of pharma companies is more or less dependent on the successful development of new products.

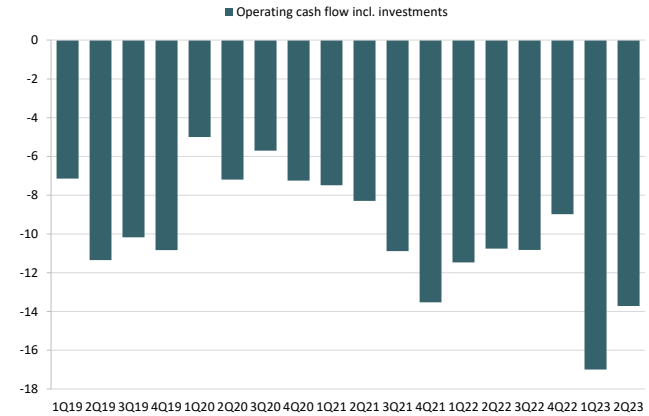
Financial forecasts

Preparation for the Tumorad clinical studies and to some extent the ongoing ph 2 with SpagoPix in endometriosis pushed up costs during H1 2023, with most of the cost burden falling in Q1. Operational costs during H1 2023 rose to SEK 28.2m (22.2m), consisting largely of higher project costs, which were up at SEK 15.1m (8.9m).

As we mentioned earlier, Spago established operations in Australia ahead of the coming ph 1/2a study in Tumorad. However, it can thus utilise the country's R&D innovation support, which offers 43.5% reimbursement of such investments. So far this year, Spago has booked SEK 1.6m in innovation support, of which SEK 0.8m was in Q2. However, the cash flow effect is delayed by one month. Cash flows have developed relatively in line with operating results over time, as shown below. We highlight that we include investments in the operating cash flow, to also include capitalised R&D.

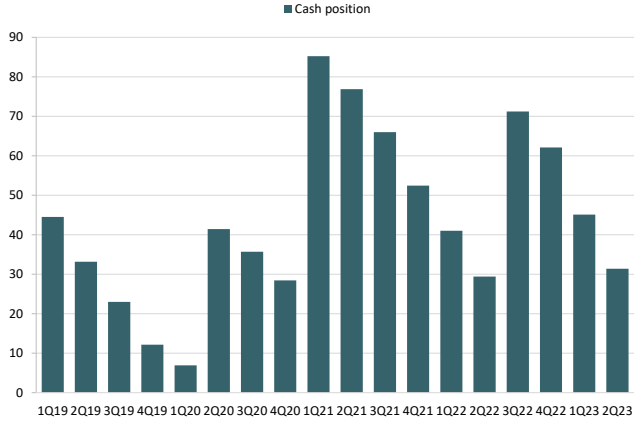
At the end of Q2, cash and cash equivalents were at SEK 31.4m. In our view, Spago's current cash position offers financing into early 2024, meaning a relatively immediate need to strengthen its finances. Our estimates thus include funding of SEK 30m this year and of a further SEK 40m in 2024. The breakdown of this may be different, though.

Operating cash flow incl. investments (SEKm), 2019–2023



Source: EPB, Company

Cash and cash equivalents (SEKm), 2019–2023



Source: EPB, Company

During H2 2023, we expect to see some increase in costs compared with Q2 2023, but no dramatic increase versus H1 2023. We anticipate a gradual increase in costs as the ph 1/2a study in Tumorad advances and more patients are included – see below.

Quarterly and full year estimates, 2022–2025 (SEKm)

	1Q23	2Q23	3Q23E	4Q23E	2022A	2023E	2024E	2025E
Net sales	0.1	0.1	0.1	0.1	1.1	0.4	0.5	0.5
Other operating income	2.5	2.8	2.4	2.8	5.4	10.4	13.7	15.2
Total income	**2.5**	**2.9**	**2.5**	**2.9**	**6.5**	**10.8**	**14.2**	**15.7**
Other externa expenses	-13.0	-6.6	-7.4	-8.0	-28.8	-35.0	-43.8	-59.1
Personnel costs	-4.1	-4.3	-4.0	-4.4	-16.8	-16.8	-18.0	-18.9
Depreciation	-0.1	-0.1	-0.1	-0.1	-0.4	-0.3	-0.4	-0.4
Operating income	**-14.6**	**-8.1**	**-9.0**	**-9.6**	**-39.5**	**-41.3**	**-47.9**	**-62.6**
Financial net	0.2	0.2	0.2	0.2	0.3	0.9	0.4	0.4
EBT	**-14.4**	**-7.9**	**-8.8**	**-9.4**	**-39.2**	**-40.4**	**-47.5**	**-62.2**
Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Profit/loss for the period	**-14.4**	**-7.9**	**-8.8**	**-9.4**	**-39.2**	**-40.4**	**-47.5**	**-62.2**

Source: EPB, Company

Valuation

Our valuation of Spago Nanomedical employs a probability-adjusted cash flow model in which we assess and evaluate each project separately before including it in a sum-of-the-parts (SOTP) model. We include the company's two active projects, SpagoPix and Tumorad, for which we see supporting data and plans for further development.

Our NPV SOTP model suggests a fundamental value of SEK 1.97 per share, with a WACC of 20%. We thus set a fundamental fair value of SEK 1.9–2.0. The share currently trades far below this fair value and a key reason for this is, we believe, the uncertainty regarding future financing. At current price levels, a WACC of around 40% is implied.

Valuation – sum-of-the-parts (SEKm)

Project	Indication	Likelihood of approval	Peak sales (USDm)	Launch	NPV*	NPV per share
SpagoPix	Breast cancer, Endometriosis	5.4%	190	2028	26	0.29
Tumorad	Solid tumours	8.5%	1,500	2030	179	1.97
Techvalue					**204**	**2.2**
Net cash					31	0.3
Shared expenses					-57	-0.6
NPV					**179**	
Number of shares					91	
NPV per share (SEK)					**1.97**	

*SEKm, USD=10,6 SEK

Source: EPB

Below, we show the sensitivity of our valuation per project to changes in the required rate of return. We also show how the company's valuation changes given different likelihoods for Tumorad. Here we want to show the value using the industry average (5.0%), in the present situation (8.5%), given early ph 1 signs that the nanoparticles are working as expected (12.0%), and a scenario in which the ph 1 study is successful and a recommended dose for ph 2a can be chosen (17%). The modelling demonstrates our view of the enormous leverage in the project as early as in ph 1 development.

Sensitivity analysis – value per project given various WACC (SEK)

	14%	17%	20%	23%	26%
SpagoPix	0.42	0.34	0.28	0.24	0.21
Tumorad	3.58	2.64	1.96	1.46	1.09
Spago Nanomedical	3.31	2.55	1.97	1.53	1.20

Source: EPB

Sensitivity analysis – different likelihoods for Tumorad

	5.0%	8.5%	12%	17%
SpagoPix	0.28	0.28	0.28	0.28
Tumorad	1.06	1.96	2.85	4.19
Spago Nanomedical	1.07	1.97	2.86	4.20

Source: EPB

Valuation of comparable companies

Below we provide a table with a few pharma companies listed in Sweden and Denmark. We have chosen companies in a similar development phase within oncology/radiotherapy. As none of them have recurring revenues and none are profitable either, we use technological value (EV) to compare them to one another. Even though they are a relatively diverse group, this highlights the low expectations that also exist for Spago. We believe the market overlooks the potential signals we will receive as to whether Tumorad can live up to its profile, which would imply a leap in value in our model. Such data would also facilitate future financing.

Valuation of comparable companies (SEKm)

Company	Market cap	Share price (SEK)	Net cash	Techvalue (EV)
Active Biotech*	231	0.87	30	200
Curasight (DK)*	563	17.8	70	493
Kancera*	408	5.00	76	331
Medivir*	418	7.37	101	317
Mean	405			335
Median	413			324
Spago Nanomedical	**39**	**0.43**	**31**	**8**

*as of Q1 2023, **therapy program

Source: EPB, Company reports, Holdings, share price based on close the 11 of august

Below, we have compiled the valuations of a selection of listed international companies active in the development of cancer radionuclide therapy. All these have progressed further than Spago, in some cases even reporting revenues on sales of image enhancement products, that are often combined with the development of therapy projects. We also point out that all the companies have projects with a targeted link to their radioactive isotope, but not using the EPR effect.

Selection of listed companies within radionuclides – international (SEKm)

Company	Listed country	Market cap	Net cash	Techvalue (EV)	Development stage
Actinium Pharmaceuticals	USA	1 821	959	862	Phase 3
Alpha Tau Medical	USA/Israel	2 854	975	1 879	Phase 3/Market
Clarity Pharmaceuticals	Australien	1 697	536	1 161	Phase 3
Fusion Pharmaceuticals	USA	2 237	1 597	640	Phase 2
POINT Biopharma Global Inc	USA	10 270	4 459	5 811	Phase 3
Radiopharm Theranostics	Australien	213	170	43	Preclin*
Telix Pharmaceuticals	Australien	22 499	748	21 751	Phase 2*
Mean		5942		4592	
Median		2237		1161	
Spago Nanomedical		**39**	**31**	**8**	

*Therapy program

Source: EPB, FactSet, share price based on close the 11 of august

Telix stands out thanks to its high market cap, stemming from the company's established sales of molecules used to enhance the imaging of tumours. Point's high market cap is the result of it having succeeded in attracting Novartis to two of its projects.

Risks in our assumptions

Investing in drug development companies involves high risk. Below, we highlight some of the most significant that we have identified and that should be considered when investing in Spago Nanomedical.

Negative study outcomes: The foremost risk with an investment in a drug development company is negative results from a clinical study, as this can spell an end to the project. Development risk is somewhat reduced as it has already been demonstrated that nanoparticles can accumulate at the tumours, which suggests that the EPR effect can be utilised.

Delays to studies: Recruiting patients for studies can be more protracted than a company expects, leading to a need for further financing to reach development goals and conclude the studies.

Financing needs: Running clinical studies is a costly business and a company like Spago has recurring capital needs. As a project advances in development, these capital needs typically increase. We believe it is positive that the company has chosen to conduct its clinical studies for Tumorad in Australia, which will nearly halve its direct costs. In our view, however, the company will need to strengthen its finances this year to be prepared for 2024.

Partner agreements fail to materialise: The company's most advanced project, SpagoPix, has shown promising results and if the ongoing study in endometriosis is successful, we expect the company to increase its efforts to secure a partnership agreement. The number of potential project partners is limited, however, and they are relatively inactive in the development of new products. We currently believe a partner is essential for the development of SpagoPix to move to the next stage.

Income statement

	2019	2020	2021	2022	2023e	2024e	2025e
Net sales	**0**	**0**	**1**	**1**	**0**	**1**	**1**
Other operating income	19	7	6	5	10	14	15
Total revenus	**19**	**7**	**7**	**6**	**11**	**14**	**16**
Gross profit	**19**	**7**	**7**	**6**	**11**	**14**	**16**
Administrative Expenses	-17	-14	-16	-17	-17	-18	-19
R & D Expenses	-22	-12	-29	-29	-35	-44	-59
EBITDA	**-20**	**-19**	**-39**	**-39**	**-41**	**-48**	**-62**
EBITDA, adjusted	**-20**	**-19**	**-39**	**-39**	**-41**	**-48**	**-62**
EBITA, adjusted	**-20**	**-19**	**-39**	**-39**	**-41**	**-48**	**-63**
EBIT	**-20**	**-19**	**-39**	**-39**	**-41**	**-48**	**-63**
EBIT, adjusted	**-20**	**-19**	**-39**	**-39**	**-41**	**-48**	**-63**
Net Financial Items	0	0	0	0	1	0	0
Profit before tax	**-20**	**-19**	**-39**	**-39**	**-40**	**-47**	**-62**
Profit before tax, adjusted	**-20**	**-19**	**-39**	**-39**	**-40**	**-47**	**-62**
Net income	**-20**	**-19**	**-39**	**-39**	**-40**	**-47**	**-62**
Net income, adjusted	**-20**	**-19**	**-39**	**-39**	**-40**	**-47**	**-62**
Sales Growth	*-*	*-62%*	*-10%*	*-1%*	*67%*	*32%*	*11%*
Gross Margin	*Neg.*	*>100%*	*>100%*	*>100%*	*>100%*	*>100%*	*>100%*
EBIT Margin, Adjusted	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
EPS, Adjusted	*-0.94*	*-0.59*	*-0.94*	*-0.43*	*-0.44*	*-0.52*	*-0.68*
EPS Growth, Adjusted	*-*	*N.m.*	*N.m.*	*N.m.*	*N.m.*	*N.m.*	*N.m.*

Source: Spago Nanomedical, EPB

Cash flow statement

	2019	2020	2021	2022	2023e	2024e	2025e
EBIT	-20	-19	-39	-39	-41	-48	-63
Other Cash flow Items	0	0	0	1	0	0	0
Changes in working capital	-1	0	3	1	-3	1	0
Cash flow from operating activities	**-21**	**-18**	**-36**	**-38**	**-44**	**-47**	**-62**
Investments in intangible fixed assets	-18	-6	-5	-4	-7	-4	-3
Cash Flow From Investments	**-18**	**-6**	**-5**	**-4**	**-7**	**-4**	**-3**
Free cash flow	**-40**	**-25**	**-40**	**-42**	**-51**	**-50**	**-64**
New share issue / repurchase	35	41	64	52	30	40	50
Cash flow from financing	**35**	**41**	**64**	**52**	**30**	**40**	**50**
Cash flow	**-4**	**17**	**24**	**10**	**-21**	**-10**	**-14**
Net debt	**-12**	**-28**	**-52**	**-62**	**-41**	**-31**	**-16**

Source: Spago Nanomedical, EPB

Balance sheet

	2019	2020	2021	2022	2023e	2024e	2025e
ASSETS							
Other intangible assets	126	132	136	140	146	148	151
Tangible fixed assets	1	1	1	1	1	0	0
Total fixed assets	**127**	**133**	**137**	**141**	**147**	**148**	**151**
Accounts receivable	0	0	0	0	0	1	1
Other current assets	1	1	2	3	4	5	6
Cash and cash equivalents	12	28	52	62	41	31	16
Total current assets	**14**	**30**	**54**	**65**	**45**	**36**	**23**
TOTAL ASSETS	**141**	**163**	**192**	**206**	**192**	**185**	**174**
EQUITY AND LIABILITIES							
Equity	138	160	185	197	185	176	163
Total equity	**138**	**160**	**185**	**197**	**185**	**176**	**163**
Accounts payable	1	1	4	5	2	4	5
Other current liabilities	2	2	3	4	4	5	6
Total current liabilities	**3**	**3**	**7**	**9**	**7**	**9**	**11**
TOTAL EQUITY AND LIABILITIES	**141**	**163**	**192**	**206**	**192**	**185**	**174**

Source: Spago Nanomedical, EPB

Growth and margins

	2019	2020	2021	2022	2023e	2024e	2025e
Revenue growth	-	-62%	-10%	-1%	67%	32%	11%
EBITDA growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.	N.m.
EBIT growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.	N.m.
EPS growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.	N.m.
Gross margin	Neg.	>100%	>100%	>100%	>100%	>100%	>100%
EBITDA margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBITDA margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBIT margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBIT margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Profit margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

Source: Spago Nanomedical, EPB

Return

	2019	2020	2021	2022	2023e	2024e	2025e
ROE, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
ROCE, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
ROIC, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

Source: Spago Nanomedical, EPB

Capital efficiency

	2019	2020	2021	2022	2023e	2024e	2025e
Accounts receivable / total revenue	-	0%	1%	1%	3%	6%	8%
Total short-term liabilities / total cost	7%	12%	15%	19%	13%	15%	14%
Working capital / total revenue	-8%	-24%	-75%	-88%	-24%	-24%	-24%
Capital turnover rate	0.1x	0.0x	0.0x	0.0x	0.1x	0.1x	0.1x

Source: Spago Nanomedical, EPB

Financial position

	2019	2020	2021	2022	2023e	2024e	2025e
Net debt	-12	-28	-52	-62	-41	-31	-16
Equity ratio	98%	98%	96%	96%	97%	95%	94%
Net debt / equity	-0.1x	-0.2x	-0.3x	-0.3x	-0.2x	-0.2x	-0.1x
Net debt / EBITDA	0.6x	1.5x	1.4x	1.6x	1.0x	0.6x	0.3x

Source: Spago Nanomedical, EPB

Per share data

	2019	2020	2021	2022	2023e	2024e	2025e
EPS	-0.94	-0.59	-0.94	-0.43	-0.44	-0.52	-0.68
EPS, adjusted	-0.94	-0.59	-0.94	-0.43	-0.44	-0.52	-0.68
FCF per share	-1.83	-0.77	-0.96	-0.46	-0.56	-0.55	-0.71
Book value per share	6.37	4.97	4.43	2.17	2.04	1.93	1.80
Number of shares, m	21.6	32.1	41.7	90.9	90.9	90.9	90.9
Number of shares after dilution, average	21.6	32.1	41.7	90.9	90.9	90.9	90.9

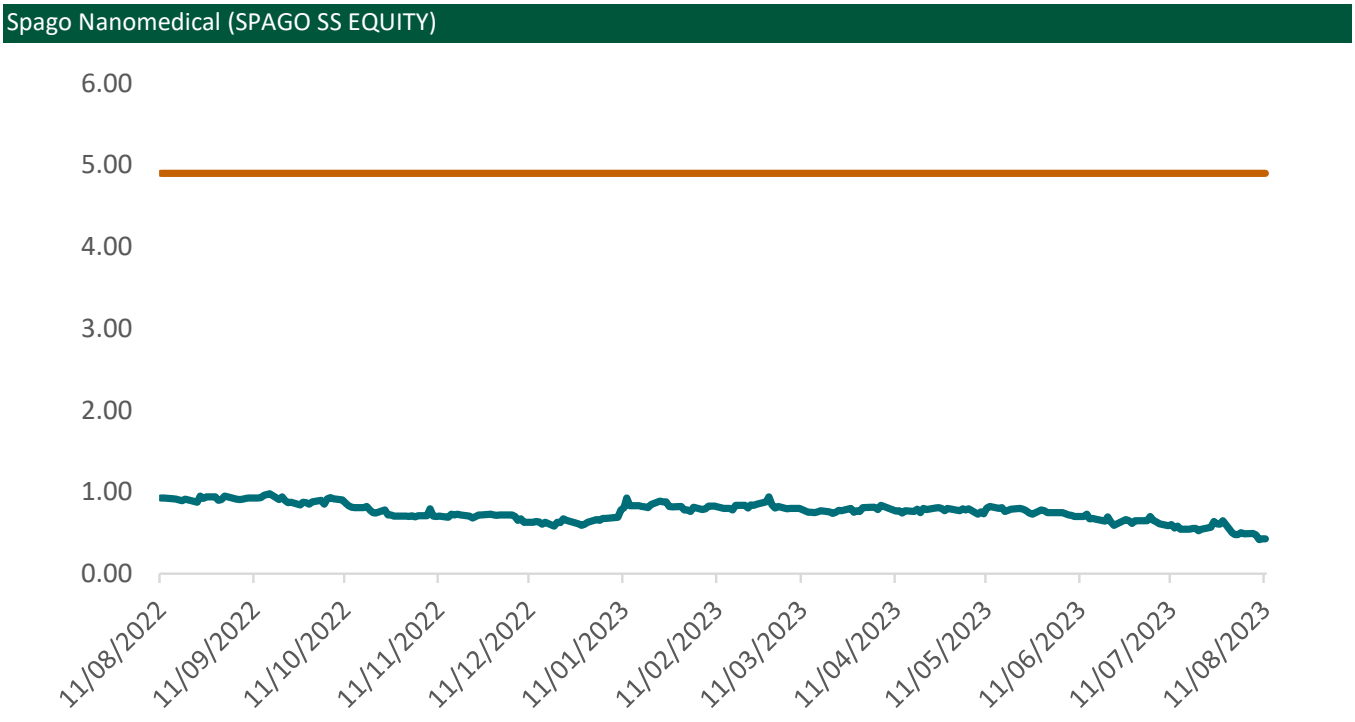
Source: Spago Nanomedical, EPB

Valuation

	2019	2020	2021	2022	2023e	2024e	2025e
P/E, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
P/BV	Neg.	Neg.	1.1x	0.3x	0.2x	0.2x	0.2x
P/FCF	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
FCF-yield	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Dividend yield	Neg.	Neg.	0.0%	0.0%	0.0%	0.0%	0.0%
Payout ratio, adjusted	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
EV/Sales	Neg.	Neg.	21.8x	Neg.	0.7x	0.5x	0.5x
EV/EBITDA, adjusted	Neg.	Neg.	Neg.	0.1x	Neg.	Neg.	Neg.
EV/EBIT, adjusted	Neg.	Neg.	Neg.	0.1x	Neg.	Neg.	Neg.
EV	Neg.	Neg.	143	-5	7	7	7
Share price, year end	-	-	4.7	0.6	0.4	0.4	0.4

Source: Spago Nanomedical, EPB

Share Price and Fair Value Chart



Source: EPB, IDC

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