EDISON

Selvita

Company outlook

New 2017-2021 strategy to boost R&D

Pharma & biotech

Selvita offers a two-pronged strategy with steady double digit growth from its drug discovery business coupled with potential upside from drug development within its broad R&D pipeline. Recently the company introduced a new strategy for 2017-2021 focused on continuing growth in the Services business and ramping up investment in the internal R&D pipeline. While this has been overshadowed somewhat by the clinical hold on the lead asset SEL24, our investment thesis for Selvita is based on supportive long-term company-specific and macro trends and we increase our valuation from PLN577m to PLN1.04bn or PLN75/share.

Year end	Revenue (PLNm)	PBT* (PLNm)	EPS* (PLN)	DPS (PLN)	P/E (x)	Yield (%)
12/15	56.1	7.5	0.84	0.0	N/M	N/A
12/16	66.7	4.6	0.64	0.0	N/M	N/A
12/17e	106.0	11.4	0.81	0.0	N/M	N/A
12/18e	99.2	0.3	0.02	0.0	N/M	N/A

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

2017-21 strategy: Organic growth and boost for R&D

Selvita has achieved rapid organic growth in its drug discovery business in recent years (2012-16 CAGR of 43%). As a result of this success and its growing in-house R&D capabilities, in August 2017 Selvita announced a new strategy for 2017-2021. The company will continue to grow the Services business and will also significantly ramp up investment in the internal R&D pipeline. Selvita estimates that the total investment over 2017-2021 will be around PLN360m, which will be financed from internal reserves (PLN78m), public grants (PLN136m), bank loans (PLN6m) and a planned share issue (PLN140m). The timing of the share issue is uncertain currently, as according to Selvita the pricing depends on the outcome of the interaction with the FDA regarding the clinical hold.

New funds to support strategic goals

The new funds will accelerate Selvita's activities. SEL24 is out-licensed to Menarini, which currently reimburses related R&D expenses. Following the handover, assuming the clinical hold is lifted by the FDA, Selvita should not incur any more costs related to this project. Second lead product SEL120 is undergoing IND enabling studies and the company has indicated that it plans to develop the product through to Phase II and, if successful, out-license then. Over the next four years, Selvita also plans to establish partnering deals for at least three projects in preclinical or clinical stages from the company's three discovery platforms.

Valuation: Increased to PLN1.04bn or PLN75/share

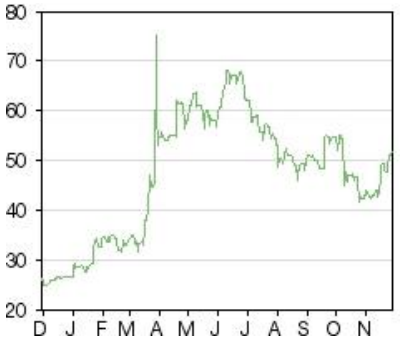
We have increased our valuation from PLN577m or PLN43/share to PLN1.04bn or PLN75/share mainly due to the addition of three new projects and substantial revision of the SEL120 project (development until Phase II, better licensing deal terms and larger market potential). Due to the near-term sensitivity related to the clinical hold on SEL24, we have reduced the probability of success to 7.5% from 15% which reduces our valuation for SEL24 to PLN5.4/share. Continued organic growth and potential collaboration deals are possible catalysts in 2018.

28 November 2017

Price	**PLN51.80**
Market cap	**PLN712m**

Net cash (PLNm) at end-Q317	32.0
Shares in issue	13.7m
Free float	45%
Code	SLV
Primary exchange	WSE
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	22.8	4.9	100.0
Rel (local)	22.3	3.8	43.9
52-week high/low	PLN75.0		PLN24.9

Business description

Selvita is a drug discovery services provider based in Poland. It employs more than 420 staff (30% with PhDs) and operates two main business units: the Innovations Platform (internal R&D pipeline) and drug discovery services (medicinal chemistry/biology, biochemistry).

Next events

FDA decision regarding clinical hold on SEL24 Phase I/II study	Est. Q417/Q118
SEL120 Phase I study start	H218
Data from preclinical projects	2018

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Edison profile page

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Company description: Ramping up the R&D plans

Selvita, founded in 2007, has become one of the largest independent drug discovery companies in Europe with a broad R&D pipeline of novel small molecules for oncology. The company is listed on the Warsaw Stock Exchange Main Market and operates in three business segments: Innovation, Services, and Bioinformatics. Innovation is responsible for the progress of Selvita's R&D pipeline, which can be broadly described by three platforms: Targeted therapies; Cancer metabolism and immunometabolism; and Immunology and immunooncology. The remaining two segments provide drug discovery (contract chemistry, biology) and bioinformatics services (Ardigen also has an internal R&D programme). Selvita employs more than 420 staff and operates out of ~4,000sq m of research facilities in Krakow and Poznan, Poland. Recently, Selvita announced 10-year expansion plans which could increase its laboratory and office space by 14,000sq m for c 1,000 new employees. Management has also recently announced an updated strategy for 2017-2021 which includes solid growth in the Services segment and Innovation to be boosted by a total investment of PLN360m, of which management estimates PLN140m ($40m) will come via a share issue.

Valuation: Upgraded to PLN1.04bn or PLN75/share

Our Selvita valuation has increased from PLN577m or PLN43/share to PLN1.04bn or PLN75/share due to our substantially revised R&D model reflecting Selvita's new strategy for 2017-2022. We have added three new projects to our valuation, namely SMARCA2, SHMT2 inhibitors and the A2A/A2B antagonist. Another significant change to our valuation relates to SEL120, which Selvita now expects to develop through to Phase II and then out-license (we previously assumed this to happen at Phase I like SEL24). If successful, this should increase the value of the asset. To reflect the clinical hold uncertainty we reduced our success probability for SEL24 from 15% to 7.5%.

Financials: Sound services business growth; R&D to ramp up

Selvita's 9M17 total revenues were PLN80.5m, up by an impressive 65% y-o-y. Commercial revenues (ie excluding subsidies/grants) were PLN68.9m, up 70%, while subsidies (allocated to both the Innovation and Services segments) accounted for PLN11.6m, up 41%. Total 9M17 operating expenses (excluding ESOP costs) increased to PLN68.7m from PLN45.2m, as Selvita has been growing its staff count and has opened new facilities in Poznan as well as new international sales offices. The 9M17 operating margin, however, increased to 15% from 8% a year ago, boosted by the Menarini licensing deal. Selvita reported cash of PLN37m in November and had PLN5.1m in debt. We forecast sales of PLN106m and PLN99m in 2017 and 2018 respectively, and break-even on operating profit in FY18 as we assume Selvita will start to ramp up its R&D activities. At present we do not include the planned share issue in our model, as according to Selvita the timing and pricing of the issue are dependent on the outcome of the interaction with the FDA regarding the clinical hold placed on the Phase I/II trial with SEL24.

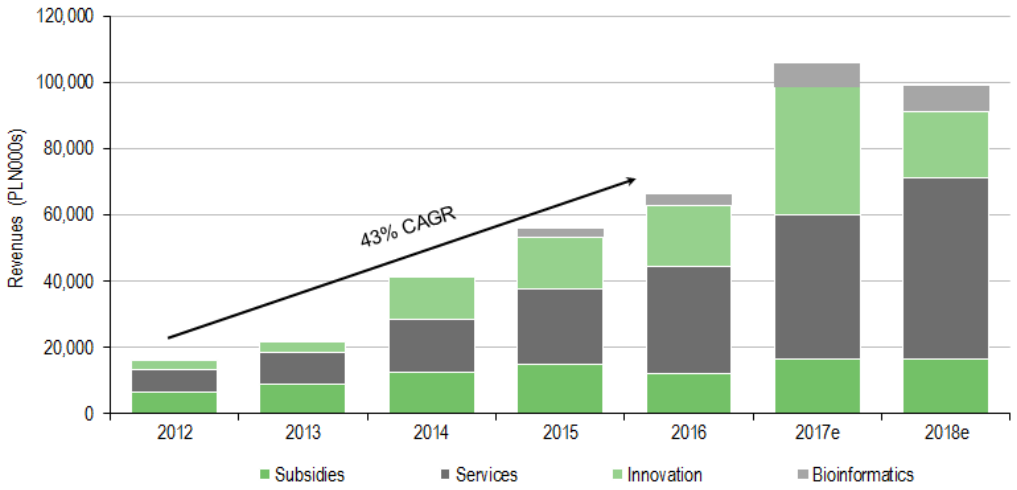
Sensitivities: Service/drug discovery mix lowers risk

Selvita operates a hybrid business model, with a largely de-risked research services business and higher-risk drug development in its innovation platform. Contract research is a highly competitive and increasingly global field. A major uncertainty in the near term relates to the clinical hold on the Phase I/II trial with SEL24. Selvita has indicated that it plans to submit the required documentation as soon as possible. The FDA will be obliged to respond to the submission within 30 days as to whether the clinical hold is lifted. Since our initiation in November 2014, the innovations pipeline has progressed to Phase I/II with the first clinical study ongoing. We have included estimates for deal metrics that Selvita could secure for the assets in our valuation, but these are indicative only, so the actual terms secured could have a materially positive or negative impact on our valuation.

Outlook: Boost for R&D in new four-year strategy

Since incorporation Selvita has seen rapid growth of its drug discovery business. We expect the services business to continue on a high-growth revenue trajectory, but in our view the innovation segment offers greater long-term potential upside, which could come from the development and licensing of a number of candidates from the diverse internal pipeline.

Exhibit 1: Selvita's growth



Source: Edison Investment Research, Selvita

As a result of the success of the Services business and in-house R&D capabilities, in August 2017 Selvita announced a new strategy for 2017-2021. The aim is to continue to grow the Services business and to significantly ramp up investment in the internal R&D pipeline (Exhibit 2). SEL24 is out-licensed to Menarini and following the handover, assuming the clinical hold is lifted by the FDA, Selvita should not incur any more costs related to this project. Second lead product SEL120 is undergoing IND-enabling studies and the company has indicated that it plans to develop the product through to Phase II and, if successful, out-license then.

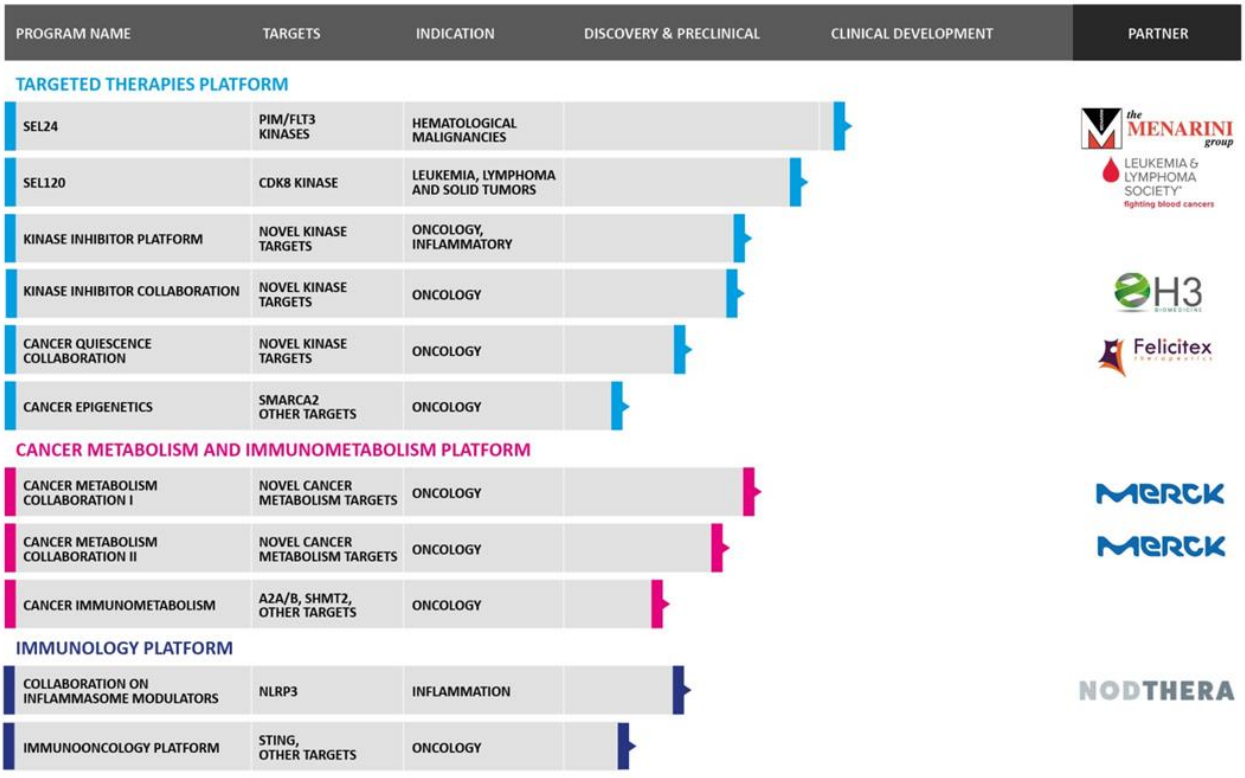
Selvita's Innovation segment can be described broadly as three discovery platforms focused on small molecules: Targeted therapeutics; Cancer metabolism and immunemetabolism; and Immunology and immunooncology. The company also expects to build biologic drug discovery capabilities in addition to its existing expertise in small molecules. Selvita's preliminary estimate is a total investment over 2017-2021 of around PLN360m, which will be financed from internal reserves (PLN78m), public grants (PLN136m), bank loans (PLN6m) and a planned share issue (PLN140m). The shareholders' meeting in August 2017 approved the issue of 2.2m new shares (compared to the current 13.7m outstanding). Pricing has not been announced and depends on the outcome of the interaction with the FDA regarding the clinical hold (see below for more details). If successful, the funding will help Selvita achieve multiple strategic goals:

- R&D related investments estimated at PLN260m (PLN140m is expected from the planned share issue if the clinical hold is lifted):
  - **Targeted therapeutics**. Total expected investment of around PLN50m. Selvita will fund the Phase I development of SEL120 which will create value; if successful, the company plans to out-license in Phase II. We assume the Phase I trial will start in 2018, ready for Phase II in 2021 and a licensing deal in the same year. Selvita also plans to partner one other research project in discovery or preclinical stage in 2018.

- **Cancer metabolism and immunometabolism**. Total expected investments of around PLN70m. One research project partnered in a preclinical or clinical stage in 2019.
- **Immunology and immunooncology**. Total expected investments of around PLN50m. One project partnered in a clinical stage in 2020.

- The remaining funds (PLN100m) will be used to develop the drug discovery services business. The expected continued rapid growth in the services business is underpinned by the investment in the expansion and optimisation of the infrastructure to increase capacity and efficiency (see more details on page 15). Selvita also expects a shift in "product mix" – increasing the number of high-margin integrated projects (higher end of drug discovery services) and less low-margin, fixed-fee projects (commodity-like services). The bioinformatics segment is also expected to grow, driven by internal R&D efforts and rolling out innovative products.
- The company also targets an increase in its market capitalisation to around PLN2bn.

Exhibit 2: Overview of Selvita's R&D pipeline



Source: Selvita

We have made a number of changes to our model to reflect Selvita's new strategy. Previously we valued only Selvita's lead products SEL24 and SEL120 and the partnering deals with Merck. With the new strategy Selvita appears to clearly commit to advancing its preclinical pipeline and provided estimated investments needed for each platform. Therefore we see the company's value as rebalancing across preclinical and clinical pipeline. Over the past few years we believe several of the projects have matured enough to be included in our valuation next to SEL24 and SEL120. We selected mainly those candidates that have published data and are identified by the company as core assets. Namely, the new additions to our valuation are SMARCA2 and SHMT2 inhibitors and A2A/A2B antagonist. We therefore provide a more detailed look at these assets.

Targeted therapeutics platform

Selvita's targeted therapeutics platform includes two lead projects SEL24 in Phase I for relapsed/refractory AML and SEL120 undergoing IND studies and could target various haematological and solid tumours in clinical development. Other strategic focus areas in this platform are synthetic lethality and epigenetic modulators in cancer. One of the other disclosed targets is BRM/SMARCA2. A preclinical candidate BRM/SMARCA2 inhibitor is expected to be identified in 2019, which we now add to our valuation. Selvita presented *in vitro* data at the American Association for Cancer Research in April 2017. Other disclosed products in earlier stages in this platform are dual MNK1/2 inhibitor and molecules active on 2HG producing IDH1/2 mutated tumours (synthetic lethality principle). Selvita has also established two collaborations for assets in this platform:

- Established in September 2013, the collaboration with H3 Biomedicine (Eisai) involves novel small molecule compounds for new kinase targets associated with cancer development.
- The collaboration with Felicitex Therapeutics was established in November 2014. It involves Selvita's cancer quiescence platform, which is a novel approach with expected efficacy against quiescent cancer cells that are not actively proliferating and therefore are less susceptible to classical chemotherapy drugs.

SEL24 – lead asset out-licensed to Menarini

Selvita's lead product SEL24 is a dual inhibitor of PIM and FLT3 kinases which is being explored in an open-label, dose escalation Phase I/II trial with relapsed/refractory AML patients. The asset was out-licensed in March 2017 to Berlin-Chemie (part of Menarini Group). The upfront payment was €4.8m, with Selvita eligible for a total of €89.1m in potential milestone payments, and non-specified single- to low-double-digit royalties and cost sharing. The terms of the deal compared well with our assumptions ie an upfront payment of $15m (€14m), R&D milestone payments of $70m (€64m) and a 5% royalty. While the upfront payment was slightly lower than our estimate, milestone payments were higher. Moreover, negotiated single- to low-double-digit royalties were higher than our 5% estimate. According to reported terms, Selvita is responsible for the continuation of the current Phase I/II trial AML until the expected takeover of the trial by Menarini after the clinical hold has been lifted.

Clinical hold introduced some uncertainty in the short term

The Phase I/II study is an open-label, multi-centre (three US centres initially planned), dose-escalation study that will seek to enrol up to 86 AML patients. Part 1 of the trial aims to establish the recommended dose, which will be further evaluated in Part 2 for safety, but also for initial efficacy. Initial plans were for a headline data readout in H218 with full results around end-2019. However, on 7 October 2017 the FDA issued a clinical hold on the Phase I/II study. The decision was based on a fatal haemorrhagic stroke after venous thrombosis in one patient enrolled in cohort 5 in part 1 of the study designed to establish the recommended dose. There were three patients enrolled in the so far highest dose (150mg) cohort 5, of whom one experienced a stroke. The fatal stroke was associated with the treatment by the investigator mainly because of the timing (the patient received four doses of SEL24). We note that from a clinical perspective, patients that have relapsed or have a refractory AML are usually frail. They also receive other medication and can have thrombosis risk factors. In this case, to prove or disprove the connection between SEL24 and the adverse event is not straightforward. Selvita indicated that as a next step it will respond to the FDA with all required data and study modification requested by the agency. Subsequently, the FDA will have 30 days to reply as to whether the hold is lifted.

SEL24 – dual inhibitor of PIM and FLT3

SEL24 has been tested extensively in *in vitro* and *in vivo* models, which confirm the drug's dual-action mechanism and demonstrate a strong cytotoxic effect in multiple haematological models, as well as potential synergy with current standard low-cost chemotherapy (cytarabine). Current drugs in development target either PIM or FLT3 kinase enzymes; therefore, SEL24 with its dual action is differentiated.

FLT3 inhibitors

FLT3 (FMS-like tyrosine kinase 3) is a kinase receptor expressed on hematopoietic progenitor cells (immature blood cells) and plays a critical role in regulating their activation, growth, proliferation, survival and differentiation into mature blood cells. The specific FLT3-ITD mutation (ITD – internal tandem duplication) results in the aggressive proliferation of immature, irregular blasts that lack the ability to differentiate into normal blood cells. Physicians, as a standard part of diagnosis, routinely test patients for the FLT3-ITD mutation, which is estimated to affect 25-35% of elderly AML patients. Patients who are FLT3-ITD positive have a significantly worse prognosis compared to FLT3-ITD negative patients. As such, FLT3 presents an obvious molecular target for new therapies. While a number of multi-kinase inhibitors on the market, including Bayer's Nexavar and Pfizer's Sutent, already act on FLT3 (as well as other receptors such as cRAF, VEGFR, c-KIT), there is only one approved drug that specifically targets FLT3 (Rydapt, midostaurin, Novartis), while others are still in the development (Exhibit 4).

An abstract presented for the 2015 ASH meeting in December revealed event-free survival and overall survival in a 717-patient midostaurin study in newly diagnosed AML patients with FLT3 mutations (Exhibit 3). The FDA granted breakthrough therapy designation and a priority review into midostaurin's NDA application and ultimately approved in April 2017. This was the first large Phase III trial to confirm a therapeutic benefit of FLT3 inhibition in AML patients. The first survival results from a large Phase III study helped to reinvigorate interest in the FLT3 target in AML. Overall survival was increased from approximately two years to just over six years and there was a 23% reduction in risk of death compared to the placebo arm (hazard ratio 0.77, p=0.0074). No statistically significant differences were observed in the overall rate of grade 3 or higher haematologic and non-haematologic adverse events in the midostaurin treatment group versus the placebo group. Consensus sales forecast Rydapt sales of $645m in 2022.

Exhibit 3: Midostaurin Phase III results

Endpoint	Arm	Median (months)	p-value	Hazard ratio	Five-year event rate (%)*
Overall survival	Midostaurin	74.7	0.0074	0.77	50.8
	Placebo	25.6			43.1
Event-free survival	Midostaurin	8.0	0.0044	0.80	26.7
	Placebo	3.6			19.1

Source: ASH Abstracts 2015. Note: *Proportion of patients with an event defined as the earliest of death, relapse or no complete response.

PIM inhibitors

The PIM family of serine-threonine kinases represents another promising target in AML, as PIMs play an important role in intracellular signalling. PIM kinases are induced by several pro-oncogenic proteins such as FLT3, PI3K kinases, JAK and NF-κB, and when overexpressed can mediate drug resistance. Researchers have found increased PIM kinase expression in relapse samples from AML patients treated with FLT3 inhibitors. This expression induces resistance to FLT3 inhibition and

that pharmacological or genetic inhibition of PIM restores cancer cell sensitivity to FLT3 inhibitors.[1] As such, targeting both PIM kinases and FLT3 mutants may improve response rates and reduce relapses. There are no approved PIM inhibitors yet. Exhibit 4 shows the most advanced candidates against PIM kinases and those against FLT3.

Exhibit 4: Competitive clinical pipeline of PIM and FLT3 kinase inhibitors

Pharma class	Product	Company	Lead indication	Status	Trial data
PIM inhibitors	LGH447	Novartis	Haematological malignancies (multiple myeloma/AML/MDS)	79-pt Phase Ib/II (multiple myeloma) 75-pt Phase I (multiple myeloma) 86-pt Phase I (AML/MDS)	H218 H218 H219
	INCB053914	Incyte	Advanced malignancies	270-pt Phase I/II	2020
FLT3 inhibitors	Midostaurin (PKC412)	Novartis	AML	Market	Consensus sales forecast of $645m in 2022*
	Quizartinib (AC220)	Ambit Biosciences/ Daiichi Sankyo	AML	367-pt Phase III	H118
	Lestaurtinib (CEP-701)	Children's Oncology Group (NCI)	Acute lymphoblastic leukaemia (ALL)	242-pt Phase III	H218
	Gilteritinib (ASP2215)	Astellas Pharma	AML	258-pt Phase I/II	Q118
	Crenolanib	Arog Pharma	AML	70-pt Phase II	Q417
	TAK-659	Takeda	AML	81-pt Phase II	2020

Source: Edison Investment Research, clinicaltrials.gov. Note: *Source: EvaluatePharma.

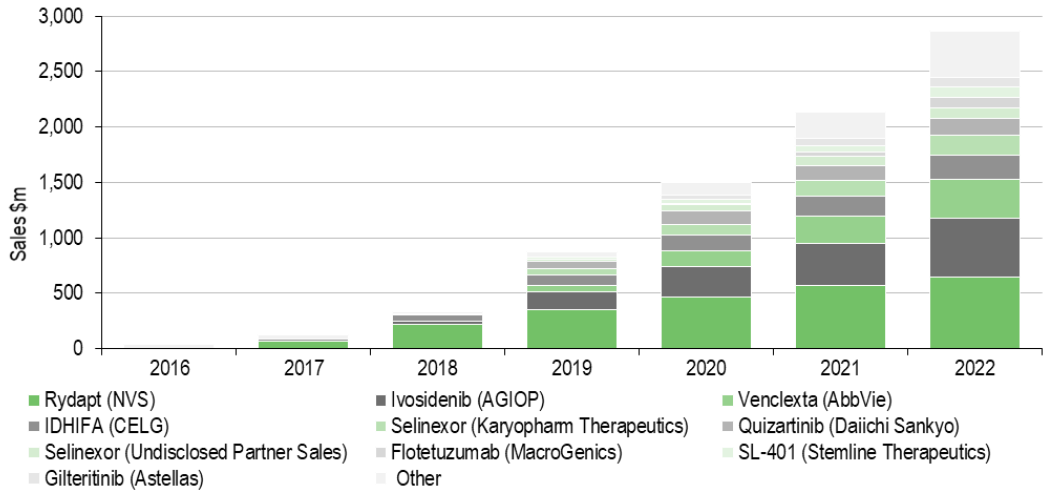
A significant unmet need in AML

AML normally originates in the bone marrow (where new blood cells are made), but often quickly moves into the blood, resulting in uncontrolled growth and accumulation of malignant white blood cells, which fail to function normally and interfere with the production of normal blood cells. AML is the most common type of acute leukaemia in adults and affects nearly 40,000 patients in the EU and US (new cases per year). The five-year survival rate for all AML patients, irrespective of age or genetic status, is around 23%. The standard-of-care treatment for AML has not changed significantly for many decades, primarily based on chemotherapy (cytarabine with anthracycline or mitoxantrone) and followed by a stem cell transplant where appropriate. The goal of treatment is to reduce the blasts in the bone marrow to below 5% and return the blood cell counts to normal levels. A bone marrow transplant is generally recognised as the only curative treatment option, but is not always appropriate.

Until recently there were no approved targeted therapies. Two novel drugs for AML are Novartis' midostaurin branded as Rydapt and enasidenib (Idhifa, Celgene/Agios). SEL24 is differentiated from midostaurin with its dual-action mechanism. Idhifa is an inhibitor of isocitrate dehydrogenase 2 (IDH2) and was first ever such drug approved by the FDA (August 2017) for relapsed or refractory AML patients with IDH2 mutation (8-19% of total population). According to the consensus the AML market is subject to rapid growth in coming years (Exhibit 5).

[1] A. S. Green et al. Pim kinases modulate resistance to FLT3 tyrosine kinase inhibitors in FLT3-ITD acute myeloid leukemia. *Sci Adv. 2015 Sep; 1(8).*

Exhibit 5: Consensus forecasts for expected top 10 products for AML



Source: EvaluatePharma

SEL120 new preclinical data, IND studies ongoing

SEL120 is a first-in-class selective CDK8 inhibitor. Depending on subtypes, cyclin-dependent kinases (CDKs) play varied roles in the control of cell cycle, proliferation and mRNA transcription. Specifically, CDK8 is uniquely differentiated and plays a part of a multi-protein complex that regulates gene expression. So far, preclinical studies point to potential efficacy in haematological malignancies and solid tumours, such as colorectal cancer or triple-negative breast cancer, which are all potential indications for the Phase I trial. There is also potential to use SEL120 in combination therapies with immunooncology products (see below). We discussed the highlights of the available preclinical data in more detail in our previous outlook report. Selvita is conducting IND enabling studies with a Phase I trial envisaged in H218. According to the R&D strategy, SEL120 could be up for out-licensing in Phase II.

Although the main concepts of CDK inhibition were discovered more than two decades ago, selective CDK8 inhibition is a fresh approach. It recently gained attention after Merck & Co in-licensed a selective CDK8/CDK19 inhibitor from Harvard University in a deal with an upfront payment of $20m and tiered royalties, which is the largest licence fee for technology developed at the university. In our view, this clearly shows that interest in selective CDK inhibitors is strong. The agreement involves compounds derived from a natural compound, cortistatin A, and recently published articles showing anti-leukaemic in vitro and in vivo efficacy, which adds to Selvita's preclinical data.

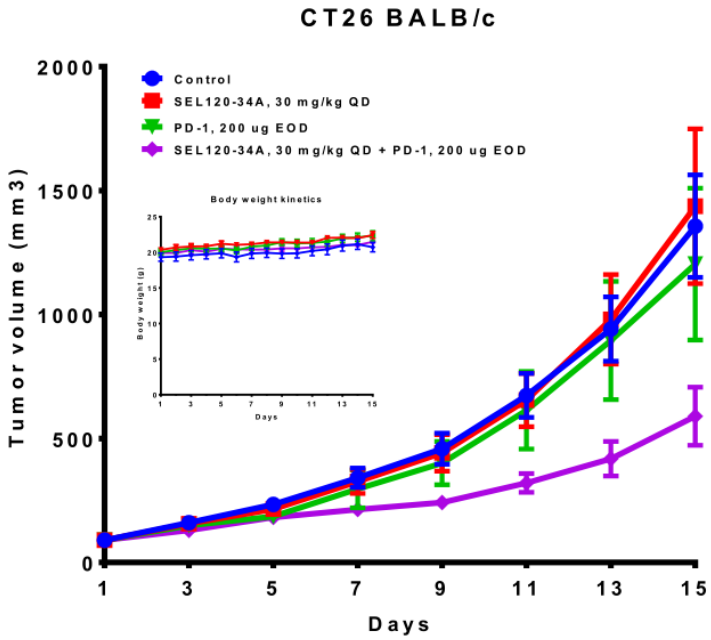
More recently Selvita released an interesting new set of data demonstrating that SEL120 acts synergistically with immune checkpoint inhibitors, such as PD-1 inhibitors (eg pembrolizumab [Keytruda, Merck & Co, expected to reach $9.9bn in sales in 2022], nivolumab [Opdivo, Bristol-Myers Squibb, estimated $9.2bn in sales by 2022[2]]). Selvita's *in vivo* experiment with a syngeneic colorectal cancer model in mice[3] demonstrated that at low doses, individually both PD-1 inhibitor and SEL120 did not substantially differ from the control in slowing down the growth of the tumour.

[2] EvaluatePharma, accessed 9 May 2017

[3] Allograft mouse tumour model, when tumour tissues are derived from the same genetic background as a given mouse strain. Tumour samples are transplanted into a host mouse and because the cancer tissues and the recipient share genetic background, the transplant is not rejected by the host's immune system. As opposed to Xenograft transplantation models, when actual human cancer samples are transplanted into a host mouse with a suppressed immune system.

But when administered together, the growth slowed down. So far, Selvita has not provided any specific future plans in immunooncology, but, in our view, this adds more options for the SEL120 programme and for partnering talks for potential IO combination treatments, a booming field right now.[4]

Exhibit 6: *In vivo* synergy of SEL120 and PD-1 inhibitor in CRC model at low doses



Source: Selvita

Deal with Leukemia & Lymphoma Society

In October 2017, Selvita announced a partnership agreement with the Leukemia & Lymphoma Society (LLS) to co-fund further preclinical development of SEL120 for AML patients. The rationale for this indication is that SEL120's unique mechanism of action does not overlap with existing therapies and may allow the development of synergistic combination treatments. According to the deal terms, LLS will provide up to $3.25m in funding over the next four years. This should allow SEL120 to progress though IND-enabling studies through to Phase I in AML. Founded in 1949, LLS is headquartered in the US and has invested over $1bn in various projects so far.

SMARCA2/SMARCA4 and synthetic lethality

The so called switch sucrose nonfermentable (SWI/SNF) complex is a large complex of proteins involved in chromatin (compact "strand" of the DNA) remodelling[5]. SMARCA2 (BRM) and SMARCA4 (BRG1) are two catalytic subunits essential for the function of the complex. An increasing number of cancers have been found to have inactivating mutations in the SMARCA4/ SMARCA2 genes. In malignant cells with the mutated SMARCA4 gene, non-mutated SMARCA2 becomes essential[6]. Therefore the inhibition of SMARCA2 causes cell death if there is an oncogenic mutation in the SMARCA4 gene. This concept of a "biological genetic flaw"

[4] S. J. Harris. Immuno-oncology combinations: raising the tail of the survival curve. *Cancer Biol Med. 2016 Jun; 13(2): 171–193.*

[5] Herpel et al. SMARCA4 and SMARCA2 deficiency in non–small cell lung cancer: immunohistochemical survey of 316 consecutive specimens. *Annals of Diagnostic Pathology 26 (2017) 47–51.*

[6] Wilson et al. Residual Complexes Containing SMARCA2 (BRM) Underlie the Oncogenic Drive of SMARCA4 (BRG1) Mutation. *Molecular and Cellular Biology p. 1136–1144.*

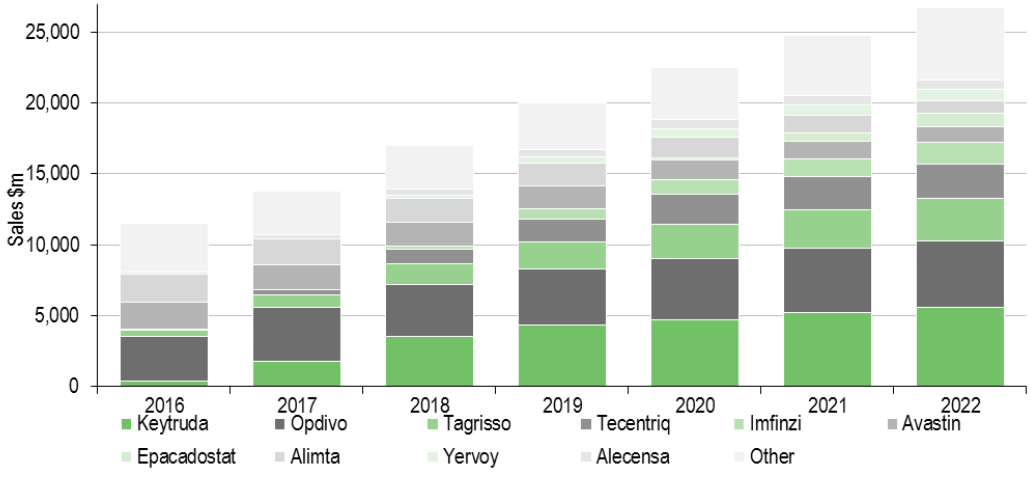
complemented by an intervention with a drug, which results in cell death, is known as synthetic lethality. This approach is very specific and potentially offers better safety profile.

Selvita is developing a first-in-class, selective SMARCA2 small molecule inhibitor, has established *in vitro* proof-of-concept and is identifying hit compounds. The company believes that the advantage of its SMARCA2 inhibitor programme is that it targets ATPase domain of SMARCA2, as opposed to bromodomain, which is the target of other SMARCA2 inhibitors. For example, both bromodomain-targeting agents from Pfizer (PFI-3) and from Genentech failed to inhibit cell growth *in vitro* studies[7]. Selvita believes its SMARCA2 ATPase inhibitors were the first to enter the hit identification stage.

When it comes to market opportunity, Selvita has indicated that the non-small cell lung cancer (NSCLC) patient population could be the first clearly defined target as SMARCA4 is mutated in around 6-8% of cases. This would correspond to more than 10,000 new patients in the US alone. Other solid tumours with inactivated SMARCA4 have also been identified. There is also the likelihood that SMARCA2 inhibition would show efficacy in tumours with mutations in other proteins from the SWI/SNF complex, which is 20% of all tumours, thus significantly expanding the market potential.

In NSCLC the top 10 drugs, which include Keytruda (pembrolizumab, Merck & Co), Opdivo (nivolumab, Bristol-Myers Squibb) and Avastin (bevacizumab, Roche) among others, are expected by the consensus to bring in sales of $21.6bn in 2022 (Exhibit 7). This translates to c $2.16bn per drug. As mentioned, SMARCA2 inhibitor would target a small subpopulation of NSCLC tumours with SMARCA4 mutations. The significant upside is, however, in other indications as discussed.

Exhibit 7: Top 10 products for non-small cell lung cancer



Source: EvaluatePharma

Cancer metabolism and immunometabolism platform

The cancer metabolism and immunometabolism platform focuses on deregulated cancer cell metabolism due to oncogenic tumour mutations or the effect of small molecule metabolites on tumour microenvironment. Major disclosed targets from this platform are A2A/A2B, CD73/CD39 (both with a role in adenosine immunosuppression) and SHMT2 (serine catabolism).

[7] B. Vangamudi. The SMARCA2/4 ATPase Domain Surpasses the Bromodomain as a Drug Target in SWI/SNF-Mutant Cancers: Insights from cDNA Rescue and PFI-3 Inhibitor Studies. *Cancer Res. 2015 Sep 15;75(18):3865-3878.*

Inhibition of adenosine-related tumour immunosuppression (A2A/A2B and CD39/CD73)

Studies over the last two decades identified extracellular adenosine as a key element in immune regulation[8]. Many cancers have the ability to accumulate natural molecule adenosine. By stimulating A2A receptors, adenosine stops T-cells within the immune system from proliferating and reduces their ability to attack cancer cells. Blocking A2A/A2B receptors can therefore promote the anti-cancer response of T-cells within the tumour microenvironment. Accumulation of adenosine is potent and prevalent mechanism tumours escape detection by the immune system.

Antagonizing adenosine receptors (A2A/A2B) or its synthesis pathway metabolites (CD39/CD73) lead to restoration of the anti-tumour response of the immune system. While this type of technology is still in early stages of clinical development, the potential has been acknowledgement by several large pharma companies:

- In 2015, Astra Zeneca in-licensed Heptares's preclinical A2A receptor antagonist programme for $10m upfront, $500m in milestones and up to double-digit royalties.
- Also in 2015, Corvus Pharmaceuticals in-licensed Vernalis's clinical stage adenosine programme for $1m in upfront and $200m in potential milestones per each indication the drug is developed for and mid-single digit royalties.
- In January 2017, Domain Therapeutics and Merck announced a collaboration agreement for the development of adenosine receptor antagonists for cancer. Upfront and royalties were not disclosed, while potential milestones to Domain could be more than €240m.
- In September 2017, Taiho announced an option agreement with Arcus Bioscience for a portfolio of regional rights in Asia (excluding China) to preclinical cancer immunotherapy candidates (targets are likely to involve CD73, CD39 and the A2A and A2B receptors). The upfront and royalties were not disclosed, but Arcus will receive $35m over three years and could get $275m for each drug programme that Taiho in-licenses.

So far deals have included mainly selective compounds. Selvita has discovered several series of A2A specific and dual A2A/A2B antagonists. The fact that Selvita's A2A/A2B antagonist is dual could be a competitive edge. Selvita's *in vivo* models showed tumour growth inhibition and increased activation and infiltration of lymphocytes into tumours. Nomination of the clinical candidate is expected in 2018. The goal of the project is to bring two programmes to clinical development in 2020. Although at an early stage, Selvita believes the relevant target populations could be broad, with the immunosuppressive environment prevalent in around 50% of all cancers. There is also a strong rationale for synergistic potential with checkpoint inhibitors.

Earlier projects in this area include inhibitors of enzymes of extracellular adenosine synthesis pathway (CD39 and CD73). In extracellular space ATP (the main molecule responsible for energy transfer in various processes) is degraded to AMP by CD39 (NTPase), and further to adenosine by CD73 (e5NT). Blocking these two enzymes is another promising way to inhibit adenosine-related tumour immunosuppression. Selvita is identifying molecules that could inhibit CD39/CD73.

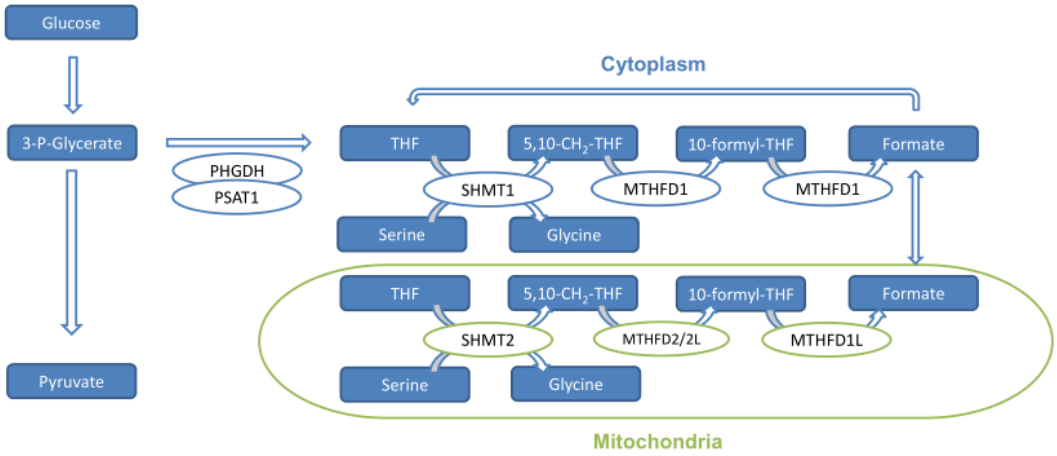
Inhibitors of serine synthesis and one-carbon metabolism pathways

Serine hydroxymethyltransferase (SHMT) plays a key role in a so-called one-carbon pathway, a group of biochemical reactions involved in amino acid metabolism (Exhibit 8). SHMT catalyses the conversion of serine to glycine and also plays a role in the folate (vitamin B9) cycle. Selvita's research focuses on the discovery of specific inhibitors of SHMT2, which is located in mitochondria (SHMT1 is found in cytoplasm). Over-activation of the serine synthesis pathway and upregulation of SHMT has been described in over 20% of solid tumours (eg breast, lung, colorectal cancers). Such

[8] Robert D. Leone et al. A2aR antagonists: Next generation checkpoint blockade for cancer immunotherapy. *Comput Struct Biotechnol J. 2015; 13: 265–272.*

cancer cells are highly dependent on serine[9]. The target population for SHMT inhibition can be well defined by using oncogene c-Myc as a biomarker. c-Myc protein is a transcription factor involved in numerous cell process and c-Myc positive tumours have been correlated with poor prognosis. Selvita's SHMT2 inhibitor is in hit-to-lead stage in vivo studies planned in upcoming months.

Exhibit 8: Serine synthesis and one-carbon pathway



Source: T. Rzymski et al. Small molecule inhibitors of SHMT1/2 validate serine metabolism as a target in the treatment of c-Myc positive solid tumours. *Poster presentation, AACR meeting, 2017.*

As mentioned above, SHMT is also important in the folate cycle. Antagonists of folate metabolism or antifolates are an established chemotherapy in certain cancers. Folate antagonism disrupts cell division, DNA/RNA synthesis and protein synthesis. Pemetrexed (for non-small cell lung carcinoma, mesothelioma) and methotreaxate (for autoimmune conditions like rheumatoid arthritis and certain cancers) are two well established and effective antifolates. The main drawback with antifolates in cancer treatment, however, is the development of resistance. Therefore, Selvita sees potential synergism of SHMT inhibitor in combination with antifolates.

Merck's collaborations provides external validation

Selvita has a long-standing relationship with Merck KGaA, which started as a drug discovery collaboration in 2013 and was extended in 2015 (Exhibit 9). Later, the two companies stepped up the relationship and signed two drug development deals, which involve undisclosed protein targets. According to the deal terms, Selvita could receive payments of up to €16.5m in each of the collaborations if the drugs are successfully commercialised.

Exhibit 9: Selvita's partnerships with Merck KGaA

Deal signed	Drug discovery collaboration October 2013	Drug discovery collaboration November 2015	Preclinical drug development deal 22 December 2015	Preclinical drug development deal 31 March 2016
Contract period	2013-15	2015-18	N/A	N/A
Details	Discovery and development of multiple NCEs against selected protein targets (two projects on two targets) involved in cancer cell metabolism.	Discovery of first-in-class NMEs as lead candidates for multiple oncology indications. Separate collaboration to that of 2013-15.	Development and commercialisation of therapeutic molecules developed by Selvita using its cancer metabolism platform for a specific target. Result of the 2013-15 collaboration with Merck.	Development and commercialisation of therapeutic molecules developed by Selvita using its cancer metabolism platform for a second specific target. Result of the 2013-15 collaboration with Merck.
Funding	PLN18.8m in research funding over 2015-18, with PLN10m funding guaranteed over 2013-15.	Milestone payments and royalties on successful development and commercialisation of products by Merck.	Signing fee €0.2m; maximum payments of €1.9m over the next five years; total milestone payments may add up to €16.5m.	Same terms as the 22 December 2015 deal.
Outcome	Selection of clinical candidates (2016-17).			

Source: Edison Investment Research, Selvita

[9] Ch. F. Labuschagne et al. Serine, but not glycine, supports one-carbon metabolism and proliferation of cancer cells. *Cell Reports, Volume 7, Issue 4, p1248–1258, 22 May 2014.*

Immunology and immunooncology platform

The two lead technologies in this platform are STING pathway modulators and NLRP3 inflammasome inhibitors. We do not include them in our valuation due to their early stage, but both assets represent cutting-edge technology and a significant part of the 2017-2021 strategy.

STING pathway modulators

STING (Stimulator of Interferon Genes) receptor is a known mediator of the immune system, which when activated induces expression of type I interferon and other T cell recruitment factors. This results in the activation of dendritic cells, which act as antigen presenting cells. The ultimate outcome is the specific immune response with "trained" CD8+ T cells attacking the cancer. Selvita has identified potentially first-in-class or best-in-class small molecule modulators of the STING signalling pathway with activity confirmed in a variety of human *in vitro* models. To our knowledge, the most advanced STING modulator is in Phase I for various solid tumours and lymphomas being developed by Aduro and Novartis. The partners signed a collaboration agreement in March 2015. Novartis paid $200m up front, invested $25m in Aduro (with a commitment for another $25m), while up to $500m are due in milestones.

Checkpoint inhibitors (CPIs) proved to be the first significant success in immunooncology, harnessing the immune system to fight cancer, and have rapidly gained popularity over the past several years because of the additional clinical benefit over standard of care cancer treatment. Yervoy (ipilimumab, anti CTLA-4, Bristol-Myers Squibb; consensus sales of $2.2bn in 2022, EvaluatePharma) was the first launched in 2011, followed by Keytruda (pembrolizumab, anti-PD1, Merck & Co; consensus sales of $9.9bn in 2022) and Opdivo (nivolumab, anti-PD1, Bristol-Myers Squibb; consensus sales of $9.6bn in 2022). However, a large proportion of patients (in certain cases more than 50%) do not respond to CPIs. While still early in the development, the strategic opportunity for STING agonists could be non-responder patients, but also there is potential for use in combination with CPIs. The strong rationale for combinations is based on the fact that CPIs act late in the immunity cycle (makes the tumour "visible" to T cells), while STING pathway appears to prime the production of cancer-specific T cells, so both technologies are potentially synergistic.

Inflammasome inhibitors and Nodthera

The lead project in immunology is SEL212, which has been spun out to Nodthera, a start-up created in July 2016 by Selvita (owns 39% stake) and a VC company Epidarex Capital and headquartered in Edinburgh, Scotland. Nodthera centres on NLRP3 inflammasome inhibitors, a first-in-class technology developed internally by Selvita. While it is still at an early preclinical stage with few details released, inflammasome's role in the immune system response and its modulation is an emerging field that has potential across several indications with high unmet need, such as cancers and non-malignant diseases like diabetes, rheumatoid arthritis and Alzheimer's disease.

The inflammasome was discovered in 2002, when researchers identified it as the molecular mechanism behind the activation cascade of interleukin (IL)-1. IL-1 is a family of pro-inflammatory cytokines (a broad term for small proteins responsible for cell signalling) that has been widely implicated in pain, inflammation and autoimmune conditions with several approved drugs targeting IL-1 subtype IL-1beta.[10,11] Nodthera's technology is a small molecule that targets NLRP3 inflammasomes, therefore it is clearly differentiated and acts more upstream than therapies targeting IL-1beta. We reviewed existing IL-1beta targeted therapies in our previous report;

[10] F. Martinon et al. The Inflammasome: A Molecular Platform Triggering Activation of Inflammatory Caspases and Processing of proIL-beta. Molecular Cell, Vol. 10, 417–426, August, 2002.

[11] M. Dagenai et al. The inflammasome: in memory of Dr. Jurg Tschopp. Cell Death and Differentiation (2012) 19, 5–12.

however, current indications are rare to extremely rare.[12] Inflammasomes can either cause the inflammation or aggravate the underlying condition; therefore, such inhibitors have potential in much more prevalent diseases, including neurodegenerative conditions (multiple sclerosis, Alzheimer's disease and Parkinson's disease) and metabolic disorders (atherosclerosis, type 2 diabetes and obesity).[13] Although neurologic and metabolic disorders are not traditionally considered to be inflammatory, the contribution of the inflammatory component is increasingly being recognised.

The inflammasome's role in immune system response is attracting private funding, with Inflazome and IFM Therapeutics being relatively recent examples. In September 2016, Dublin-based Inflazome closed a Series A funding round with €15m in new capital co-led by Novartis Venture Fund and Fountain Healthcare Partners. IFM Therapeutics finalised a Series A financing round with $27m co-led by Atlas Venture and Abingworth in June 2016. The company was developing inflammasome modulators for cancer and inflammatory diseases and also had a STING agonist programme. IFM was seeded with just $2m in October 2015 and in August 2017 Bristol-Myers Squibb acquired the company for $300m upfront and potential milestones of up to $1.01bn.

Services and bioinformatics

Selvita's drugs discovery services business has been growing at an impressive pace (43% CAGR 2012-2016). Going forward we find both macro trends and company specific characteristics as beneficial to maintain the rapid organic growth.

Macro trends: Secular growth of the drug discovery market

Several sources provide different estimates of the drug discovery outsourcing market size (Research and Markets $8.3bn in 2017, Visiongain $19.2bn in 2016), but all point to will be a high growth space (Reasearch and Markets estimates CAGR of 11.6% over 2017-2022). The main macro trends that underpin the drug discovery outsourcing market's growth are:

- **Efficiency, expertise of the provider, access to novel technologies**. A specialised service provider accumulates expertise in specific research stages and becomes expert in certain therapeutic areas. To maintain the competitive advantage, the provider has to employ cutting-edge technologies, which may not be owned by outsourcing companies. Established providers can also attract top talent in the industry.
- **Need for R&D cost reduction and increasing comfort with outsourcing**. The need to control rising costs is a compelling incentive to look for ways of outsourcing at least part of the R&D activities. This has become especially acute with the decreasing efficiency of the in-house R&D efforts at large pharma companies. Biotech and pharma started outsourcing a range of different activities with varying degrees of complexity and, with increasing complexity, the quality of the service provider becomes crucial.
- **Flexibility with different outsourcing models**, which range from typical fee-for-service contracts (eg outsourcing of synthesis of a library of compounds) to fully integrated drug discovery projects, through different FTE-based partnership structures involving research fees, milestones and royalties (margins increase accordingly).
- **Scalability**. Outsourcing allows for fixed costs to be converted to variable costs. The extent of the work can be rapidly increased or decreased, while accomplishing this in-house would involve hiring, reassigning or laying off personnel. This is especially true when the outsourcing

[12] L. Campbell. The Relationship between NALP3 and Autoinflammatory Syndromes. Int. J. Mol. Sci. 2016, 17, 725.

[13] H. Guo. Inflammasomes: mechanism of action, role in disease, and therapeutics. Nature Medicine 21, 677–687 (2015).

company is of smaller scale or so called 'virtual', in which case all the R&D activities are outsourced.

Company-specific trends: Growing faster than the market

Selvita's Services division operates out of a research facility in Krakow and Poznan, Poland. The division is split into two main units – Chemistry and Biology – each run as separate businesses within the group. Selvita's client list for its services is extensive, ranging from big pharma, to generics, to biotech companies. A range of contract options are offered – fixed price, to FTE, to integrated – which generate increasing revenues, costs and complexity, as illustrated in Exhibit 10. Fixed price contracts normally involve fierce price competition from lower-cost Asian countries, while FTE contracts and integrated projects are more of a value proposition and compete with Western drug discovery services providers such as Evotec, Charles River Laboratories and Covance. In line with its strategy of moving away from fixed-priced contracts, Selvita has been increasing the percentage of FTE contracts signed. One of Selvita's significant competitive edges is its lower cost base, while at the same time the country's large population means that there should be enough MSc and PhD life sciences professionals to join the company during the expansion stage.

Exhibit 10: Contract types and sales cycle

Typical sales cycle in services

	Customer identified	Meeting	CDA	Pilot project awarded	Pilot project completed	Regular projects	FTE collaboration	Integrated project
Months from start	0	2	4	6	10	12-24	25	60
Profitability	Cost investment	Cost investment	Cost investment	Cost investment	Cost investment	5-10%	10-20%	30%
Revenues	0	0	0	0	Marginal	Slow growth	Dynamic growth	Dynamic growth plus milestones

Source: Selvita

Ardigen is recognized as a third business segment. The bioinformatics company was spun out in October 2015 (currently Selvita holds 51% of shares). The logic behind its spin out was to increase the range of services within the bioinformatics and IT solutions offering, but also to expand into new areas rapidly evolving with the global precision medicine trends. Ardigen now has stable existing business, which provides revenues and can explore expansion opportunities.

Expansion plans: New chapter in Selvita's story

Selvita added around 70 employees in 2016 bringing the total number to c 370, and expanded to a new location in Poznan. In September 2016 the company announced its long-term expansion plans, which include a new laboratory infrastructure development close to the current Selvita facilities in Krakow with a total area of c 14,000sq m and space for c 1,000 employees. The first stage includes one new, fully equipped facility covering c 3,000sq m; the company estimates that work will be completed in 2019. To finance the project, Selvita will use a mix of cash, bank financing, tax incentives (the property is located in a special economic zone) and public grants. The total costs of this first stage are estimated at around PLN73m (including the land cost). We have already included the first stage of this expansion in our model (for more details, see our previous report).

Sensitivities

Selvita operates a hybrid business model, with a largely de-risked research services business and higher-risk drug development in its innovation platform. Contract research is a highly competitive and increasingly global field, which may put pressure on this side of its business. Since our initiation in November 2014, the innovations pipeline has progressed to Phase I/II with the first clinical study ongoing. We have included estimates for deal metrics that Selvita could secure for the assets in our valuation, but these are indicative only, so the actual terms secured could have a materially positive or negative impact on our valuation. A major uncertainty in the near term is related to the clinical hold on the Phase I/II trial with SEL24. Selvita indicated that it aims to submit required documentation as soon as possible. The FDA is obliged to respond within 30 days as to whether the clinical hold is lifted.

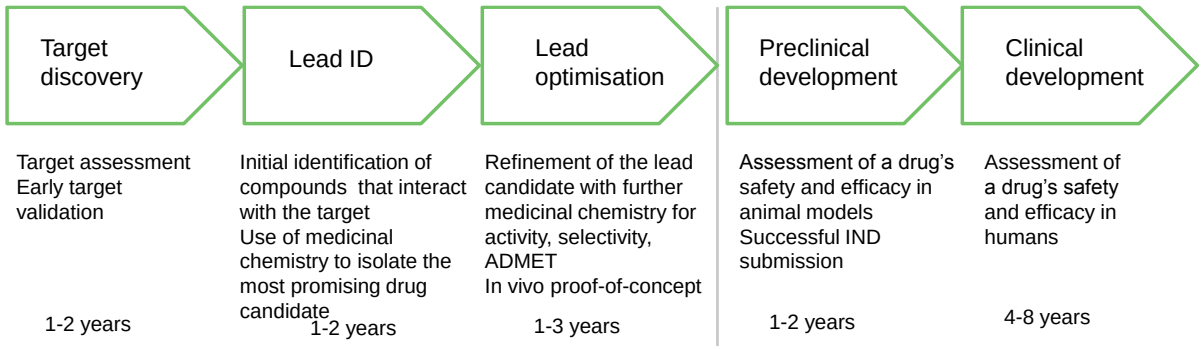
Valuation

Our Selvita valuation has increased from PLN577m or PLN43/share to PLN1.04bn or PLN75/share mainly due to our substantially revised R&D model. At present we do not include the planned share issue in our model as according to Selvita, the timing and pricing of the issue are dependent on the outcome of the interaction with the FDA regarding the clinical hold placed on the Phase I/II trial with SEL24. We use DCF-based calculations with a discount rate of 10% to value the core drug discovery services business and research collaborations. Separately we use risk-adjusted NPV models with a discount rate of 12.5% for Selvita's R&D projects in various stages. These projects include allocated R&D costs (based on our assumptions, Exhibit 14), which are excluded from the DCF model to avoid double accounting.

For the R&D pipeline valuation, we have made a number of changes to reflect Selvita's new strategy for 2017-2022. Previously we valued only Selvita's lead products SEL24 and SEL120 and the partnering deals with Merck. With the new strategy Selvita has committed to advancing its preclinical pipeline and provided estimated investments needed for each platform. Therefore, the company's valuation has been rebalanced across the preclinical and clinical pipeline.

Exhibit 11 summarises the stages of the drug discovery process. Selvita has assets across all these stages and over the past few years we believe several of the projects have matured enough to be included in our valuation with SEL24 and SEL120. We have selected those projects that have published data and are identified by the company as core assets. Namely, SMARCA2 and SHMT2 inhibitors and A2A/A2B antagonist.

Exhibit 11: Overview of the drug discovery process



Source: Edison Investment Research

Our valuation and assumptions for the projects are summarised in Exhibits 12, 13 and 14. Due to the early stage of the assets (we assign 2% success probability for the newly added projects) to

evaluate market potential we used top-down approach and looked at how benchmark or relevant products are performing in the market. Associated R&D costs are estimated from those Selvita provided with its new strategy. R&D model changes include:

- **R&D expenditure**. With its strategy update, Selvita provided R&D cost estimates for the period 2017-2021. For the targeted therapies platform costs are estimated at $13.7m; for cancer metabolism and immunometabolism – $19.3m; for the immunooncology platform – $13.7m. We have split some these costs per products to calculate rNPV values (described in Exhibit 14), but note that we included in our valuation only more advanced projects in the preclinical and clinical stages. Selvita is also working on a number of earlier projects, disclosed and undisclosed, although these are likely less costly. Clinical stage trials should account for the bulk of the R&D spend.
- **SEL24 success probability** reduced to 7.5% from 15% to reflect the clinical hold uncertainty. As a result we value SEL24 at PLN5.4/share. If the hold is lifted and we increase the probability back to 15%, the value would be PLN9.2/share.
- **SEL24 deal terms revision**. Following the licensing deal with Menarini, we have revised the deal structure in our model for SEL24. As discussed above, the terms were broadly in line in overall value terms with our assumptions, therefore the revision did not have a substantial effect on the rNPV for this project.
- **Licensing deal for SEL120**. In line with Selvita's strategy we postponed the licensing deal until Phase II. This also means that the deal terms should be more favourable than those of Menarini deal, assuming the data are positive. As detailed in Exhibit 12, we use Novartis/Astex Therapeutics licensing deal for CDK4/6 inhibitor as a benchmark.
- **Revised SEL120 market potential.** We have revised our assumptions for the potential sales of SEL120. For comparison we looked at other CDK inhibitors in the market. Pfizer's Ibrance (*palbociclib*) was the first CDK4/6 inhibitor approved in February 2015 for HR+/HER2- advanced or metastatic breast cancer. According to EvaluatePharma, the drug brought $723m in sales in 2015 and $2.1bn in 2016. The consensus estimate is sales of $7.4bn by 2022. In March 2017, the US FDA approved a close competitor Kisqali (*ribociclib*, Novartis, consensus sales of $1.5bn in 2022), while Eli Lilly's Verzenio (*abemaciclib*, consensus sales $1.8bn in 2022) was approved in September. These new drugs represent a breakthrough in the treatment of advanced breast cancer, as, for example, in Pfizer's Phase III trial PALOMA-2 with breast cancer patients progression-free survival was 24.8 months in the Ibrance + letrozole (aromatase inhibitor) arm compared to 14.5 months in the placebo + letrozole arm. According to consensus expectations the sales of the three drugs could total $10.5bn by 2022. However, the main issues with this first generation of CDK inhibitors are the lack of selectivity within the CDK family and inhibition of other kinases leading to a variety of side effects, with bone marrow suppression and neutropenia being the main one. In general, depending on subtypes, CDKs play varied roles in the control of cell cycle, proliferation and mRNA transcription. SEL120 is a uniquely differentiated selective CDK8 inhibitor mainly regulating mRNA transcription; therefore it is not directly comparable to CKD4/6 inhibitors. We nevertheless view such a strong performance of the first wave of CDK4/6 inhibitors as indicative of a large potential within the CDK family, especially since they can be developed for a variety of solid and haematological cancers. While SEL120 is about to enter Phase I and precise indications are still not clear, we have tentatively increased our peak sales assumption for SEL120 from $750m to $1.5bn to reflect its blockbuster potential.

Exhibit 12: Selected licensing deals used as benchmarks for relevant products

Date	Licensor	Licensee	Product	Stage	Upfront, $m	Deal value (excl. upfront), $m
SEL120						
December 2005	Astex Therapeutics	Novartis	Kisqali (ribocilicb) – CDK4/6 inhibitor	Phase I	Undiscl.	520
November 2017	Loxo Oncology	Bayer	Larotrectinib – tropomyosin receptor kinase inhibitor	Phase 1/2	400	1,150
SMARCA2 inhibitor						
September 2016	Hanmi Pharmaceuticals	Genetech (Roche)	HM95573 – RAF kinase inhibitor	Phase I	80	830
December 2016	Dong-A ST	AbbVie	Mer TK inhibitor	Preclin.	40	485
A2A antagonist						
August 2015	Heptares	AstraZeneca	HTL-1071 – A2A receptor antagonist,	Preclin.	10	500
February 2015	Vernalis	Corvus Pharmaceuticals	CPI-444 – adenosine antagonist	Phase I	1	200 per indication
January 2017	Domain Therapeutics	Merck KGaA	Adenosine receptor antagonists		Undiscl.	280
September 2017	Arcus Bioscience	Taiho	Targets likely involve CD73, CD39 and the A2A and A2B receptors.	Preclin.		$35m over 3 years $275m for each drug programme
SHMT2 inhibitor						
April 2010, amended several times since	Agios Pharmaceuticals	Celgene	AG-881 – pan-IDH mutant inhibitor AD-120 – IDH1 mutant inhibitor AG-221 – IDH2 mutant inhibitor			70 120 120

Source: EvaluatePharma

Exhibit 13: Sum-of-the-parts Selvita valuation

Product	Launch	Peak sales, $m	NPV (PLNm)	NPV/sh. (PLN)	Probability	rNPV (PLNm)	rNPV/sh. (PLN)
Innovation							
SEL24	2023	750	642.6	46.7	7.5%	74.3	5.4
SEL120	2025	1,500	1,346.1	97.7	10%	153.3	11.1
SMARCA2 inhibitor	2030	1,000	580.5	42.1	2%	91.9	6.7
A2A/A2B antagonist	2030	1,000	646.9	47.0	2%	89.3	6.5
SHMT2 inhibitor	2031	1,000	393.3	28.6	2%	61.9	4.5
Merck collaborations	2026	2,000	45.3	3.3	5%	8.6	0.6
Services (incl. Ardigen)	Market			DCF (Q417-2027)	100%	168.8	12.3
				Terminal value	100%	356.9	25.9
Net cash					100%	32.0	2.3
Valuation			**3,654.6**	**265.4**		**1,037.0**	**75.3**

Source: Edison Investment Research. Note: WACC = 12.5% for product valuations, WACC = 10% for Services segment.

Exhibit 14: Assumptions for R&D projects and services business

Product / stage / indication	Comments
Targeted therapeutics platform	
SEL24 - *Phase I/II* - *r/r AML*	Market potential: $750m indicative peak sales. AML treatment currently dominated largely by traditional chemotherapy drugs. Two novel drugs were approved in 2017 and the consensus expects rapid market growth (Exhibit 5) to $2.9bn in 2022 as more novel drugs are expected to be approved in coming years. R&D costs and timelines: according to the agreement, Menarini is due to take over the development by the end of 2017 and Selvita will not incur any R&D costs afterwards. We assume launch in 2023 with peak sales reached in six years. Licensing terms: Menarini deal terms include an upfront payment of €4.8m, a total of €89.1m in potential milestone payments and non-specified single- to low-double-digit royalties (we assume up to 10%) and cost sharing. Market protection: until mid-to-late 2030.
SEL120 - *IND studies* - *Cancer*	Market potential: $1.5bn indicative peak sales. While SEL120 (CDK8 inhibitor) is not directly comparable to CKD4/6 inhibitors, we nevertheless view the strong the strong performance of the first CDK4/6 inhibitors (Ibrance, Kisqali and Verzenio) as indicative of a large potential within the CDK family, especially since they can be developed for a variety of solid and haematological cancers. R&D costs and timelines: $19m in R&D costs for Selvita (partly funded by LLS, see below) to develop the drug to Phase II in 2020. Then out-licensing. The partner continues the development and launches in 2027 with peak sales reached in six years. Licensing terms: According to the deal terms, LLS will provide up to $3.25m in funding over the next four years. This should allow Selvita to progress SEL120 through IND-enabling studies through to Phase I in AML. In Phase II (2020) we assume a licensing deal with terms similar to Novartis/Astex deal. Upfront was undisclosed, we use 5% of the milestone value $26m (Exhibit 12). We assume up to 15% royalty rates. Market protection: until mid-to-late 2030.
BRM/SMARCA2 - *Identification of lead compounds* - *Various cancer, primary indication could be NSCLC*	Market potential: Selvita has identified NSCLC with mutated SMARCA4 as clear initial target. Average sales of the top 10 drugs in NSCLC are estimated to reach $2.16bn. The target population of NSCLC is only around 8% with SMARCA4 mutations; however, there is potential that SMARCA2 inhibition would show efficacy in tumours with mutations in other proteins from SWI/SNF complex, which is 20% of all tumours thus significantly expanding the market potential. To account for the overall potential, but erring on the conservative side we use an assumption of $1bn in peak sales for Selvita's SMARCA2 inhibitor. R&D costs and timelines: Selvita indicated that a clinical candidate could be identified in 2019, we therefore assume Phase I to start in 2021 and an out-licensing deal the same year, as the company indicated that an early partnership will be needed. R&D cost of $3m to reach Phase I. The partner continues the development and launches in 2030 with peak sales reached in six years. Licensing terms: $40m upfront and $485m in milestones split over clinical development and commercialisation. We use AbbVie/Dong-A ST deal as a benchmark from Exhibit 12. We assume 7-10% royalty rates. Market protection: we assume market protection until late 2030.
Cancer metabolism and immunometabolism platform	
Merck deals #1 and #2 - *Preclinical* - *cancer*	Technology remains undisclosed. Assume two projects in Phase I in 2020 with launch in 2028 and peak sales of $1bn in each project in 2034. Licensing fee €0.2m; total milestone payments could add up to €16.5m in each deal. Royalties have not been disclosed, we assume up to 2%.
A2A/A2B antagonist - *Identification and optimization of lead compound* - *Various cancers*	Market potential: Selvita believes the relevant target populations could be broad with the immunosuppressive environment prevalent in around 50% of all cancers. There is also a strong rationale for synergistic potential with checkpoint inhibitors. Because checkpoint inhibitors have gained widespread recognition, but suffer from non-responder issues, combination treatments are likely the future of immunooncology. Because of the lack of detail about potential specific indications, but to reflect the broad potential, we use $1bn as our peak sales assumption. R&D costs and timelines: We assume that a clinical candidate could be identified in 2018 and partnered in 2019. We assume an R&D cost of $2m for Selvita to develop the asset to partnership deal. Phase I to start in 2021 and the partner continues the development and launches in 2030 with peak sales reached in six years. Licensing terms: We use the Heptares/AstraZeneca deal as a benchmark. $10m upfront and $500m in milestones split over clinical development and commercialisation. We assume 7-10% royalty rates. Market protection: we assume market protection until late 2030.
SHMT2 inhibitor - *Identification and optimization of lead compound* - *Various cancers*	Market potential: Overactivation of serine synthesis pathway and upregulation of SHMT has been described in over 20% of solid tumours therefore, while it is still not clear what could be primary indications, the potential seems wide. As in the case of A2A/A2B antagonist, we assume $1bn in peak sales. R&D costs and timelines: We assume that a clinical candidate could be identified in 2018/19 and partnered in 2020. We assume the R&D cost for Selvita to develop the asset to partnership deal is $3m. Phase I to start in 2022 and the partner continues the development and launches in 2031 with peak sales reached in six years. Licensing terms: We use the value of Agios/Celgene deals involving three separate products, but all focusing on isocitrate dehydrogenasemutant (IDH) mutant inhibitors. $10m upfront and $310m in milestone payments split over clinical development and commercialisation. We assume 7-10% royalty rates. Market protection: we assume market protection until late 2030.
Drug discovery services collaborations	Services: sliding scale pa growth from c 25% in 2018 to 12% in 2027; research collaborations: +10-5% pa growth to 2027; subsidies: +5-3% pa growth; tax = 2-11% sliding scale (2017-27); 10% WACC. For terminal value calculation we use 0.75% growth on 2025 FCF.

Source: Edison Investment Research.

Financials

Selvita's 9M17 total revenues were PLN80.5m, up by impressive 65% y-o-y. Commercial revenues (ie excluding subsidies/grants) were PLN68.9m, up 70%, while subsidies (allocated to both the

Innovation and Services segments) accounted for PLN11.6m, up 41%. Total 9M17 operating expenses (excluding ESOP costs) increased to PLN68.7m from PLN45.2m, as Selvita has been growing its staff count and has opened new facilities in Poznan as well as new international sales offices. The 9M17 operating margin, however, increased to 15% from 8% a year ago, boosted by the Menarini deal. Selvita reported 9M17 capex (tangible and intangible) of PLN15.1m versus PLN10.6m a year ago reflecting mainly organic growth. Selvita's new strategy provided more details about the funding sources for the first stage of capacity expansion (page 15). We have already included that in our model and for the time being maintain our approach and assume that this will be funded using debt. Selvita reported cash of PLN37m in November and had PLN5.1m in debt.

Segment performance

Commercial revenues from the **Innovation segment** grew 118% to PLN32.7m in 9M17. The segment's 9M17 net profit was PLN7.3m, up from PLN3.5m a year ago. Notably, Innovation includes Selvita's own R&D pipeline activities so developing it is a long-term strategic goal. Commercial revenues from this segment come from payments related to different partnerships, such as milestone payments from drug discovery collaborations, and therefore tend to be volatile from quarter to quarter, but offer potentially higher margins. The out-licensing of SEL24 to Menarini is the main reason for such a strong performance this year (deal details described on page 5). The upfront payment was PLN20.3m, but because Selvita has capitalised certain costs associated with SEL24 development, the profit booked in the P&L was PLN13m. Selvita will also receive milestone payments if the development of SEL24 is successful.

The profitability-driving **Services segment** reached 9M17 sales of PLN30.5m (excluding subsidies), an increase of 31% y-o-y, which reflects solid organic services business growth. The segment's net profit was PLN2.9m compared to PLN567k a year ago. Business portfolio expansion, entering new markets and an increasing number of FTE and integrated contracts were the growth drivers indicated by Selvita.

While a small business on an absolute basis (5.0% of total Selvita revenues in FY16) the **Bioinformatics (Ardigen) segment** has been a positive surprise to us since the spinout in October 2015 (Selvita has 51%, consolidates the accounts and reports as a third business segment). 9M17 sales were PLN5.3m, a 159% increase versus a year ago.

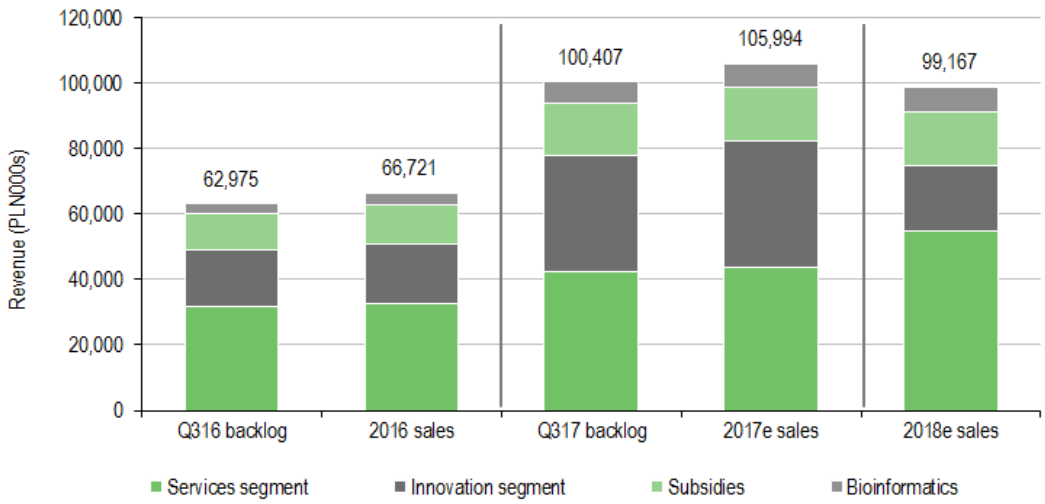
Record backlog for 2017

Together with its Q317 results, Selvita reported a record order backlog of PLN100.4m for this year. Exhibit 15 provides a breakdown of the backlog per sector and comparison to end-year sales. Backlogs of all three business segments, including subsidies (which are allocated to segments), have increased substantially year-on-year, with Innovation and Bioinformatics leading. We expect sales of PLN106m and PLN99m in 2017 and 2018 respectively. The large up-front payment from Menarini is the main reason for our flattish forecast in 2018. Notably, we do not include in our financial forecasts any subsequent milestone payments from Menarini, as Selvita did not provide any guidance, so the visibility is low (we include risk-adjusted milestones in our rNPV model).

On the cost side, Selvita presented a breakdown of expected investments associated with its new strategy for 2017-2021. As mentioned (page 3) Selvita's preliminary estimate is a total investment of around PLN360m financed from internal reserves, public grants, bank loans and a planned share issue (PLN140m). As the green light for the share issue depends on the outcome from the interactions with the FDA, we do not include this in our model. Of the total amount, the company expects PLN260m will be used for the development of the internal R&D pipeline. This translates roughly to PLN65m per year for the next four years and means a substantial ramp up in R&D activities. For comparison, costs associated with the Innovation segment were PLN36m in 9M17. At

present we have not revised our estimates to fully reflect the new investment plans, but we do anticipate a pick-up in R&D spend, especially with SEL120 as the company plans to initiate a Phase I trial next year. We therefore forecast break-even on operating profit in FY18. Once all funding sources are in place and more details emerge about the ongoing R&D activities, we will look to revise our estimates.

Exhibit 15: Backlog and year-end sales

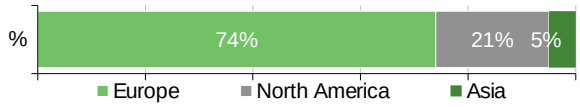


Source: Selvita's accounts

Exhibit 16: Financial summary

PLN'000s	2013	2014	2015	2016	2017e	2018e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	21,914	41,557	56,077	66,721	105,994	99,167
of which: Services (research outsourcing)	9,812	16,121	23,052	32,404	43,746	54,682
Innovation platform	3,241	12,744	15,416	18,353	38,638	20,189
Subsidies	8,688	12,430	14,700	12,067	16,290	16,290
Bioinformatics			2,561	3,431	6,855	7,541
EBITDA	(146)	7,626	10,235	8,264	17,915	5,770
Operating Profit (before GW and except.)	(2,228)	5,272	6,802	4,646	13,212	1,067
Intangible Amortisation	0	0	0	0	0	0
Exceptionals/Other*	0	0	(4,729)	(5,860)	(583)	0
Operating Profit	(2,228)	5,272	2,073	(1,214)	12,629	1,067
Net Interest	(198)	155	748	947	(1,050)	20
Share in profit/(loss) of asocs. and JVs**	0	0	0	(1,016)	(808)	(808)
Other	0	0	0	0	0	0
Profit Before Tax (norm)	(2,427)	5,427	7,550	4,577	11,354	279
Profit Before Tax (reported)	(2,427)	5,427	2,821	(1,283)	10,771	279
Tax	(19)	(45)	(5)	0	(323)	(14)
Deferred tax	0	468	3,417	3,968	0	0
Profit After Tax (norm)	(2,445)	5,850	10,962	8,545	11,031	265
Profit After Tax (reported)	(2,445)	5,850	6,233	2,685	10,448	265
Average Number of Shares Outstanding (m)	10.5	10.5	13.1	13.4	13.6	13.6
EPS - normalised (PLN)	(0.23)	0.56	0.84	0.64	0.81	0.02
EPS - reported (PLN)	(0.23)	0.56	0.48	0.20	0.77	0.02
Dividend per share (PLN)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	7,067	9,494	16,718	41,451	46,543	85,140
Intangible Assets	282	331	2,274	6,640	435	435
Tangible Assets	4,932	6,845	8,597	21,833	33,130	71,727
Other	1,854	2,318	5,847	12,979	12,979	12,979
Current Assets	11,191	17,310	48,524	47,669	60,692	49,882
Stocks	391	706	1,174	1,403	1,384	1,365
Debtors	5,161	10,314	17,961	16,320	16,320	16,320
Cash	5,418	4,878	28,807	29,095	40,688	29,897
Other	221	1,411	582	851	2,300	2,300
Current Liabilities	(11,401)	(15,271)	(16,319)	(18,933)	(23,665)	(23,355)
Creditors	(3,481)	(6,055)	(3,927)	(7,883)	(9,400)	(9,400)
Provisions	(2,104)	(2,801)	(3,327)	(3,600)	(6,650)	(6,650)
Deferred revenues	(5,455)	(4,617)	(7,384)	(5,469)	(5,069)	(5,069)
Short term borrowings	(161)	(91)	(33)	(859)	(950)	(950)
Other	(200)	(1,708)	(1,648)	(1,122)	(1,595)	(1,286)
Long Term Liabilities	(3,454)	(2,278)	(2,043)	(14,477)	(13,728)	(38,728)
Long term borrowings	0	0	0	(4,792)	(4,200)	(29,200)
Deferred revenues	(3,222)	(2,010)	(1,513)	(6,382)	(6,700)	(6,700)
Other long term liabilities	(232)	(268)	(529)	(3,303)	(2,828)	(2,828)
Net Assets	3,403	9,254	46,880	55,710	69,843	72,939
CASH FLOW						
Operating Cash Flow	(7,198)	(4,902)	(16,430)	(6,280)	12,176	(8,459)
Net Interest	0	0	0	0	0	0
Tax	0	0	0	0	0	(323)
Capex	(2,167)	(3,610)	(5,190)	(21,210)	(16,000)	(43,300)
Acquisitions/disposals	0	0	0	0	0	0
Financing	0	0	27,314	303	328	0
Dividends	0	0	0	0	0	0
Other (incl. subsidies)	9,567	7,972	18,354	21,859	15,590	16,290
Net Cash Flow	202	(540)	24,049	(5,329)	12,094	(35,791)
Opening net debt/(cash)	(5,192)	(5,257)	(4,787)	(28,773)	(23,445)	(35,538)
HP finance leases initiated	0	0	0	0	0	0
Exchange rate movements	0	0	0	0	0	0
Other	(137)	71	(63)	1	(1)	0
Closing net debt/(cash)	(5,257)	(4,787)	(28,773)	(23,445)	(35,538)	253

Source: Edison Investment Research, Selvita accounts. Note: *Non-cash cost related to the employee stock options programme. **Profit and loss from 2016 include share in Nodthera's earnings according to an equity method valuation. Please note that the share changed in 2017 as a result of Nodthera's capital increase.

Contact details	Revenue by geography (2016)
Park Life Science ul. Bobrzyńskiego 14 30-348 Kraków Poland +48 12 297 47 00 www.selvita.com	

Management team

Chief executive officer (co-founder): Paweł Przewięźlikowski

Paweł Przewięźlikowski co-founded Selvita in 2007. From 1994 to 2007 he worked at Comarch, a Polish information technology company, becoming VP on the management board in 1996. While at Comarch, he was also the co-founder and the first CEO of Interia.pl, the third largest portal in Poland. He holds an MBA and MSc in information technology.

Chief operating officer (co-founder): Bogusław Sieczkowski

Bogusław Sieczkowski co-founded Selvita in 2007. From 2001 to 2007 he was VP and sub-section director at Comarch. Previously he was IT manager at Bahlsen Polska (1995-99). He holds an MBA and MSc in information technology.

Chief scientific officer: Krzysztof Brzózka

Krzysztof Brzózka joined Selvita in 2007, became project manager (oncology compound) in 2009 and was appointed CSO in 2012. From 2003 to 2007 Krzysztof worked on a broad immunology research programme at Ludwig Maximillian University (Munich). He holds a PhD (molecular biology), an MSc and an MBA.

Director of chemistry department: Mirosława Zydroń

Mirosława Zydroń joined Selvita in 2009 and was appointed to the management board in 2013. From 2005 to 2009 Mirosława held various roles at Pliva (now Teva), including head of the R&D laboratory. She holds a PhD (analytical chemistry), an MSc and an MBA.

Director of biology department: Miłosz Gruca, PhD

Miłosz Gruca was appointed director of biology in 2010 (appointed to the management board in 2012), having worked at Selvita and BioCentrum (a Selvita subsidiary) since 2007, responsible for the introduction of complex biological and analytical services at Selvita. He holds a PhD (biochemistry), an MSc and an MBA.

Principal shareholders	(%)
Paweł Przewięźlikowski (co-founder, CEO)	36.2
Tadeusz Wesołowski	8.2
Nationale Nederlanden PTE S.A.	6.9
Bogusław Sieczkowski	6.7

Companies named in this report

Merck KGaA; H3 Biomedicine (Eisai), Merck & Co, Novartis, AstraZeneca, Incyte, Ambit Biosciences (Daiichi Sankyo), Astellas Pharma, Arog Pharma, Strategia Therapeutics, Takeda