EDISON

Selvita

Company outlook

SEL24 enters Phase I/II

Pharma & biotech

Selvita delivered on both fronts in 2016. We expect sales to have grown a solid 21% y-o-y, with an R&D milestone met and the FDA accepting an investigational new drug application for the company's lead drug candidate, SEL24, which now proceeds through Phase I/II. We have increased our valuation to PLN577m, which includes the first stage of Selvita's long-term expansion plans. Continued organic growth and potential collaboration deals for Selvita's innovation platform are likely catalysts in 2017.

Year end	Revenue (PLNm)	PBT* (PLNm)	EPS* (PLN)	DPS (PLN)	P/E (x)	Yield (%)
12/14	41.6	5.4	0.56	0.0	67.9	N/A
12/15	56.1	7.5	0.84	0.0	45.2	N/A
12/16e	67.6	3.7	0.28	0.0	N/A	N/A
12/17e	76.9	3.3	0.24	0.0	N/A	N/A

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

SEL24 moves to clinic; FLT3 inhibitors in spotlight

SEL24 is a dual PIM/FLT3 inhibitor and the first such compound to progress to Phase I/II, to our knowledge. Selvita started recruiting acute myeloid leukaemia (AML) patients into Phase I/II in March 2017. Standalone FLT3 inhibitors are at a peak of interest in blood malignancies, after a seven-year Phase III study with midostaurin from Novartis showed survival benefit and a 23% reduction in risk of death for AML patients. The FDA granted breakthrough therapy designation and a priority review in November to midostaurin's NDA application. Given SEL24's differentiated dual-action mechanism, this bodes well for potential partnering opportunities, in our view.

Third-party PIM/FLT3 combo inhibition data at ASH

An interesting set of data was presented at the annual meeting of the American Society of Hematology (ASH) in December 2016, where AstraZeneca's pan-PIM inhibitor AZD1208 was tested *in vitro* in combination with FLT3 inhibitor quizartinib (Ambit Biosciences/Daiichi Sankyo) in AML cells. The researchers managed to gather evidence that the combination of both PIM and FLT3 inhibitors produces additional effects, ie decreases the level of a specific protein, which could promote survival of the malignant cells. No such effect was observed after the treatment with either inhibitor individually. The authors concluded that this approach could have clinical promise, a conclusion that Selvita made three years ago when nominating SEL24 as the preclinical candidate.

Valuation: PLN577m or PLN43/share

Our valuation is increased to PLN577m or PLN43/share from PLN427m or PLN32/share. Using a DCF model we value Selvita's operations at PLN348m (PLN25.9/share), while for the lead candidates SEL24 and SEL120 we employ an rNPV method and derive indicative values of PLN69m (PLN5.1/share) and PLN35m (PLN2.6/share) respectively. Continued organic growth and potential collaboration deals are likely catalysts in 2017.

20 March 2017

Price	**PLN38.0**
Market cap	**PLN509m**

Estimated net cash (PLNm) at 31 December 2016	26.1
Shares in issue	13.4m
Free float	45%
Code	SLV
Primary exchange	WSE
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	18.6	43.6	72.7
Rel (local)	13.0	19.9	46.2
52-week high/low	PLN38.0	PLN20.8	

Business description

Selvita is a drug discovery services provider based in Poland. It employs c 370 staff (34% with PhDs) and operates two main business units: the Innovations Platform (internal NME pipeline) and Research Services (medicinal chemistry/biology, biochemistry).

Next events

Q416 results and 2016 annual report	19 April 2017
SEL120 IND studies start	H117

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Edison profile page

Investment summary

Company description: CRO with innovative R&D pipeline

Selvita, founded in 2007, has become one of the largest independent drug discovery companies in Europe. It employs c 370 staff (c 30% with PhDs), operates out of a ~30,000sq ft modern research facility in Krakow, Poland, and decided to open a new facility in Poznan adding another 5,500sq ft, with operations to start in early 2017. Recently Selvita also announced 10-year expansion plans and could increase laboratory and office space by 150,000sq ft for c 1,000 new employees. The internal pipeline is focused on novel small molecules for cancer. The research outsourcing business covers contract chemistry, biology and bioinformatics (clients from a range of big biopharma companies). Selvita listed on the Warsaw Stock Exchange NewConnect Market in July 2011 and upgraded its listing to the WSE Main Market in December 2014 with the successful offering and placing of 2.65m shares at PLN10.3 per share and gross proceeds of PLN27.3m. Selvita operates a capital-efficient financial model, although fresh funds may be sought to advance its internal pipeline.

Valuation: Upgraded to PLN577m or PLN43/share

Our valuation increased to PLN577m or PLN43/share from PLN427m or PLN32/share, which is mainly due to rolling our model forward and extending our DCF model to include 2024-2025. In line with Selvita's long-term expansion plans we forecast a solid growth for the foreseeable future (more details in our previous report). Existing operations (services, collaborations, subsidies) constitute 76% of the total valuation, while SEL24 and SEL120 account for 12% and 6%, respectively. We note that due to the early stage of the lead R&D projects, the success probabilities typically range from 5% to 15%. In other words, if all innovative programmes in our model were to be successful, the valuation would be PLN1.2bn.

Financials: Strong organic growth to continue

Selvita has demonstrated consistently strong performance, with 2012-15 annual revenues growing at a CAGR of 51% and a solid 21% estimated growth to PLN67.6m in 2016. Selvita reached positive net profit in 2014 and 2015, while we forecast a modest net loss of PLN2.0m in 2016 (this includes an estimated PLN5.9m non-cash cost related to the employee stock options programme). In our last report we had already included the estimated cost (c PLN70m) related to the first stage of long-term expansion plans in our model, which suggests that long-term sales from the Services and Innovation segments could more than double over the next six years, with a long-term operating margin of around 30%. Selvita's cash position is strong, with an estimated PLN26.1m at the end of 2016. There is sufficient cash to progress the internal drug candidates SEL24 and SEL120 to complete Phase I/II and pre- Phase I respectively, although for these programmes to progress further, we would anticipate additional financing and/or a collaborative deal.

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, 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 SEL24 and SEL120, but these are indicative only, so the actual terms secured could have a materially positive or negative impact on our valuation.

Outlook: Major expansion started

Selvita has established a good track record with its Services business, which has enabled it to also develop its own pipeline of novel small molecule programmes. The Services business (Exhibit 1) is expected by us to continue on a high-growth revenue trajectory (>20%) over the next two years, but greater potential long-term upside could come from the development and licensing of a number of candidates from the internal pipeline (Innovation platform). Key among these are SEL24 and SEL120 in the near term, but Selvita has other preclinical programmes in oncology, which may also offer partnering potential or other innovative funding solutions, for example like the formation of Nodthera in August 2016.

Exhibit 1: Overview of Selvita's divisions and R&D programmes

Division	Key features	Examples
Innovations Platform	Multiple wholly owned preclinical programmes in oncology	SEL24 (PIM/FLT3 inhibitor – blood cancer); SEL120 (CDK8 inhibitor – blood cancer, solid tumours); SEL201 (MNK1/2 inhibitor – various cancers); SEL303 (HO-1 inhibitor - cancer); EPTHERON (Cancer epigenetics platform); immuno-oncology platform (GCN2 and STING targets); immuno-metabolism platform (SHMT2)
	Research collaborations with big pharma/biotech	Merck KGaA (cancer metabolism collaboration I signed October 2013). Merck KGaA (cancer metabolism collaboration II signed November 2015). H3 Biomedicine/Eisai (kinase discovery collaboration signed September 2013). Felicitex Therapeutics (cancer quiescence collaboration signed in November 2014).
	Nodthera (49% owned)	SEL212 (NLRP3 inflammasome – autoimmune diseases)
Research Services	Contract chemistry	Custom organic synthesis; medicinal chemistry; scale-up/process chemistry; industrial chemistry.
	Biology	Cell and molecular biology; biochemistry; analytical chemistry; ADME and pharmacokinetics; method validation.
	Bioinformatics* - 60% stake in Ardigen JV	LIMS systems; bioinformatics solutions; document management; big data solutions for precision medicine.

Source: Edison Investment Research, Selvita. Note: *Spun into Ardigen in October 2015.

Expansion plans: New chapter in Selvita's story

Selvita added around 70 employees, with the total number rising to c 370 in 2016 alone, and initiated expansion at a new location in Poznan with operations starting in early 2017. Furthermore, on 21 September 2016 Selvita announced its long-term expansion plans with the first step approved at the extraordinary general meeting on 25 October. The expansion plans include a new laboratory infrastructure development close to the current Selvita facilities in Krakow over the next 10n years, with a total area of c 150,000sq ft and space for c 1,000 employees. The first stage includes one new fully equipped facility covering c 54,000sq ft; 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 purchase price for the land is PLN7.5m, and while the total costs of this first stage are still being refined, a rough estimate is around PLN70m (including the land cost). We have included the first stage of this expansion in our model, resulting in our updated long-term sales estimates from the Services and Innovation segments more than doubling over the next six years, with an increase in operating costs starting in 2019 when the development of the first building is expected to be completed (for more details, see our previous report).

Nodthera – innovative financing of internal projects

In July 2016, Selvita, together with Epidarex Capital, announced the formation of a new company, Nodthera (Selvita owns 49%), 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. Epidarex is a specialist, early-stage life sciences investor and we view the solution of carving out the asset and funding the research together with specialist investors as innovative, with the potential to speed up the preclinical development in Selvita's portfolio. See Nodthera and inflammasome technology on page 8 for more details.

Collaboration progress with Merck KGaA

Selvita's partnership with Merck has been progressing in 2016. The two companies signed a second preclinical drug development deal in March, which involved an undisclosed protein target with potential therapeutic compounds initially developed by Selvita using its cancer metabolism platform. Similarly to the previous deal with Merck, announced on 22 December 2015, Selvita may receive up to €1.9m in payments during the first five years depending on undisclosed R&D milestones. Total payments may amount to €16.5m if the drug is successfully commercialised.

These two preclinical drug development deals stem from the original drug discovery collaboration with Merck established in October 2013 with the goal of collaborating on the discovery and development of multiple new compounds. This two-year agreement has clearly been successful, with the two new drug development programmes now ongoing. Furthermore, in November 2015 a second drug discovery collaboration was agreed with Merck to identify first-in-class small molecules as lead candidate drugs for multiple oncology indications. This indicates that we could see more development deals in the near term. We summarise the collaboration and drug development agreements with Merck in Exhibit 2.

Exhibit 2: 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; max 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

Selvita also collaborates with H3 Biomedicine (Eisai). While the details remain undisclosed, the collaboration involves novel small molecule compounds for new kinase targets associated with cancer development. Another partnership with Felicitex Therapeutics, established in November 2014, centres on Selvita's cancer quiescence platform, which is a novel approach with expected efficacy against quiescent cancer cells that are not actively proliferating and thus less susceptible to classical chemotherapy drugs. These more resistant malignant cells may cause tumour relapse once the treatment ends.

SEL24: A unique dual PIM/FLT3 inhibitor

SEL24 is Selvita's most advanced oncology programme, focused on developing a compound with a dual-action mechanism to target two kinases, namely PIM (1, 2 and 3 isoforms) and FLT3 mutants, which have been shown to be important in the development of AML and other haematological

malignancies (eg diffuse large B-cell lymphoma, multiple myeloma, follicular lymphoma).[1] 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, but SEL24 has the ability to inhibit both families of kinases at therapeutic doses.

In August 2016, Selvita announced that the FDA has accepted the investigational new drug application (IND) for SEL24. This is the first of Selvita's R&D assets being tested in a clinical study and enrolment started in March 2017. With its dual-action mechanism, SEL24 is the first such compound to progress to Phase I/II to our knowledge. The 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 will establish the recommended dose, which will be further evaluated in Part 2 for safety, but also for initial efficacy. Headline data could be reported in H218, while full results could be published around end-2019.

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. To date there are no targeted agents approved for the treatment of AML, although many are in development and Novartis's midostaurin is now under a priority review by the FDA after demonstrating survival benefit in a Phase III study. Midostaurin inhibits FLT3, but not PIM, so SEL24 is differentiated with its dual-action mechanism.

PIM – a promising target downstream of FLT3

The PIM family of serine-threonine kinases plays 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. As such, targeting both PIM kinases and FLT3 mutants may improve response rates and reduce relapses. Overexpression of PIM has been reported in a variety of haematological malignancies[2] (eg AML, CLL, B-cell lymphoma), as well as some solid tumours (pancreatic, liver). Exhibit 3 shows the most advanced candidates against PIM kinases and those against FLT3. AstraZeneca's AZD1208[3] completed a Phase I study, but terminated clinical development in Q314 due to efficacy and safety reasons (no further explanation provided). Novartis has launched a number of Phase I and Phase I/II studies with LGH447, so data over the next 12-18 months will provide greater insight into the viability of specifically targeting PIM kinase.

[1] Levis, M and Small, D (2003). FLT3: ITDoes matter in leukemia. Leukemia (2003) 17, 1738–1752.

[2] Alvarado Y, Giles FJ, Swords RT (2012). The PIM kinases in hematological cancers. Expert Rev Hematol. 2012 Feb; 5(1):81-96.

[3] Keeton EK, et al (2014). AZD1208, a potent and selective pan-Pim kinase inhibitor, demonstrates efficacy in preclinical models of acute myeloid leukemia. Blood. 2014 Feb 6; 123 (6): 905-13.

Exhibit 3: 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)	20-pt Phase I/II (multiple myeloma) 75-pt Phase I (multiple myeloma) 86-pt Phase I (AML/MDS)	Completed, data not reported H117 H118
	AZD1208	AstraZeneca	Malignant lymphoma	43-pt Phase I	Discontinued Q314
	INCB053914	Incyte	Advanced malignancies	135-pt Phase I	H217
	TP-3654	Tolero	Haematological malignancies, prostate cancer, urothelial carcinomas	Preclinical	N/A
FLT3 inhibitors	Midostaurin (PKC412)	Novartis	AML	717-pt Phase III	Dec 2015 (ASH)
	Quizartinib (AC220)	Ambit Biosciences (Daiichi Sankyo)	Acute myeloid leukaemia (AML)	363-pt Phase III	H118 (interim analysis H117)
	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 III	H219
	Crenolanib	Arog Pharma	AML	70-Pt Phase II	H116
	E6201	Strategia Therapeutics	AML	62-Pt Phase II	H119
	TAK-659	Takeda	AML	81-Pt Phase II	H217

Source: Edison Investment Research, clinicaltrials.gov

FLT3 – a natural dual target

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), compounds that specifically target FLT3 are still in clinical development (Exhibit 3).

Positive midostaurin Phase III and priority review

Ambit Biosciences' quizartinib (AC220) and Novartis's midostaurin (PKC412) are the most advanced FLT3 inhibitors in AML. 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 4). In February 2016 the FDA granted breakthrough therapy designation and a priority review in November 2016 to midostaurin's NDA application, which implies a possibility of the FDA response within a six-month period.

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.

Exhibit 4: 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.

In our view, these data improve the chances of Selvita finding a suitable partner and of progressing SEL24 through clinical development. FLT3 plays an important role in leukemogenesis and its presence is associated with poor prognosis in acute myeloid leukemia (AML). PIM-1 was found to be one of the most significantly downregulated genes on FLT3 inhibition. Midostaurin inhibits FLT3 but not PIM. SEL24 inhibits both, so could offer improved efficacy. It is too early to say based on clinical evidence to date, but the midostaurin data are supportive to SEL24, in our view.

Ambit/Daiichi Sankyo plans interim analysis of quizartinib's Phase III trial in H117. We note that Ambit secured a co-development deal with Astellas Pharma in 2009 for quizartinib, when the drug was undergoing Phase II studies, with Astellas paying a $40m upfront fee as part of a $390m total deal value. Astellas subsequently returned rights to the compound in 2013, but in September 2014 Daiichi Sankyo agreed to purchase Ambit for $315m, with a further $95m payable depending on commercial milestones being achieved.

Third-party preclinical data with combo inhibition of PIM/FLT3

An interesting set of data was presented at ASH in December 2016, where AstraZeneca's pan-PIM inhibitor AZD1208 was tested *in vitro* in combination with Ambit's FLT3 inhibitor quizartinib in AML cells. The researchers sought to establish the effect on the expression of several anti-apoptotic (those that prevent cell death) and pro-apoptotic (those that promote cell death) proteins. They found that the expression of one anti-apoptotic protein Mcl-1 decreased when the cells were cultured with both inhibitors, but the protein level did not change when treated with either inhibitor alone. Mcl-1 is thought to play a critical role in regulating the death of immune cells and could promote the survival of the malignant AML cells. While this is basic preclinical research and the effect the combination might have in humans cannot be directly extrapolated, the importance of this study is that the authors managed to gather evidence that the combination of both PIM and FLT3 inhibitors produces additional effects relative to treatment using either one of them separately. The researchers concluded that this approach could have clinical promise, a conclusion that Selvita made three years ago when nominating SEL24 as the preclinical candidate.

SEL120: A selective CDK8 inhibitor

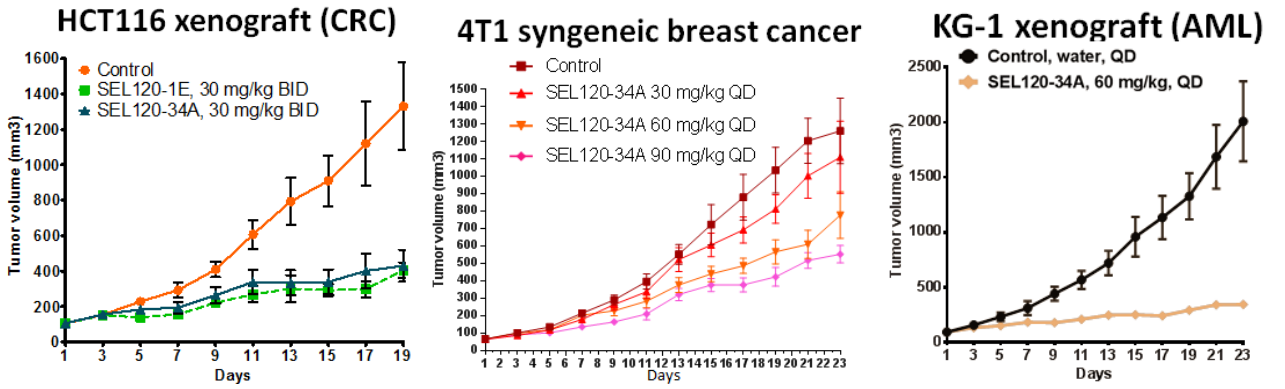
SEL120 is a first-in-class selective CDK8 inhibitor. Depending on subtypes, cyclin-dependent kinases (CDKs) play varied roles in the control of cell cycle, proliferation and mRNA transcription.[4] A number of CDK inhibitor candidates are in advanced stages of clinical trials or approved, but the majority of them target a range of CDK subtypes, such as CDK4/6 (eg palbociclib/Pfizer, abemaciclib/Eli Lilly, LEE011/Novartis). The main issues with the first generation of CDK inhibitors were not only the lack of selectivity within the CDK family, but they also inhibit numerous other kinases leading to a variety of side effects in clinical trials, most often bone marrow suppression, anaemia and leukopenia.

[4] Cicenas, J and Valius, M (2011). The CDK inhibitors in cancer research and therapy. J Cancer Res Clin Oncol. 2011 Oct;137 (10):1409-18.

SEL120 is a uniquely differentiated selective CDK8 inhibitor mainly regulating mRNA transcription and shown to have a favourable safety/efficacy profile in non-GLP studies in two species, and the company is now preparing for IND-enabling studies. 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 a natural compound, cortistatin A, and recently published articles show anti-leukaemic *in vitro* and *in vivo* efficacy, which adds to Selvita's preclinical data.

Selvita currently is in the process of CRO selection for performance of the required IND-enabling studies in 2017. So far, preclinical studies from the company (Exhibit 5) and from third parties point to potential efficacy in haematological malignancies, colorectal cancer or triple-negative breast cancer. Selvita aims to secure a partner for further development of the SEL120 programme and, given Merck & Co's interest in CDK8 inhibitors, we believe that other large pharma companies may also be interested in this area.

Exhibit 5: SEL120 inhibits tumour survival in multiple *in vivo* cancer models



Source: Selvita. Note: HCT116=CRC, KG-1=AML (xenograft models – human tumour tissue transplanted in animals); 4T1=breast cancer (syngeneic model – tumour derived from same strain animals).

Nodthera and inflammasome technology

As mentioned before, in July 2016, Selvita and Epidarex Capital announced the formation of a new company, Nodthera, headquartered in Edinburgh, Scotland. Nodthera (Selvita owns 49%) centres on NLRP3 inflammasome inhibitors, a first-in-class small-molecule technology developed internally by Selvita.

Inflammasomes: Recent discovery with accumulating data

The inflammasome was discovered (and given its name) by a team led by Professor Jurg Tschopp at the University of Lausanne in 2002, when his team 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.[5,6]

[5] 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.

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

There are several classes of innate immune system (in-born, as opposed to acquired, eg vaccination) receptors, with the two most researched ones being toll-like receptors (TLRs), located on cell membranes; and nucleotide-binding oligomerization domain-like receptors (NLRs) located inside the cells.[7] Both classes recognise microbial infection, which leads to secretion of pro-inflammatory cytokines like IL-1beta. Inflammasomes (there are several subtypes described) are molecular mechanisms in the middle of this cascade and in some cases can also be stimulated by internal chemical signals without the presence of an infection. This may lead to autoimmune disorders. A unique subtype of inflammasomes – NLRP3 – is able to sense both external and internal signals.

Potential therapeutic areas for targeting inflammasomes

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; however, current indications are rare to extremely rare (cryopyrin-associated autoinflammatory syndrome (CAPS), familial Mediterranean fever, pyogenic sterile arthritis, hyperimmunoglobulinemia D syndrome and TNF receptor-associated syndrome).[8] 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).[9] Although neurologic and metabolic disorders are not traditionally considered to be inflammatory, the contribution of the inflammatory component is increasingly being recognised.[9]

The inflammasome's role in immune system response and its modulation is attracting private funding, with Inflazome and IFM Therapeutics being 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 is developing inflammasome modulators for cancer and inflammatory diseases. Notably, IFM was seeded with just $2m in October 2015.

Valuation

Our valuation has increased to PLN577m or PLN43/share from PLN427m or PLN32/share, which is mainly due to rolling our model forward and extending our DCF model to include 2024-2025. In line with Selvita's long-term expansion plans we forecast solid growth for the foreseeable future (more details in our previous report). We value the existing operations (services, collaborations, subsidies) at PLN286m (PLN21.2/share) or 76% of the total valuation, while SEL24 and SEL120 are valued at PLN5.1/share and PLN2.6/share or 12% and 6% respectively. Our key assumptions and valuation metrics are summarised in Exhibit 6. We note that due to the early stage of the lead R&D projects, the success probabilities typically range from 5% to 15%. In other words, if all programmes in our model were to be successful the valuation would be PLN1.2bn.

[7] H. Hoffman and A. Wanderer. Inflammasome and IL-1β-Mediated Disorders. Curr Allergy Asthma Rep (2010) 10:229–235.

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

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

Exhibit 6: Selvita valuation model

Division	Metric	Non risk-adj. value (PLNm)	Probability of success (%)	Risk-adj. value (PLNm)	Value per share (PLN)	Notes
Services/ research collaborations	DCF (2017-2021)	91	100%	91	6.78	Services: sliding scale pa growth from c 25% in 2017 to 20% in 2025; research collaborations: +10% pa growth; subsidies: +5.0% pa growth; tax = 2-11% sliding scale (2017-25); 10% WACC.
	Terminal value	348.1	100%	348.1	25.89	0.75% growth on 2025 FCF
	Subtotal	**439.2**		**439.2**	**32.67**	
Internal pipeline	SEL24	318.9	15%	69.1	5.14	$750m indicative peak sales (2029); launch in 2023; 5% royalty (preclinical); 15% probability of success (preclinical). Includes deal milestone estimates: $15m upfront in 2017 (60%); $10m on start of Phase II in 2018 (60%); $20m on start Phase III in 2020 (15%); $40m on NDA filing/approval in 2022 (7.5%). 12.5% WACC. Internal R&D Phase I/II costs of $5m over 2016/2017.
	SEL120	292.8	5%	34.6	2.58	$750m indicative peak sales (2029); launch in 2023; 5% royalty (preclinical); 5% probability of success (preclinical). Includes deal milestone estimates: $3m upfront in 2017 (60% probability); $5m on IND/Phase I start in 2017 (50%); $15m on start Phase II in 2018 (25%); $20m on start Phase III in 2020 (10%); $40m on NDA filing/approval in 2022 (5%). 12.5% WACC. Internal R&D pre-Phase I costs of $1m in 2016.
	Collaborations	87.0	5%	8.2	0.61	Indicative oncology projects to reflect the value of the partnership with Merck KGaA. Assume two projects in Phase I in 2020. Milestones of up to $31.5m each relate to candidate selection, start of Phase I, initiation of pivotal trials, launch in major regions and sales thresholds. Royalties on annual sales of 0.5% up to $500m, 1% on $500m-1bn and 2% on sales greater than $1bn. Probability of 5% to market.
	Subtotal	**698.7**		**111.9**	**8.33**	
Est. net cash at end-2016		26.1		26.1	1.94	
Selvita total		**1,164.0**		**577.2**	**42.9**	Based on 13.4m shares outstanding.

Source: Edison Investment Research

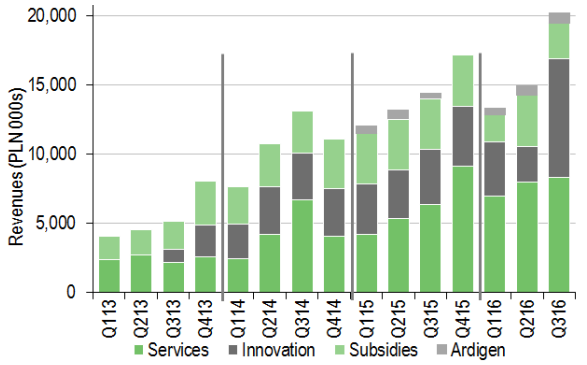
Financials

Selvita has three business segments: Innovation, Services and Bioinformatics (Ardigen). Besides sales to external customers, the company also receives subsidies, which are allocated to the Innovation and Services segments (Exhibits 7 and 8).

Selvita has demonstrated a consistently strong performance with 2012-15 annual revenues growing at a CAGR of 51% and solid 21% estimated growth to PLN67.6m in 2016 (Exhibit 8). Selvita reached positive net profit in 2014 and 2015, while we forecast a modest net loss of PLN2.0m in 2016. This includes an estimated PLN5.9m non-cash cost related to the employee stock options programme (ESOP; PLN4.7m in 2015). We calculate adjusted profit after tax at PLN3.8m. As mentioned, Selvita has been expanding in 2016, including preparations to open new facilities in Poznan and the number of employees rising by around 70 new hires to c 370. This meant a near term cost hit, with total operating costs rising from PLN49.3m in 2015 to PLN63.5m in 2016.

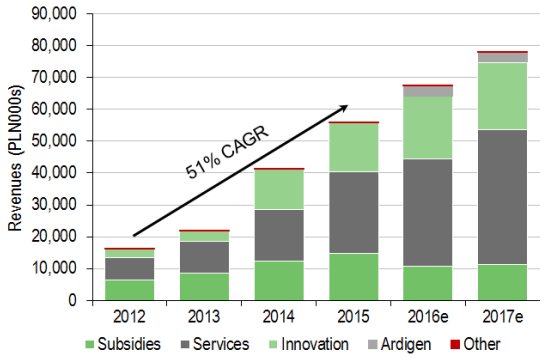
We have already included the estimated cost (c PLN70m) related to the first stage of long-term expansion plans in our model (for a more detailed breakdown, see our previous report). Overall, our updated long-term estimates include sales from the Services and Innovation segments more than doubling over the next six years, with an increase in operating costs starting in 2019 when the development of the first building is expected to be completed. We model a long-term group operating margin of 30%.

Exhibit 7: Quarterly revenue performance



Source: Edison Investment Research, Selvita

Exhibit 8: Annual revenue performance



Source: Edison Investment Research, Selvita. Note: Other is unallocated income.

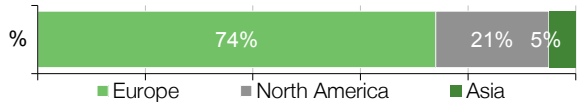
Selvita's spin-out bioinformatics company Ardigen delivered a positive surprise with Q316 sales of PLN810k topping our expectations of PLN725k. Selvita has a 60% stake in the company. Ardigen was established to diversify from laboratory software and IT support services to develop new solutions and leverage the emerging bid data applications tailored for precision medicine. Our initial 2016 expectations were for flattish sales with a small addition to the top line and a neutral effect on the bottom line. However, the segment has consistently performed better than expected and our 2016 sales estimate now stands at PLN3.1m, albeit a small portion, 4.6%, of total sales. Selvita expects new leads in the US will allow the delivery of additional sales already logged in Q416 to continue into 2017.

Selvita's cash position is strong, with, we estimate, PLN26.1m at the end of 2016. There is sufficient cash to progress the internal drug candidates SEL24 and SEL120 to complete Phase I/II and pre-Phase I respectively. For these programmes to progress further, we would anticipate additional financing and/or a collaborative deal.

Exhibit 9: Financial summary

PLN'000s	2013	2014	2015	2016e	2017e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	21,914	41,557	56,077	67,642	76,935
of which: Services (research outsourcing)	9,812	16,121	25,612	33,729	42,161
Innovation platform	3,241	12,744	15,416	19,560	16,416
Subsidies	8,688	12,430	14,700	10,818	14,824
EBITDA	(146)	7,626	10,235	7,640	10,685
Operating Profit (before GW and except.)	(2,228)	5,272	6,802	4,161	5,945
Intangible Amortisation	0	0	0	(0)	(0)
Exceptionals/Other*	0	0	(4,729)	(5,857)	(586)
Operating Profit	(2,228)	5,272	2,073	(1,696)	5,359
Net Interest	(198)	155	748	805	13
Share in profit/(loss) of assocs. and JVs**	0	0	0	(1,307)	(2,613)
Other	0	0	0	0	0
Profit Before Tax (norm)	(2,427)	5,427	7,550	3,660	3,345
Profit Before Tax (reported)	(2,427)	5,427	2,821	(2,197)	2,759
Tax	(19)	(45)	(5)	164	(83)
Deferred tax	0	468	3,417	0	0
Profit After Tax (norm)	(2,445)	5,850	10,962	3,824	3,262
Profit After Tax (reported)	(2,445)	5,850	6,233	(2,033)	2,676
Average Number of Shares Outstanding (m)	10.5	10.5	13.1	13.3	13.4
EPS - normalised (PLN)	(0.23)	0.56	0.84	0.28	0.24
EPS - reported (PLN)	(0.23)	0.56	0.48	(0.16)	0.20
Dividend per share (PLN)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	7,067	9,494	16,718	30,655	40,891
Intangible Assets	282	331	2,274	5,274	5,274
Tangible Assets	4,932	6,845	8,597	15,799	26,035
Other	1,854	2,318	5,847	9,583	9,583
Current Assets	11,191	17,310	48,524	43,062	40,178
Stocks	391	706	1,174	1,158	1,142
Debtors	5,161	10,314	17,961	14,385	14,385
Cash	5,418	4,878	28,807	26,066	23,198
Other	221	1,411	582	1,453	1,453
Current Liabilities	(11,401)	(15,271)	(16,319)	(16,154)	(16,237)
Creditors	(3,481)	(6,055)	(3,927)	(6,854)	(6,854)
Provisions	(2,104)	(2,801)	(3,327)	(4,375)	(4,375)
Deferred revenues	(5,455)	(4,617)	(7,384)	(4,061)	(4,061)
Short term borrowings	(161)	(91)	(33)	(197)	(197)
Other	(200)	(1,708)	(1,648)	(666)	(749)
Long Term Liabilities	(3,454)	(2,278)	(2,043)	(6,940)	(12,565)
Long term borrowings	0	0	0	0	(5,625)
Deferred revenues	(3,222)	(2,010)	(1,513)	(4,172)	(4,172)
Other long term liabilities	(232)	(268)	(529)	(2,768)	(2,768)
Net Assets	3,403	9,254	46,880	50,622	52,267
CASH FLOW					
Operating Cash Flow	(7,198)	(4,902)	(16,430)	(12,504)	(8,340)
Net Interest	0	0	0	0	0
Tax	0	0	0	(4)	0
Capex	(2,167)	(3,610)	(5,190)	(13,680)	(14,976)
Acquisitions/disposals	0	0	0	0	0
Financing	0	0	27,314	0	0
Dividends	0	0	0	0	0
Other (incl. subsidies)	9,567	7,972	18,354	23,449	20,449
Net Cash Flow	202	(540)	24,049	(2,740)	(2,867)
Opening net debt/(cash)	(5,192)	(5,257)	(4,787)	(28,773)	(25,868)
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	0	0	0	0	0
Other	(137)	71	(63)	(165)	0
Closing net debt/(cash)	(5,257)	(4,787)	(28,773)	(25,868)	(23,001)

Source: Edison Investment Research, Selvita accounts. Note: *Non-cash cost related to the employee stock options programme. **Profit and loss estimates from 2016 now include 49% share in Nodthera's earnings according to equity method.

Contact details	Revenue by geography (2015)
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)	39.0
Tadeusz Wesołowski	9.5
Other members of the Management and Supervisory Board	7.8
Bogusław Sieczkowski (Co-founder, COO)	7.2

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

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