EDISON

Crossject

Initiation of coverage

Making injections simple, quick and needle-free

Pharma & biotech

Crossject has developed a deep pipeline of products that are based on its proprietary needle-free injection system, ZENEO, across a variety of indications. The benefits of ZENEO include no need for needles, as well as a simple and quick (~1/10th of a second) delivery of the drug. Its first commercial product, ZENEO Methotrexate for rheumatoid arthritis, should reach the market in 2017. We value the company at €11.96 per share, which is based on the value of four of its nearer-term disclosed programmes.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/14	1.7	(5.3)	(0.66)	0.0	N/A	N/A
12/15	2.4	(6.7)	(0.85)	0.0	N/A	N/A
12/16e	3.1	(4.6)	(0.53)	0.0	N/A	N/A
12/17e	3.0	(8.9)	(0.97)	0.0	N/A	N/A

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

The ZENEO platform is broadly applicable

According to Crossject, around 200 injectable compounds meet the criteria for use in the ZENEO platform, providing a deep well of markets to target, though Crossject is focused on acute treatments. Also, unlike powder-based injection systems, no reformulation of the reference product is needed.

First product to be commercialised in 2017

ZENEO Methotrexate is expected to be commercialised in H217. Over the course of 2018 and 2019, Crossject expects to launch proprietary versions of sumatriptan (acute migraine), L15 (an undisclosed niche product), adrenaline (anaphylactic shock), midazolam (epileptic seizures), naloxone (opioid overdose) and apomorphine (Parkinson's disease) through a series of regional partnerships.

An accelerated approval process

As Crossject is focusing on including already approved drugs in its ZENEO platform, the clinical development programme is extremely abbreviated through a 505(b)2 process. For example, Zogenix was able to get its needle-free version of sumatriptan approved simply through bioequivalence and device usability studies. In total, the cost to develop a product is estimated at €4-6m per compound.

Valuation

Using a risk-adjusted NPV method valuing Crossject's disclosed nearer-term products (methotrexate, sumatriptan, adrenaline and midazolam), we value the company at €81.1m or €11.96 per basic share. As of 2015 year-end, the company had €5.2m in cash. It expects to receive an additional €3.1m in grants in 2016 and has also recently announced an equity line, which could provide up to ~€10m. Between now and projected profitability in 2018, we forecast a total funding need of €15m for all projects. This would be mitigated in part by additional upfront payments from partners, as well as milestone payments on product approvals.

13 June 2016

Price	**€7.70**
Market cap	**€52m**

Net cash (€m) as of 31 December 2015	5.2
Shares in issue	6.7m
Free float	72.3%
Code	ALCJ
Primary exchange	Euronext
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(11.3)	(9.9)	3.1
Rel (local)	(10.2)	(9.4)	17.6
52-week high/low	€11.06		€3.52

Business description

Crossject has several programmes in development based on its proprietary needle free injection system, ZENEO. The first to market will be ZENEO Methotrexate, which is expected to be commercialised in 2017. Over the course of 2018 and 2019, the company expects to launch proprietary versions of six other products on its ZENEO platform.

Next event

Launch of MTX	H217

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Edison profile page

Crossject is a research client of Edison Investment Research Limited

Investment summary

Company description: A platform company with a deep pipeline

Crossject is a needle-free drug delivery company that was founded in Dijon, France, in 2001 as a spinout from Fournier Laboratories (which has since been acquired by Abbott) and went public on the Paris exchange in 2014 in a €17m offering. It is a low overhead company with 23 employees.

Crossject has seven programmes in development, all using its proprietary needle-free injection system, ZENEO. Its lead programme is ZENEO Methotrexate for rheumatoid arthritis (RA), which is expected to be commercialised in Europe in H217 and in China sometime in 2017. It already has regional partnerships in France, India and China and will likely sign additional agreements to commercialise the product in other regions (as it likely will with all of its products). The next product to reach the market will likely be ZENEO Sumatriptan for the acute treatment of migraine, which is expected to be commercialised in H118. Crossject is also developing a product dubbed ZENEO L15, which is an undisclosed emergency product for a relatively niche market, and is expected to launch in H118. Crossject will be targeting the billion-dollar epinephrine market with ZENEO Adrenaline, with a commercial launch targeted for H218. ZENEO Midazolam for the acute treatment of epileptic seizures is expected to also hit the market in the second half of 2018. Finally, the company is developing ZENEO Naloxone for drug overdose and ZENEO Apomorphine for temporary paralysis associated with Parkinson's disease (PD), with commercial launches targeted for 2019.

Valuation: €11.96 per basic share

Using a risk-adjusted NPV model, we value the company at €81.1m or €11.96 per basic share. We currently assign no value to the L15 programme, as we don't have knowledge of what the product is or what indication it is for; once this information is available, we will likely include it in our valuation. Also, we are not including the naloxone and apomorphine products as there is significantly less visibility. Also, much of our valuation is dependent upon successful launches in the US as pricing in Europe, according to company comments, will likely be a fraction of that in the US and in the rest of the world. Potential catalysts will likely include the announcement of additional partnerships for Crossject's various products as well as product approvals, which should start in earnest in H217.

Financials: Near-term funding secured

As of year-end 2015, Crossject had €5.2m in cash and cash equivalents on hand. The company expects to receive an additional €3.1m in grants in 2016 and recently announced an equity line, which could provide ~€10m. Between now and projected profitability in 2018, we predict a total capital need of €15m for Crossject. This requirement would be mitigated somewhat by additional upfront payments from partners as well as milestone payments upon product approvals.

Sensitivities: Commercialisation risk prevails

As Crossject is focusing on well characterised and approved generic drugs, there should be very little clinical risk, with only positive bioequivalence and device usability studies likely needed in healthy volunteers. The main risk will come on the commercialisation front, as Crossject is completely dependent upon partners to market the products. Also, Crossject is generally focused on areas that are heavily genericised with multiple dosage forms available. In the case of sumatriptan, there are oral, injectable (both with a needle and needle-free) and intranasal forms available. Making headway may be extremely difficult and will likely depend heavily on physician and patient preference. However, Crossject diversifies the commercialisation risks and its dependence on any single product by having a deep product pipeline, with the total cost of developing each product estimated to be in the €4-6m range per compound.

A productive platform

Crossject's proprietary needle-free injection platform, ZENEO, can be used for up to 200 drugs (both small molecule and biologic) that the company identified, although currently the company is focusing mainly on acute treatments (except for its methotrexate product for rheumatoid arthritis) where the speed of treatment is an important factor for patients.

Exhibit 1: Crossject pipeline

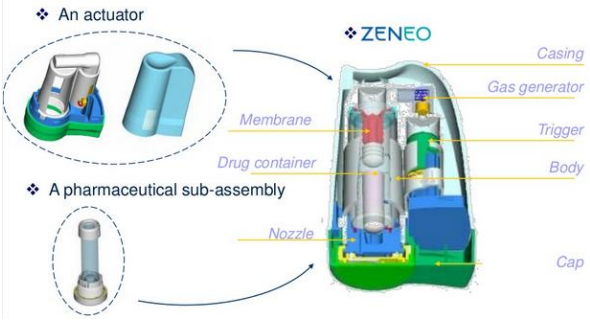
Drug	Indication	Potential commercial launch timing	Partners
ZENEO Methotrexate	Rheumatoid arthritis	H217	Biodim (France), Sayre (India), Xi'an Xintong (China)
ZENEO Sumatriptan	Acute migraine	H118	
ZENEO L15	Undisclosed	H118	
ZENEO Adrenaline	Anaphylactic shock	H218	Undisclosed (worldwide)
ZENEO Midazolam	Acute epileptic seizures	H218	
ZENEO Naloxone	Opioid overdose	H119	
ZENEO Apomorphine	Temporary paralysis associated with Parkinson's	H219	

Source: Crossject

Broadly, ZENEO offers a number of advantages over conventional syringes:

- Greater compliance, as ZENEO has been designed to reduce human factor risk on self-administration. For example, there is less risk of going too deep or not deep enough – just place and push down.
- A very fast ~1/10th of a second injection, instead of a possibly prolonged push on the needle. The pain related to injection is approximately the same though.
- Eliminates risk of needle injury during use and/or disposal. While there is no data on needle injuries among patients, the Centers for Disease Control (CDC) estimates that there are 385,000 needlestick injuries per year among hospital-based personnel alone.
- Avoids needle-phobia/aversion. The number of people with needle-phobia is unknown. Historically, 10%[1] of people were thought to be needle-phobic, however more recent data suggest an even higher prevalence. In a study of 400 travellers visiting a travel health clinic, 21.7%[2] indicated being afraid of injections. In a study of 177 patients at a general practice in Australia, 22.0% indicated a fear of needles and 20.5%[3] of those reported having fainted.
- In total, ZENEO allows for a very easy-to-use and simple injection process driving a greater acceptance of self-injection.

Exhibit 2: The ZENEO device



Source: Crossject

1 Hamilton J et al. Journal of Family Practice, 1995;41-169-75

2 Nir Y et al. American Journal of Tropical Medicine and Hygiene, 2003;68:341-4

3 Wright S et al. Australian Family Physician, 2009; Vol. 38, No. 3, March 2009

The device itself is disposable, pre-filled and single-use. It generally works in a similar fashion to other needle-free devices as it involves an energy source (gas), a volume of drug and a nozzle. However, unlike other systems, the gas to power the drug through the skin is generated at the time of injection through a controlled chemical process. This avoids the need for special storage and transportation of a pressurized system. Also, unlike certain other needle-free technologies, such as powder-based injection systems, no reformulation of the reference product is needed, making both clinical development and commercial manufacturing cheaper and easier. It is also adaptable to various product viscosities and can be discharged subcutaneously, intramuscularly or intradermally. The mechanism was adapted from air bag systems technology and can be manufactured in a mass and low-cost fashion. It is covered by 403 patents, with patent protection running into 2035.

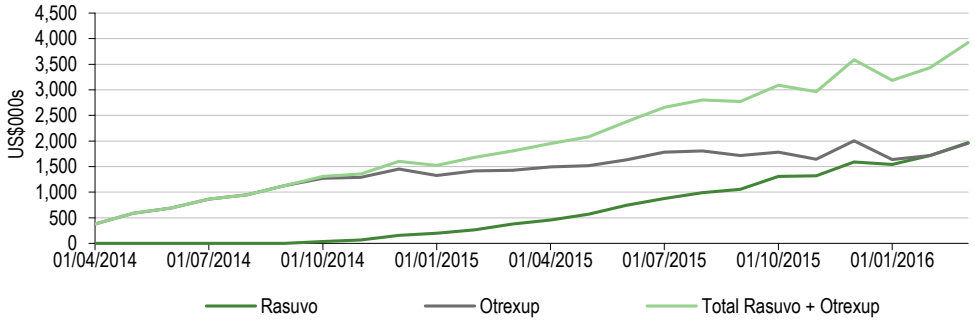
First commercial product: ZENEO Methotrexate for RA

RA is an auto-immune inflammatory arthritis that affects 1.3 million[4] adults in the United States. Internationally, the prevalence rate is between 0.4-1.3% according to the CDC. Methotrexate is generally recommended as the first-line therapy for these patients and comes in both oral and injectable forms. Although the vast majority of patients (~80%[5]) in the United States take the oral version, the injectable version has shown to have greater bioavailability and dose response than the oral version (oral methotrexate exposure plateaus at doses of 15mg and above) due to absorption issues that the injectable version bypasses.[6]

One of the problems with the traditional injectable version is the multistep process that had to happen before the patient could dose themselves. Patients had to gather multiple supplies (eg syringe, vial, alcohol swab for vial top cleaning, sharps container and potentially a bandage as well), prepare both the syringe and vial, draw the methotrexate, expel air from the syringe and only then inject themselves.

In order to help make injections more convenient and also less painful, two pre-filled disposable autoinjector versions were launched in 2014, Otrexup from Antares Pharma and Rasuvo from Medac Pharma. Antares reported 2015 US sales of $13.2m for Otrexup, while Medac, a private company, does not report sales but likely had ~$10m in sales in 2015 based on prescription data.

Exhibit 3: Monthly sales of Rasuvo and Otrexup (US$000s)



Source: Wolters Kluwer

Sales for Otrexup and Rasuvo have been modest (though currently approaching a combined $50m annualised rate) for three major reasons:

1. In order to get coverage for these autoinjectors, insurers typically ask patients to first try the traditional injectable version as part of step therapy.

4 Helmick C et al., Arthritis Rheumatology 2008 Jan;58(1):15-25

5 DiBenedetti et al., Rheumatology and Therapy 2015 June; Vol 2, Issue 1, pp 73-84

6 Schiff M et al., Annals of the Rheumatic Diseases 2014;0:1-3

2. The entire sales and marketing effort of Antares consists of only around 50 people in total while Medac's is estimated to be half that.
3. While traditional syringes are definitely inconvenient, in a study of 500 methotrexate oral and injectable users and treatment adherence,[7] complaints regarding injections were not listed, which could be a sign of low demand for alternative injection methods. In the study, people were non-compliant typically because they simply forgot, were feeling well, had safety concerns or suffered from side effects (see Exhibit 4).

Exhibit 4: Reasons for non-compliance to methotrexate therapy

	Percent responding
Forget or cannot remember	33
Do not need it when feeling well	24
Concern about long-term safety	24
Side effects	18
Costs	18
Can't drink alcohol	16
Too many lab visits	14
Doctor's recommendation	13
Take too many other medications	12
Does not treat arthritis symptoms well	10
Other	4

Source: DiBenedetti et al., Rheumatology and Therapy 2015 June; Vol 2, Issue 1, pp 73-84

Crossject will likely have to face similar hurdles as Antares and Medac, but would have one key marketing advantage of being needle free. We currently assume approval in the US in 2019 and in the EU in H217 (the company has already been able to demonstrate bioequivalence of its product to the injectable version) for the product with pricing of €100 (which is approximately in line with Otrexup pricing) and €20 per dose respectively. Peak sales are estimated at €82.2m in the US (2% peak penetration of the methotrexate market) and €17.8m in the EU (6% peak penetration of the methotrexate market). We assume greater penetration in the EU market as injectable methotrexate in general has garnered greater acceptance in that market, while in the US injectable methotrexate is only ~20% of the market. We are not currently modelling product sales outside the US and EU as there is little visibility in those markets, especially since patients typically will not be reimbursed for the use of ZENEO Methotrexate.

Unlike with Antares and Medac, we do not expect Crossject to market ZENEO Methotrexate by itself and the company has already signed local partnership deals with Biodim for France, with Sayre for India and with Xi'an Xintong for China. Crossject will receive €1m per pre-commercialisation milestone from Biodim and €3m for Chinese approval from Xi'an Xintong. Sayre milestones for India are unknown. For the United States, we expect a partner to pay a total of €2m upfront/approval and an additional €10m in commercial based milestones. For both the US and EU markets we have assumed a 20% royalty.

Treating migraines in minutes: ZENEO Sumatriptan

Migraines are a very common and debilitating ailment often lasting between four and 72 hours, with prevalence of around 13% in the US[8] and around 15%[9] in the EU, totalling over 100 million sufferers across the two regions. Sumatriptan was the first drug within the triptan class available for the treatment of migraines and has been the standard of care since. There are a number of different dosage forms available, including traditional injectable, needle-free, nasal, patch, oral tablet and oral melt (see Exhibit 5). The oral forms together dominate the market, accounting for over 95% of all doses according to Symphony Health. Injectable forms (both traditional and needle-

7 DiBenedetti et al., Rheumatology and Therapy 2015 June; Vol 2, Issue 1, pp 73-84

8 Victor T et al., Cephalgia 2010 Sep;30(9):1065-72

9 Stovner L et al., Journal of Headache Pain (2010) 11:289-299

free) are less than 3% of the market (around four million doses per year according to Symphony Health data) despite having a much faster onset of action, with migraine relief coming in a matter of minutes instead of a matter of hours.

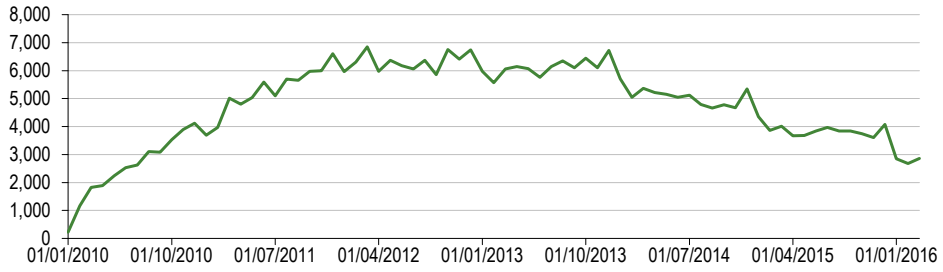
Exhibit 5: Triptan competitive landscape for migraine

Drug	Brand	Route of administration	Time to peak concentration (Tmax)	Relief at 1 hour	Relief at 2 hours
Sumatriptan	Sumavel DosePro	Needle-free	12 minutes	70%	81-82%
Sumatriptan	Imitrex	Autoinjector pen	12 minutes	70%	81-82%
Sumatriptan	Imitrex	Nasal	N/A	38-46%	43-64%
Zolmitriptan	Zomig	Nasal	3 hours	60%	69-70%
Sumatriptan	Zecuity	Patch	1.1 hours	N/A	53%
Zolmitriptan	Zomig-ZMT	Oral melting tablet	3 hours	33-43%	63%
Rizatriptan	Maxalt-ZMT	Oral melting tablet	1.6-2.5 hours	38-43%	59-74%
Sumatriptan	Imitrex	Oral	2-2.5 hours	28-36%	50-62%
Sumatriptan + naproxen sodium	Treximet	Oral	1 hour	28%	57-65%
Zolmitriptan	Zomig	Oral	1.5 hours	35-45%	59-67%
Rizatriptan	Maxalt-ZMT	Oral	1-1.5 hours	38-43%	60-77%
Naratriptan	Amerge	Oral	2-3 hours	19-21%	50-66%
Almotriptan	Axert	Oral	1-3 hours	32-36%	55-65%
Frovatriptan	Frova	Oral	2-4 hours	12%	37-46%
Eletriptan	Relpax	Oral	1.5 hours	20-30%	47-77%

Source: FDA, Zogenix

The needle-free version of sumatriptan currently on the market, Sumavel DosePro, was originally developed by Zogenix and has been approved since 2009. It was launched in January 2010 by both Zogenix and Astellas as part of a co-promotion agreement. Astellas terminated the agreement in 2012, but then Mallinckrodt took up the product with a similar arrangement, which ended in early 2014. Eventually, Endo purchased the programme outright for $85m in April 2014. As Endo does not break out Sumavel DosePro sales, the last firm data point we have is the $31.7m in sales that Zogenix reported for 2013. The product had been doing well while Astellas was promoting the drug, but then flattened out after changing hands to Mallinckrodt and is falling now that it is with Endo.

Exhibit 6: Sumavel DosePro total monthly prescriptions



Source: Wolters Kluwer

From the point of view of providing fast relief for migraines, injectable forms are superior to the other various forms. And based on the initial launch trajectory of Sumavel DosePro, there is a market for needle-free injection products, though their success will likely depend on a quality partner. We currently assume approval in the US and EU in 2018 for Crossject's ZENEO Sumatriptan with pricing of €100 (which is approximately in line with Sumavel DosePro pricing) and €25 per dose, respectively. Peak sales are estimated at €73.0m in the US (8% peak penetration of the injectable triptan market) and €8.8m in the EU (12% peak penetration of the injectable triptan market). Our estimates for injectable market penetration are conservative due to its competitive nature and the fact that there is already a needle-free option. We assume greater penetration in the EU due to the fact that Crossject is a European company. For both the US and EU we expect regional partnerships to help sell the products. For the US, we assume a €2m upfront/approval

milestone and an additional €4m in commercial milestones with a 20% royalty. For the EU, we assume a €2m upfront/approval milestone with a 20% royalty. As a reference, Astellas paid $2m upfront and another $18m in milestones in exchange for a service fee of 45-55% of net sales of Sumavel DosePro to physicians who were in the Astellas target market (primary care physicians, OB/GYNs, emergency physicians and urologists).

L15: The mystery programme

Crossject's next product, which is currently expected to be launched commercially in H118, is known as L15. It is an acute/emergency treatment product for a niche indication with 600,000 patients in both the US and EU. The company is guiding pricing of $100 in the US and €60 in Europe. Assuming an even split in the population between the US and EU, this is a potential ~$500m addressable market. We are currently not including L15 in our valuation given the lack of visibility, but will do so once Crossject defines the market and discloses the molecule that is included in the ZENEO device.

Breaking into the EpiPen market: ZENEO Adrenaline

An estimated 1.6%[10] of the US population has had an episode of anaphylactic shock (which could potentially be fatal), with allergic reactions to medication, food and insect stings being the most common reasons. This might be an underestimate as data suggests that just food allergy prevalence is 6% in children and 4% in adults.[11] Mylan currently dominates this market with its EpiPen product, which accounts for ~93% of prescriptions and had over $1.1bn in 2015 US sales.

A major issue with the EpiPen is that only a minority of patients and physicians know how to use it correctly. According to one study, just 18% of participants were able to perform all steps correctly (one of the major weaknesses being not keeping the EpiPen in place for the full 10 seconds recommended).[12] In another study, 32% of participants were able to, but only 18% of paediatricians were able to correctly demonstrate use of the device.[13]

In order to combat this, Sanofi launched Auvi-Q, an autoinjector that is voice-guided to help with compliance, in 2013. There was a manufacturing related recall in October 2015, but prior to this, it had achieved €113m in sales through the first nine months of 2015, up 52.4% on a constant currency basis over the prior year. This level of sales indicates that there is room in the market for a compliance and user friendly product, such as ZENEO Adrenaline, which is very easy to use and does not need to be held in place for 10 seconds as the product is injected in ~1/10th of a second.

Crossject currently has a worldwide commercial agreement with an undisclosed partner for this product. The partner will be responsible for all R&D expenses related to the product and will pay double-digit royalties and up to approximately $470m in milestones. Crossject received €1m upfront and will receive an additional €8m upon EMA and FDA approvals.

We currently assume approval in the US and EU in H218 for the product, with pricing of €100 (which is approximately half of EpiPen pricing) and €33 per dose, respectively. Peak sales are estimated at €127.3m in the US (8% peak penetration) and €5.8m in the EU (6% peak penetration). Our estimates are conservative due to the strength of the EpiPen brand, which has been able to withstand previous competitors. In terms of milestones, we model €8m upon EMA and FDA approvals (€3m and €5m respectively) and a further €10m in commercial milestones. We estimate royalties of 25% in the US and 20% in the EU, where the product will be less profitable to the partner.

10 Wood R. et al., The Journal of Allergy and Clinical Immunology 2014 Feb;133(2):461-7

11 Dreborg S. et al., Allergy, Asthma & Clinical Immunology (2016) 12:11

12 Sicherer S. et al., Journal of Pediatrics 2012 Apr;160(4):651-6

13 Sicherer S. et al., Journal of Pediatrics 2000 Feb;105(2):359-362

Helping to quickly stop epileptic seizures: ZENEO Midazolam

According to the Centers for Disease Control (CDC), 2.9 million people have active epilepsy in the United States. The prevalence of epilepsy in Europe is 3.4 million with 20-30% having more than one seizure per month.[14] The average seizure lasts less than two minutes[15] but the longer a seizure does last the harder it is to stop with treatment and the greater the likelihood of complications. For seizures lasting 10-29 minutes, only 43% cease without treatment and once they reach 30 minutes in length (officially known as status epilepticus), only 7% cease without treatment, with 19% of effected patients dying.[16]

Optimally, the patient would be treated at home as the trip to the hospital can waste very valuable time. However, only one at-home treatment is approved in the US, a rectal gel version of diazepam, which is part of the benzodiazepine class along with midazolam.

Exhibit 7: Profiles of acute treatments for epileptic seizures

	Time to response (in minutes)	Duration (in hours)
Lorazepam (iv)	3–10	12–24
Diazepam (rectal)	5–15	<1
Diazepam (iv)	1–5	<1
Midazolam (im)	5–10	<1
Midazolam (buccal)	5–10	<1
Midazolam (iv)	10–30	12–2
Phenytoin (iv)	10–30	12–24
Fosphenytoin (iv)	10–30	12–24
Phenobarbitone (iv)	5–30	48–72

Source: Cherian A. et al., Annals of Indian Academy of Neurology 2009 Jul-Sep; 12(3): 140-153

While rectal diazepam does work quickly (see Exhibit 7), it is not patient friendly as it involves injecting a liquid inside the rectum of a patient while they are having a seizure, which may be convulsive. Nevertheless, rectal diazepam achieved over $100m in sales before going generic in 2010.

In Europe, a buccal form of midazolam, known as Buccolam, is marketed by Shire. It is a liquid that needs to be inserted slowly into the space between the gum and cheek, again possibly not the most convenient way to administer a drug to someone with a convulsive seizure. According to EvaluatePharma, sales in 2015 were $18m, though Shire does not disclose sales specifically for that product, given its small size.

Crossject's ZENEO Midazolam should have a similar profile to intramuscular and buccal midazolam, with a 5-10 minute onset but short duration of action, ideal for home use. Given the quick and easy administration of midazolam via the ZENEO device, Crossject should have an advantage over the competition.

We currently assume approval in the US and EU in late 2018 for the product, with pricing of €100 and €25 per dose, respectively (approximately the average price of Buccolam in Europe). Peak sales are estimated at €50.8m in the US (8% peak penetration) and €6.8m in the EU (12% peak penetration). Our penetration estimates are conservative due to the competitive and genericised nature of the market. We believe Crossject will require a marketing partner in the different regions. In terms of milestones, we model €2m upfront/approval milestones for EMA and FDA approval and a further €4m in commercial milestones. We estimate royalties of 20% for both the US and EU.

14 Forsgren L. et al., European Journal of Neurology 2005 Apr;12(4)245-53

15 Alford E et al., Journal of Pediatric Pharmacology and Therapeutics 2015;20(4):260-289

16 DeLorenzo R. et al., Epilepsia 1999 Feb;40(2):164-9

ZENEO Naloxone and ZENEO Apomorphine

Crossject is also working on a needle-free naloxone, which is intended for the acute treatment of opioid overdose, and needle-free apomorphine, which reverses hypomobility ("off episodes") associated with Parkinson's disease (PD).

Naloxone is an opioid antagonist that is able to reduce the respiratory and mental depression due to opioids and hence can be very useful in saving lives when available. The need is clear; according to the Drug Abuse Warning Network, in 2011 there were 258,482 emergency room visits in the United States due to heroine and another 488,004 due to nonmedical use of prescription opioids.

Due to these numbers, naloxone kits are now available without prescription in 14 states (naloxone has no side effects in people without opioids in their system) and can usually be obtained for $20-40 per kit, which includes two doses. They are available in traditional intramuscular, intramuscular/subcutaneous auto-injector and intranasal forms, all of which work within 6-8 minutes of administration.

Apomorphine is a dopamine agonist and is used to treat/manage sudden and unexpected bouts of hypomobility associated with PD. According to the Parkinson's Disease Foundation the prevalence of Parkinson's is one million people in the United States, with 7-10 million people worldwide suffering from the disease. Once patients are on standard PD drug treatments for four to five years, they experience bouts of hypomobility, including the inability to rise from a chair, to speak or walk. Often these can be treated by changing their treatment regimen. However, according to BlueShield of Northeastern New York, approximately 12,000 patients have severe hypomobility that requires apomorphine, which reverses symptoms in 7-14 minutes. As a month's supply is typically ~$2,000/month, the addressable market approaches $300m per year in the United States alone.

As previously mentioned, we are not including ZENEO Naloxone or ZENEO Apomorphine in our valuation as they are currently not expected to reach the market until 2019 and there is little visibility as to their status. We will include these programmes in our valuation model once their advancement is announced by the company.

Sensitivities

As Crossject is focusing on well-characterised and approved generic drugs, there should be very little clinical risk for any one of its programmes. All that will likely be needed will be bioequivalence and device usability studies. The main risk will come on the commercialisation front as Crossject, at least at this point, is completely dependent upon partners to market the products and will need partners for each product in each region. Also, Crossject is generally focused on areas that are heavily genericised, with lots of different dosage forms for the product it is putting onto the ZENEO platform. In the case of sumatriptan, there are oral, injectable (both with a needle and needle-free) and intranasal forms available. Making headway may be extremely difficult and will likely depend heavily on simply physician and patient preference. Pricing/reimbursement will be another issue, as pricing outside the United States is likely to be challenging, leading to minimal market opportunity for its products. In the United States on the reimbursement front, Crossject products will likely be placed in "Tier 3" with higher co-pays and need for prior authorisation. This would limit the opportunity for its products. However, Crossject does not depend on any one of its products to be extremely successful in order for it to be successful as a company, due to its deep pipeline, with the total cost of developing each product estimated to be in the range of €4-6m per compound.

Valuation

Using a risk-adjusted NPV approach, we value the company at €81.1m or €11.96 per basic share (€82.8m or €11.18 per diluted share). We currently assign zero value to the L15 programme, as we have no knowledge of what the product is or what indication it is for. Also, we are not including the naloxone and apomorphine products as they are further out and visibility on them is limited. In addition, much of our valuation is dependent upon successful launches in the US as pricing is often a fraction of the US value in Europe and in the rest of the world. We assume 60% probabilities of success. Clinical risk is low as Crossject is simply taking a well-characterised generic molecule that is already given intramuscularly or subcutaneously and using propulsion instead of a physical needle to get beneath the skin. However, commercial risk is greater due to the need for the right partner, who would need to have a large enough salesforce focused on the indication that Crossject is targeting (~100-200 salespeople in the US for a speciality indication and ~1,000 for a more generalised indication). Potential catalysts will likely include the announcement of additional partnerships for the various products as well as product approvals, which should start in earnest within the developed countries in H217.

Exhibit 8: Crossject valuation table

Product	Main Indication	Prob. of success	Launch year	WW Peak sales (€m)	Patent protection	Royalty	rNPV (€m)
Methotrexate	Rheumatoid Arthritis	60%	2017	€100	2034	20%	€18.4
Sumatriptan	Acute Migraine	60%	2018	€82	2034	20%	€14.1
Adrenaline	Anaphylactic shock	60%	2018	€133	2034	25% US/20% EU	€36.3
Midazolam	Acute epileptic seizures	60%	2018	€58	2034	20%	€8.3
Total							€77.2
Cash and cash equivalents (Q116e) (€m)							€3.96
Total firm value (€m)							**€81.14**
Total basic shares (m)							6.78
Value per basic share (€)							**€11.96**
Stock options (3/2016e, m)							0.62
Weighted average exercise price (€)							€2.68
Cash on exercise (€m)							€1.67
Total firm value (€m)							**€82.81**
Total number of shares							7.4
Diluted value per share (€)							**€11.18**

Source: Edison Investment Research

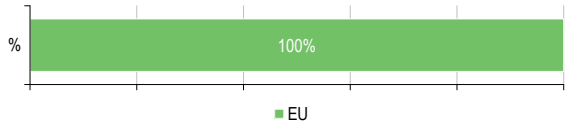
Financials

As of year-end 2015, Crossject had €5.2m in cash and cash equivalents on hand. The company expects to receive an additional €3.1m in grants in 2016 and recently announced an equity line from Kepler Cheuvreux, which could provide ~€10m. The terms are that Kepler Cheuvreux has committed to subscribe over the next 24 months to a maximum of 1.2m shares at a 7% discount. Between now and expected profitability in 2018, we project a total funding need of €15m for Crossject and have modelled this via an illustrative long-term debt. This need would be mitigated somewhat by additional upfront payments from partners as well as milestone payments upon product approvals. We expect €9m total in R&D expenses in 2016 and 2017 and an additional €9m in SG&A.

Exhibit 9: Financial summary

€000s	2014	2015	2016e	2017e	2018e
Year end 31 December	French GAAP	French GAAP	French GAAP	French GAAP	French GAAP
PROFIT & LOSS					
Revenue	1,744	2,370	3,100	3,000	14,309
Cost of Sales	0	(0)	0	0	0
Gross Profit	1,744	2,369	3,100	3,000	14,309
R&D Expenses	(2,421)	(3,077)	(2,921)	(6,000)	(6,600)
SG&A and Other Expenses	(3,388)	(4,808)	(4,354)	(4,702)	(6,079)
EBITDA	(4,066)	(5,516)	(4,175)	(7,702)	1,630
Operating Profit (before GW and except.)	(5,108)	(7,013)	(4,175)	(7,702)	1,630
Intangible Amortisation	0	0	0	0	0
Other	(0)	0	0	0	0
Exceptionals	0	0	0	0	0
Operating Profit	(5,108)	(7,013)	(4,175)	(7,702)	1,630
Net Interest	(36)	(19)	(400)	(1,200)	(1,199)
Other	(160)	299	0	0	0
Profit Before Tax (norm)	(5,334)	(6,720)	(4,575)	(8,902)	431
Profit Before Tax (FRS 3)	(5,304)	(6,732)	(4,575)	(8,902)	431
Tax	968	1,045	876	1,800	1,980
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(4,366)	(5,675)	(3,699)	(7,102)	2,411
Profit After Tax (FRS 3)	(4,336)	(5,687)	(3,699)	(7,102)	2,411
Average Number of Shares Outstanding (m)	6.7	6.7	6.9	7.3	7.6
EPS - normalised (€)	(0.66)	(0.85)	(0.53)	(0.97)	0.32
EPS - FRS 3 (€)	(0.65)	(0.86)	(0.53)	(0.97)	0.32
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	5,521	5,936	7,521	8,726	9,642
Intangible Assets	2,327	2,330	2,330	2,330	2,330
Tangible Assets	888	1,727	3,313	4,518	5,433
Other	2,305	1,878	1,878	1,878	1,878
Current Assets	12,853	7,943	7,672	9,365	10,860
Stocks	0	761	761	761	761
Debtors	1,926	1,991	1,991	1,991	1,991
Cash	10,927	5,139	4,867	6,560	8,056
Other	0	52	52	52	52
Current Liabilities	(2,907)	(3,261)	(3,261)	(3,261)	(3,261)
Creditors	(2,907)	(3,261)	(3,261)	(3,261)	(3,261)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(982)	(1,820)	(6,820)	(16,820)	(16,820)
Long term borrowings	0	0	(5,000)	(15,000)	(15,000)
Other long term liabilities	(982)	(1,820)	(1,820)	(1,820)	(1,820)
Net Assets	14,484	8,797	5,112	(1,991)	421
CASH FLOW					
Operating Cash Flow	(3,163)	(4,796)	(3,285)	(6,307)	3,495
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(4,770)	(1,805)	(2,000)	(2,000)	(2,000)
Acquisitions/disposals	0	0	0	0	0
Financing	17,873	0	0	0	0
Dividends	0	0	0	0	0
Other	0	483	0	0	0
Net Cash Flow	9,940	(6,118)	(5,285)	(8,307)	1,495
Opening net debt/(cash)	(2,468)	(10,927)	(5,139)	133	8,440
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	0	0	0	0	0
Other	(1,481)	330	13	0	0
Closing net debt/(cash)	(10,927)	(5,139)	133	8,440	6,944

Source: Company accounts, Edison Investment Research

Contact details	Revenue by geography
Crossject 60L avenue du 14 Juillet 21300 Chenove France 03 80 54 98 50 www.crossject.com	

Management team

CEO: Patrick Alexandre	Chief Business Officer: Tim Muller
Patrick Alexandre is a co-founder of the company. He has been the driving force in the development of Crossject's technology since its inception 1997 when it was a research effort at Fournier Laboratoires. He has over 15 years' experience in the pharmaceutical industry. He also has 10 years' industrial R&D experience in the steel industry and graduated as an engineer from Supelec.	Tim Muller has been CBO since 2012. He is responsible for partnering and business development. His career also includes being the founding CEO of Scientex, a healthcare dedicated transition management company. Prior to Scientex, Tim worked at both CDC group and Sofimac Partners as a venture capitalist between 1999 and 2006.
Head of Pharmaceutical Projects: Xavière Castano	**Head of Engineering: Xavier Vigot**
Xavière Castano is a co-founder of Crossject, where she has been responsible for building and managing the company's research development and validation laboratory. She graduated as a pharmacist from the University of Lyon and is also a qualified engineer specialising in materials.	Xavier Vigot joined the company in 2013 and since then he has been responsible for driving the technical and industrial development of ZENEO. He has 20 years of experience in mechanical engineering in various companies in consumer and automotive industries, including five years as head of mechanical engineering at TRW. He graduated as a mechanical engineer from the Ecole Nationale Supérieure de Micromécanique et Microtechnique (Besançon).

Principal shareholders	(%)
Gemmes Venture	21.54
A Plus Finance	10.55
IDEB	5.61
Sofigexi	4.68
Sofimac	3.96
Crossject Investment Partners	2.63
La Banque Postale Asset Management	2.55

Companies named in this report

Abbott (ABT), Antares (ATRS), Zogenix (ZGNX), Astellas (4503), Mallinckrodt (MNK), Endo (ENDP), Mylan (MYL), Sanofi (SNY), Shire (SHPG)

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