EDISON

Creo Medical

Initiation of coverage

Providing energy for endoscopic surgery

Healthcare equipment & services

We are initiating coverage of Creo Medical, which is developing and commercialising minimally invasive electrosurgical devices. Its CROMA platform delivers a combination of bi-polar radiofrequency (RF) and microwave energy for the purpose of dissection, resection, ablation and haemostasis of diseased tissue. The initial focus will be on gastrointestinal (GI) procedures but will expand into soft tissues (such as the pancreas) and pulmonology. The company has had all six products within the CROMA platform CE marked and four are also cleared for use by the FDA, with the other two expected to be cleared in the coming months.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/19	0.0	(18.6)	(13.1)	0.0	N/A	N/A
12/20	9.4	(23.0)	(12.7)	0.0	N/A	N/A
12/21e	25.9	(22.7)	(12.3)	0.0	N/A	N/A
12/22e	28.4	(24.4)	(13.3)	0.0	N/A	N/A

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

Allowing for quicker and safer procedures

Creo Medical's flagship Speedboat product allows for incision, dissection and coagulation to be accomplished with one device, leading to more efficient use of the surgeon's time as there is less switching of instruments. With bi-polar RF, the current is restricted to a specific area, which should help reduce complications compared to monopolar RF, which drives energy across relatively large areas.

A large addressable market

Creo Medical products are in a large and lucrative market. Conmed estimates the GI endoscopic technologies market is approximately $3.0–3.2bn with the RF energy-based surgical device market at $2.7–2.9bn per year.

Albyn acquisition provides products and a salesforce

In July 2020, Creo Medical announced the acquisition of Albyn Medical, which commercialises products for the urology, gynaecology and GI endoscopy markets. Albyn Medical was purchased for €24.8m plus up to €2.7m in performance-related milestones. While full year revenues have not been disclosed, Albyn Medical was profitable with €1.7m in profit before tax (PBT) for FY19 and contributed £12.8m in sales to Creo in H121. Importantly, with this acquisition, Creo has also acquired Albyn Medical's 70-person European sales and marketing team.

Valuation: £434m or 240p per basic share

We value Creo Medical at £434m or 240p per basic share using a risk-adjusted net present value (NPV) model. The vast majority of the value is attributable to the CROMA platform (especially the GI market) with the remainder divided between the value of Albyn Medical and net cash. Creo Medical had reported that it had £30.6m in cash and £10.7m in debt at the end of H121 and raised £36.3m in gross proceeds in a Q321 placement and open offer.

4 October 2021

Price	**171.5p**
Market cap	**£310m**

Net cash (£m) at 30 June 2021 + offering	56.1
Shares in issue	180.9m
Free float	75.9%
Code	CREO
Primary exchange	AIM
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(6.0)	(13.7)	2.2
Rel (local)	(3.7)	(13.0)	(16.5)
52-week high/low		234p	144p

Business description

Creo Medical is a UK-based healthcare company focusing on the development and commercialisation of minimally invasive electrosurgical devices. It has six products in the flagship CROMA platform, all of which have been CE marked and four of which have been cleared by the FDA. The company recently acquired Albyn Medical, which provides it with profitable products and a direct sales force in Europe.

Next events

Update on commercial launch	2021

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Edison profile page

Creo Medical is a research client of Edison Investment Research Limited

Investment summary

Creo Medical is a UK-based medical device company that was founded in 2003 and went public in 2016 on the AIM market. It is focused on the development and commercialisation of minimally invasive electrosurgical devices for a variety of indications in the GI, soft tissue and pulmonological areas. Its CROMA platform delivers a combination of bi-polar RF and microwave energy for the purpose of dissection, resection, ablation and haemostasis of diseased tissue. Products include the Speedboat Inject, Speedboat Slim, SpydrBlade Flex, SlypSeal Flex, MicroBlate Fine and MIcroBlate Flex. All six products have been CE marked and four are also cleared for use by the FDA, with the remainder expected to be cleared in the coming months. In July 2020, Creo Medical announced the acquisition of Albyn Medical, which commercialises products for the urology, gynaecology and GI endoscopy markets. Albyn Medical was purchased for €24.8m plus up to €2.7m in performance related milestones. With this acquisition, besides acquiring profitable products, Creo has also acquired Albyn Medical's 70-person strong EU sales and marketing team.

Valuation: £434m or 240p per basic share

We value Creo Medical at £434m or 240p per basic share using a risk-adjusted NPV model utilizing a 12.5% discount rate on the CROMA platform products and a 10% discount rate for Albyn Medical products (as they are more mature). Approximately 75% of the value is attributable to the CROMA platform (focused on the GI market) with the remainder divided between the value of Albyn Medical and net cash. We attribute a 70% probability of success for the CROMA platform as it is still in the early phases of adoption. We forecast that sales will start to mature in 2026, when we expect revenues for the platform to hit £347m, with £205m coming from the US. We will adjust our assumptions as we are further updated on the progress of commercialisation.

Financials: Well capitalised

The company reported that it had £30.6m in cash and £10.7m in debt as of 30 June 2021 with £12.9m in sales for H121, nearly all of which was attributable to Albyn Medical. The company raised £36.3m in gross proceeds in a Q321 placement and open offer and we project a financing need of an additional £30m before profitability (£10m in 2022 and £20m in 2023), which we expect in 2025. Sales have been minimal historically, but that has changed with the inclusion of Albyn Medical sales and we expect will increase further with the expected penetration of CROMA products.

Sensitivities: Commercialisation risk dominates

Although Creo's products are unique in their use of bi-polar RF and other design elements, the competitive landscape in GI endoscopy and energy products is crowded with a large number of large and legacy players. Even with a better device, it is not an easy to convince surgeons to switch brands or move to a new type of procedure. One of the focus procedures for Creo is endoscopic submucosal dissection (ESD), which has gained limited traction in the US mainly because of generally longer procedure times and somewhat higher adverse events (although Creo's products address both), despite better outcomes from patients versus the standard of care. Creo Medical may need to meaningfully increase its investment in US sales and marketing to gain significant penetration. This can be done organically or through acquisition, as Creo has done with its Albyn Medical purchase. Reimbursement may also be an issue as there is no separate payment for use of Creo products and they are bundled into a total payment for the entire procedure. Gaining reimbursement will likely make adoption easier as financial considerations often dominate in the US healthcare industry.

Company description: Innovative medical devices

Creo Medical is a UK-based medical device company focused on the development and commercialisation of minimally invasive electrosurgical devices for a variety of indications in the GI, soft tissue and pulmonological areas.

Exhibit 1: The CROMA Advanced Energy Platform

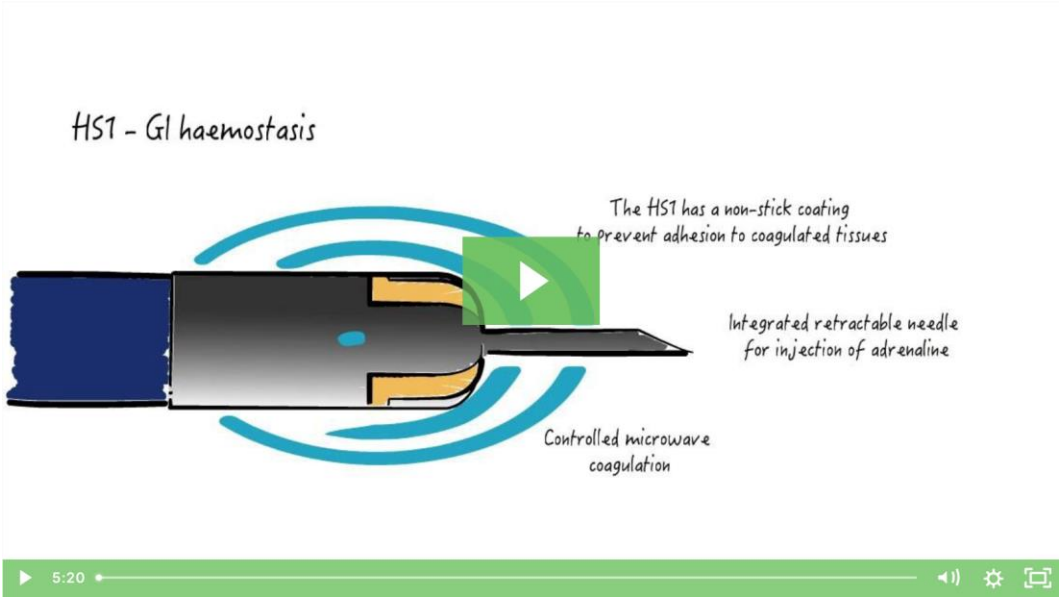
Source: Creo Medical

Exhibit 2: Creo's suite of products

Source: Creo Medical

Its CROMA platform is at the heart of the company's surgical products and delivers a combination of bi-polar RF (while use of RF in endoscopic procedures is common, it is usually delivered as monopolar RF; Creo appears to be unique in using bi-polar RF in its stated target indications), which is used for endoscopic cutting, resection and dissection, and microwave energy, for coagulation and ablation. Products using the CROMA platform include the Speedboat Inject, Speedboat Slim, SpydrBlade Flex, SlypSeal Flex, MicroBlate Fine and MIcroBlate Flex.

Exhibit 3: Video of Creo's products and what they do



Source: Creo Medical

All six products have been CE marked and four of them are also cleared for use by the FDA via the 510(k) pathway, with the other two expected to be cleared in the coming months.

Exhibit 4: Description of Creo Medical's products

Product	Description	Indications	Availability	Comments
Speedboat Inject	Flagship product. Multimodal bipolar RF and focused microwave energy blade antenna with an integrated needle injection capability. Enabling surgeons to lift tissue with a retractable needle, cut tissue using bipolar RF energy delivered along the edge of the instrument for localised energy transfer, reducing the adverse events associated with monopolar tissue resection, and deliver high frequency controlled and focused coagulation, all within a single instrument.	Dissection of pre-cancerous and cancerous lesions in the lower and upper GI tracts	US, EU/UK, India, South Africa, Australia, New Zealand	CE marked for lower GI tract use, FDA clearance in both upper and lower GI tract. Commercially launched October 2019
Speedboat Slim	Similar to Speedboat Inject except has a narrower diameter of 3.2mm to allow use in narrower and more flexible scopes.	Dissection of pre-cancerous and cancerous lesions in the lower and upper GI tracts	EU/UK	CE marked in EU
MicroBlate Fine	Microwave needle ablation device designed to same form and dimensions as a standard biopsy needle. Has a diameter of less than 1mm (likely the smallest diameter for a microwave ablation device) allowing the ablation of tumours in a wide range of tissue types.	Ablation of soft tissue such as pancreas, liver, kidney, lung and muscle	US, EU/UK	CE marked in the EU and FDA clearance in the US since October 2020
MicroBlate Flex	Flexible version of MicroBlate fine for use when a flexible device is needed for access. May be particularly useful to treat nasopharyngeal cancer and nasal polyps.	Ablation of soft tissue such as pancreas, liver, kidney, lung, muscle as well as nasal indications	US, EU/UK	CE marked in the EU and FDA clearance in the US since January 2021
SlypSeal Flex	Flexible microwave haemostasis device designed for treatment of bleeds in the GI tract, such as stomach ulcers and bleeding polyps. Non-stick feature lowers risk of re-bleeds.	Haemostasis in the GI tract	US, EU/UK	CE marked in EU and FDA clearance in the US since March 2020
SpydrBlade Flex	Flexible bi-polar RF and microwave scissor device for grasping, cutting and coagulating highly perfused tissue.	Highly perfused tissue in the colon, stomach, liver and spleen, among other areas	EU/UK	CE marked in EU

Source: Creo Medical

Initial focus on the GI Endoscopy market

Although the company's approvals span a variety of indications and organs the initial commercial focus will mainly be in the GI endoscopy market, which is what the Speedboat products, with the first launch in Q419, are approved for. And within the GI endoscopic market, the focus of the company is to increase penetration within the ESD and peroral endoscopic myotomy (POEM) procedures.

ESD is a relatively new up-and-coming outpatient procedure (most patients go home the same day) to remove early-stage cancerous tumours or polyps from the GI tract. A typical ESD procedure involves marking the perimeter of the lesion, use of a lifting agent around the perimeter of the lesion, the mucosa around the lesion is cut, the submucosa beneath the lesion is dissected and any intraprocedural bleeding is managed with a water jet and haemostatic devices.

Historically, endoscopic mucosal resection (EMR) procedures have been the most used technique for removing early-stage tumours and polyps in the GI tract but it has difficulty in reducing adenomas larger than 2cm.[1] Meta-analysis comparing the procedures indicate that ESD has a much higher rate of en bloc resection (where the entire tumour is taken out) than EMR, 91.7% versus 46.7%, respectively. Additionally, the rate of recurrence is much lower in patients who receive ESD at only 0.9% versus the 12.2% recurrence rate for patients receiving EMR.

Two aspects of the procedure although have limited adoption despite the higher rates of efficacy. First, the procedure time is much longer than EMR, with EMR generally taking 30 minutes on average while ESD can take between one and two hours[2] likely due to the need for precision as

1 Backes et al., Endoscopic mucosal resection (EMR) versus endoscopic submucosal dissection (ESD) for resection of large distal non-pedunculated colorectal adenomas (MATILDA-trial): rationale and design of a multicenter randomized clinical trial. *BMC Gastroenterology* (2016) 16:56

2 Fujiya et al., Efficacy and adverse events of EMR and endoscopic submucosal dissection for the treatment of colon neoplasms: a meta-analysis of studies comparing EMR and endoscopic submucosal dissection. *Gastrointestinal Endoscopy* 2015;81(3):583–95.

well as the need for frequent instrument changes.[3] The extra time is generally worth it for the patient but financial considerations at hospitals and outpatient surgical centres (time per procedure is higher due to the longer procedure time and a surgeon can perform fewer per day, affecting revenue) make this a more difficult sell. That said, an ESD is still significantly cheaper than more traditional surgical colectomy (€3190 vs €8,490).[4]

Complication rates are also higher with ESD procedures, with a perforation rate of 5.7% versus 1.4% for EMR[5] although most perforations are small and can be identified/treated during the procedure using a clip.[6] Procedures to treat distal colorectal cancers (involving the descending colon, sigmoid colon, rectosigmoid and rectum) appear to have fewer perforations that proximal colon cancers (involving the cecum, ascending colon and transverse colon).[7] There is also a higher bleeding risk of 4.8–5.7% compared to 0.9–1.4% for EMR.[8]

Creo Medical's Speedboat can help with both drawbacks of the ESD procedure, which may increase its use. It uses a bipolar RF energy blade, while typically commonly used ESD cutting instruments use monopolar RF. Monopolar RF knives use significantly higher voltages and direct current and heat across the bowel wall, increasing the risk of injury. With the Speedboat, the current is restricted to a specific area, which should help reduce complications[9]. Also, as the Speedboat incorporates cutting, coagulation and fluid injection devices in one product, procedure times are shorter due to less frequent instrument changes.

With regards to the market size, there are approximately 19m colonoscopies performed annually in the United States with approximately 1.5m procedures performed on US Centers for Medicare & Medicaid Services (CMS) patients that involve removal of polyps, growths or tissue from the large bowel, according to the federal agency. As these numbers are just for Medicare and Medicaid patients, the total number of procedures such as these performed in the US is likely double. While the incidence of new cases of colorectal cancer are approximately 150,000 per year, a large number of people have polyps or adenomas. Adenomas are found in 20–53% of the US population over the age of 50 (approximately 33 million to 62 million people in the US alone).[10]

The Speedboat is also being used in POEM procedures, a minimally invasive procedure for the treatment of achalasia, an incurable condition that is marked by a failure of the smooth muscle fibres to relax, impairing a patient's ability to squeeze food down into the stomach, causing an inability to swallow, regurgitation/vomiting, heartburn, gas, chest pain and progressive weight loss. Achalasia can happen at various points along the GI tract such as the myoenteric plexus of the

3 Tsiamoulos et al., A novel multimodality endoscopic device for colonic submucosal dissection using a combination of bipolar radiofrequency and microwave modalities. Endoscopy 2016; 48: 271–276

4 Dahan et al., What is the cost of endoscopic submucosal dissection (ESD)? A medico-economic study. *United European Gastroenterology Journal* 0(0) 1–8

5 Backes et al., Endoscopic mucosal resection (EMR) versus endoscopic submucosal dissection (ESD) for resection of large distal non-pedunculated colorectal adenomas (MATILDA-trial): rationale and design of a multicenter randomized clinical trial. *BMC Gastroenterology* (2016) 16:56

6 Fukami, Surgery Versus Endoscopic Mucosal Resection Versus Endoscopic Submucosal Dissection for Large Polyps Making Sense of When to Use Which Approach. *Gastrointestinal Endoscopy Clinics* (2019) 675–685

7 Backes et al., Endoscopic mucosal resection (EMR) versus endoscopic submucosal dissection (ESD) for resection of large distal non-pedunculated colorectal adenomas (MATILDA-trial): rationale and design of a multicenter randomized clinical trial. *BMC Gastroenterology* (2016) 16:56

8 Fukami, Surgery Versus Endoscopic Mucosal Resection Versus Endoscopic Submucosal Dissection for Large Polyps Making Sense of When to Use Which Approach. *Gastrointestinal Endoscopy Clinics* (2019) 675–685

9 Tsiamoulos et al., A novel multimodality endoscopic device for colonic submucosal dissection using a combination of bipolar radiofrequency and microwave modalities. Endoscopy 2016; 48: 271–276

10 Strum, Colorectal Adenomas, *NEJM* 2016;374:1065-75.

oesophagus, lower oesophageal sphincter, the vagal trunks and the dorsal vagal nucleus.[11] Prevalence of the condition appears to be around 10.82 per 100,000, which would indicate around 36,000 cases in the United States.[12]

Historically, this condition was treated with non-surgical approaches including Botox, balloons and pharmacologic therapy (muscle relaxants). Each of these have significant weaknesses. Botox tends to not have a long-lasting impact on the condition. Symptomatic improvement is 78.6% at one month but then degrades to 40.6% at one year. A second treatment is required in 46.6% of patients.[13]. Endoscopic balloon dilation (EBD) has a similar issue, although it is typically more efficacious. Symptom relief has been shown to be 84.8% at month one and 68.2% at one year with 25% of patients requiring subsequent dilations. This procedure also has some side effects such as a 1.6% risk of perforation as well as a significant increase in heartburn episodes (approximately one-third of patients studied).[14]

Pharmacologic agents such as nitrates have been used but efficacy tends to be of very short duration (as low as 30 minutes) and have a high incidence of headache and hypotension. Calcium channel blockers have also been used with some efficacy in 50–90% of patients. However, up to 30% of patients experience significant side effects such as peripheral oedema and headaches.[15] Pharmaceutical agents are only typically used in mild disease and when more invasive procedures are inappropriate.

There have been a variety of different surgical approaches used, with laparoscopic myotomy being most popular. 89.3% of laparoscopic myotomy procedures in patients with achalasia were successful. In total, 6.9% of patients treated with this procedure have had perforations, with another 6.3% having further complications. As with EBD, there can be a significant number of heartburn episodes (31.5% without an anti-reflux procedure and 8.8% when this preventative procedure is conducted).[16]

POEM procedures, unlike ESD (but similar to laparoscopic myotomy), is performed under general anaesthesia and requires a hospital stay (median of one day[17]). In the procedure a flexible scope is inserted through the mouth to avoid cutting the chest or abdomen. It involves a submucosal injection of saline to create a mucosal bulge, followed by a cut to the oesophageal mucosa. Then a submucosal tunnel is made followed by dissection of submucosal fibres to weaken the sphincter so that food may pass. The success rate of 91.5% at two months and 88.5% at three years is comparable to laparoscopic myotomy.[18] However, procedure length tends to be shorter than for

11 Campos et al., Endoscopic and Surgical Treatments for Achalasia: A Systematic Review and Meta-Analysis. *Annals of Surgery*, Volume 249, Number 1, January 2009

12 Sadowski et al., Achalasia: incidence, prevalence and survival. A population-based study. *Neurogastroenterology and Motility* (2010) 22, e256–e261

13 Nassri et al., Pharmacotherapy for the management of achalasia: Current status, challenges and future directions. *World Journal of Gastrointestinal Pharmacology and Therapeutics* 2015 November 6; 6(4): 145-155

14 Campos et al., Endoscopic and Surgical Treatments for Achalasia: A Systematic Review and Meta-Analysis. *Annals of Surgery*, Volume 249, Number 1, January 2009

15 Nassri et al., Pharmacotherapy for the management of achalasia: Current status, challenges and future directions. *World Journal of Gastrointestinal Pharmacology and Therapeutics* 2015 November 6; 6(4): 145-155

16 Campos et al., Endoscopic and Surgical Treatments for Achalasia: A Systematic Review and Meta-Analysis. *Annals of Surgery*, Volume 249, Number 1, January 2009

17 Ashrava et al., Per oral endoscopic myotomy: early experience and safety of a multispecialty approach. *Surgical Endoscopy* 2018 Jul;32(7):3357-3363

18 Inoue et al., Per-Oral Endoscopic Myotomy: A Series of 500 Patients. *Journal of the American College of Surgeons* 2015;221:256e264

laparoscopic myotomy (120 minutes versus 149 minutes) and hospitalisation tends to be shorter (one day versus two days). Complications of the procedure are broadly similar.[19]

Use of Speedboat in POEM procedures has similar benefits to use in ESD, reduced procedure time due to less need to switch instruments and less risk of injury through the use of bipolar RF.[20] Procedure durations are usually around an hour and some of the procedures can be completed in as little as 25 minutes.[21] As procedure times can be a major component of a decision whether to use a certain approach, we would expect both Speedboat use in POEM procedures and the overall share of POEM of the achalasia market to increase.

Commercial penetration assumptions

Our assumptions are focused on the market for ESD procedures as POEM procedures are treating a relatively niche market with generally poor data sources. As mentioned, there are approximately 19m colonoscopies performed annually in the United States, with approximately 1.5m procedures performed on US CMS patients that involve removal of polyps, growths or tissue from the large bowel, according to the federal agency. As the median age of people who receive EMR and ESD procedures is around retirement age,[22] the total number of procedures such as these in the US is likely double that, at around 3m per year.

We do not have these data for the other major markets but assume a per-capita reduction of 40% in the EU and Japan as they typically perform fewer colonoscopies.[23] We assume peak penetration of around 9% as although Speedboat has advantages, ESD will be one of several potential approaches. Additionally, following discussions with the company and in reviewing the market environment, we assume Creo Medical will book approximately £730 per procedure. There is also a fee for the CROMA energy platform device (approximately £22,000) but the future economics are uncertain. Often medical device companies will give these types of permanent-use devices away for free or for nominal amounts to accelerate penetration of their single-use devices (such as Speedboat). Based on these assumptions, our 2026 sales estimate (which is when we forecast the products reaching maturity) is £347m for the US, EU/UK and Japan (representing approximately 475,000 procedures). Any sales outside these regions would provide upside to our estimates. Note that achieving these estimates would likely require significant additional investment in the US sales and marketing team (as assumed in our model) to drive growth in that important market among gastroenterologists.

To give a reference point for this peak sales estimate, Conmed, a major surgical device supplier, estimates the GI endoscopic technologies market is approximately $3.0–3.2bn with the RF energy-based surgical device market valued at $2.7–2.9bn per year.

Additionally, Creo Medical has a vast patent portfolio. As of 31 December 2019, it had 188 granted patents and another 599 pending applications around the world. With this in mind, we are modelling patent protection until 2040.

19 Bhayani et al., A Comparative Study on Comprehensive, Objective Outcomes of Laparoscopic Heller Myotomy With Per-Oral Endoscopic Myotomy (POEM) for Achalasia. *Annals of Surgery* Volume 259, Number 6, June 2014

20 Patil et al., Feasibility of Speedboat RS2 with bipolar radiofrequency energy for peroral endoscopic myotomy in patients with achalasia. *Endoscopy International Open* 2020; 08: E998–E1001

21 Nabi et al., Endoscopic submucosal dissection and tunneling procedures using a novel all-in-one bipolar device. *Endoscopy International Open* 2020; 08: E1302–E1307

22 Choi et al., Safety and effectiveness of endoscopic mucosal resection or endoscopic submucosal dissection for gastric neoplasia within 2 days' hospital stay. *Medicine* (2019) 98:32(e16578)

23 Audibert et al., Global perspective on colonoscopy use for colorectal cancer screening: A multi-country survey of practicing colonoscopists. *Contemporary Clinical Trials Communications*, 7 (2017), 116–121

The opportunity outside GI

Outside of the GI space, Creo Medical has also stated an intention of expansion into lung and pancreatic cancers among others. However, these are much more niche markets because colorectal cancer screening guidelines are quite broad and include all adults aged 50–75 years in the United States. For lung cancer, the guidelines only recommend screening for people with a history of smoking at least 20 packs per year or more, who are current smokers or have smoked in the last 15 years and are aged 50–80 years. There are no guidelines for pancreatic cancer screening. Less screening means fewer growths and polyps discovered, functionally reducing the size of the market.

For lung cancer, the total potential screening population is around 15 million[24] people compared to 83–85 million for colorectal cancer.[25] The current screening standard is low-dose computed tomography (LDCT), which effectively takes x-rays of the chest to detect lesions. The big issue with LDCT is that there is a dose of radiation involved, which in itself may increase the incidence of lung cancer. The typical dose of radiation is 2 millisieverts (mSv), which is equivalent to 243 days of natural background radiation. Follow-up exams, such as full chest CT, would involve a typical dose of 8mSv or 2.7 years of natural background radiation. Over time and if repeated this would lead to unnecessary cumulative radiation exposure greater than that of nuclear industry workers and atomic bomb survivors.[26] Another issue with LDCT is that as an imaging technology, even skilled readers can miss a 3mm (or smaller) nodule. Due to this and other reasons, only about 14.4% of the eligible population is generally screened[27] (note that this percentage estimate is based on older and more restrictive 2013 guidelines whereas the screening criteria was recently significantly expanded in March 2021). This has a knock-on effect that once the cancer is detected, it has likely already progressed past the point of surgical intervention. According to the National Cancer Institute, only 18% of lung cancer at diagnosis is at the localised stage, where surgery would be most effective (as compared to 37% of colorectal cancers). We estimate approximately 20,000–40,000 surgical procedures for lung cancer per year.

Unlike colorectal and lung cancer, there are no official screening guidelines for pancreatic cancer. According to the consensus reached at the International Cancer of the Pancreas Screening Consortium summit, screening is not recommended for the general population, instead focusing on those with first-degree relatives (parents, siblings and offspring) with pancreatic cancer, a very limited segment of the population. Those with two first-degree relatives with pancreatic cancer have a 6.4-fold greater risk of pancreatic cancer (8–12% lifetime risk) than the general population. Those with three or more first-degree relatives with pancreatic cancer have a 32-fold greater risk (40% lifetime risk).[28] Gene testing can provide a signal of risk as well but it is thought it is of limited use at the moment as the genetic basis for susceptibility to pancreatic cancer is unclear.

Endoscopic ultrasound is generally the procedure performed to screen patients for pancreatic cancer. It is similar to colonoscopy as it requires sedation and sometimes general anaesthesia. It involves the insertion of a tube into the mouth, down to the stomach and into the first part of the

24 Meza et al., Evaluation of the Benefits and Harms of Lung Cancer Screening With Low-Dose Computed Tomography: A Collaborative Modeling Study for the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (US); 2021 Mar. (Evidence Syntheses, No. 198tr.)

25 Piscitello et al., Estimating the Screening-Eligible Population Size, Ages 45–74, at Average Risk to Develop Colorectal Cancer in the United States. *Cancer Prevention Research* 2020;13:443-8

26 McCunney et al, Radiation risks in lung cancer screening programs: a comparison with nuclear industry workers and atomic bomb survivors. *Chest.* 2014; 145(3):618-624.

27 Zahnd et al., Lung Cancer Screening Utilization: A Behavioral Risk Factor Surveillance System Analysis. *American Journal of Preventive Medicine* 2019;57(2):250−255

28 Canto et al., International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer *Gut* 2012; 0:1-9

small intestine. Risks are bleeding and GI perforation, and sometimes infection. So, while accurate, it is far from perfect or patient friendly, which at least partially explains why such a high percentage of pancreatic patients are detected late (only 11% are diagnosed when the tumour is localised). Given there are 60,000 new cases per year of pancreatic cancer, we believe there are fewer than 10,000 pancreatic cancer surgical procedures per year.

Given that lung and pancreatic cancer are much smaller opportunities and will likely take Creo Medical years to develop a market within these indications (although MicroBlate Fine and MicroBlate Flex can already be used in the lung and pancreas in the US and EU/UK), we are not including these in our forecasts. However, that may change as the company provides more evidence of effectiveness and gains momentum with oncologists treating those diseases.

Albyn Medical

In July 2020, Creo Medical announced the acquisition of Albyn Medical, which designs, manufactures and commercialises a wide variety of products that broadly cover the endourology, urology, urogynaecology, endoscopy, GI motility and coloproctology areas (see Exhibit 5) although 90% of revenues come from the GI endoscopy space.

Exhibit 5: Albyn Medical products

Type	Product/item
Ureteroscopy	WiScope Ureteroscope
	Peditrol irrigation system
Endourology accessories	Nitinol stone retrieval basket
	Ureteral catheters
	Ureteral stents
	Nephrostomy sets
	Needles & dilators
	Guidewires and special wires
Cystoscopy	WisScope cystoscope
Biofeedback-Stimulation	BioSmart
	AROS
	Femiscan
Bladder Cancer	Elmedical thermochemotherapy system
Procedure tables	SmartDyn integrated
	Examination tables and chairs
	Urodynamics table/chair
	Video fluoroscopy table
Ultrasound	Pinit
	Albit
Urodynamics	Hermes
	SmartDyn
	SmartDyn integrated
	SmartFlow
	SmartScale
	Consumables
Endoscopy	Premier Endoscopy
	Endoscopy (ENDO-FLEX)
	Endoscopy (FORESIGHT)
	Gastric balloon removal kit
	Gold hpdry
pH and impedance	SmartpH
	Vizion
	pH impedance catheters and buffer solutions
Manometry	SmartGI
	Isolab HR
	GI manometry catheters
Transit markers	Gastric transit markers
	Colon transit markers

Source: Albyn Medical/Creo Medical

Albyn Medical was purchased for €24.8m plus up to €2.7m in performance related milestones. Albyn Medical was profitable with €1.7m in PBT for FY19 and contributed £12.8m in sales to Creo in H121. Importantly, with this acquisition, Creo has also acquired Albyn Medical's 70-person EU sales and marketing team, which has a direct presence in Spain, France, Germany and the UK, effectively increasing its sales and marketing presence by tenfold. In November 2020, Creo Medical announced it was acquiring the Belgian medical device company Boucart Medical SRL for €4.5m in cash and up to €0.5m in additional considerations and folding it into its Albyn Medical subsidiary. Boucart supplies products for the GI market in the Belgium and Luxembourg area and reported PBT of €0.6m in 2019. The Boucart acquisition added a further 10 sales and marketing personnel to the team.

Sensitivities

Although Creo's products are unique in their use of bi-polar RF and other design elements, the competitive landscape in GI endoscopy and energy products is crowded, with a large number of large and legacy players. One of Creo's biggest competitors is Olympus, which had £5.3bn in 2020 sales (over half from their endoscopy division) and has a plethora of products serving the GI

endoscopy space and ESD procedures. Further, even with a better device it is not an easy undertaking to convince surgeons to switch brands or move to a new type of procedure. Creo is focused on the ESD procedure, which has gained limited traction in the US mainly because of generally longer procedure times and somewhat higher adverse events (although Creo's products address both), despite better outcomes from patients versus the standard of care. Creo Medical may need to meaningfully increase its investment in US sales and marketing to gain significant penetration as it is currently limited to only a few sales and marketing personnel in the important region. This increase can be achieved organically or through acquisition, as Creo has done with its Albyn Medical purchase, which has helped it acquire a 70-person EU sales and marketing team. Reimbursement may also be an issue as there is no separate payment for use of Creo products and they are bundled into a total payment for the entire procedure. However, according to the company, an ESD conducted using Creo products is still significantly cheaper than surgical colectomy (around £10,000 cheaper per procedure), mainly due to lower downstream costs associated with lesion recurrence and a lower number of procedure-related complications. Gaining reimbursement will likely make adoption easier as financial considerations often dominate the decision-making process in the US healthcare industry.

Valuation

We value Creo Medical at £434m or 240p per basic share using a risk-adjusted NPV model utilising a 12.5% discount rate on the CROMA platform products and a 10% discount rate for Albyn Medical products (as they are more mature). Approximately 75% of the value is attributable to the CROMA platform (especially the GI market), with the remainder divided between the value of Albyn Medical and net cash. We attribute a 70% probability of success to the CROMA platform as it is still in the early phases of adoption (Speedboat only launched in Q419). Additionally, our 2026 sales estimate (which is when we forecast the CROMA products reaching maturity) for the platform is £347m, with £205m coming from the US. We will adjust our assumptions as we are updated on the progress of commercialisation and as additional studies are published using the CROMA devices (both company and physician sponsored).

Exhibit 6: Creo Medical valuation

Product	Main indication	Status	Probability of successful commercialisation	2026 sales (£m)	rNPV (£m)
CROMA Platform	GI, soft tissues and pulmonology	Market/registration	70%	347	334.7
Albyn Medical	Urology, gynaecology and GI	Market	100%	30	43.6
Total					378.3
Net Cash (30 June 2021 + offering)					56.1
Total firm value					**434.5**
Total basic shares (m)					180.9
Value per basic share (£)					**2.40**
Options (m)					11.7
Total number of shares (m)					192.6
Diluted value per share (£)					2.26

Source: Edison Investment Research

Financials

Creo Medical reported that it had £30.6m in cash and £10.7m in debt as of 30 June 2021 with £12.9m in sales for H121, most of which was attributable to Albyn Medical. The company reported an H121 operating loss of £11.1m (vs £10.6m in H120). It raised £36.3m in gross proceeds in a

recent placement and open offer and we project a financing need of an additional £30m before profitability (£10m in 2022 and £20m in 2023). We model this need as illustrative long-term debt.

Sales have historically been minimal but this has changed with the inclusion of the sales of Albyn Medical Products and will change further upon penetration of the CROMA products, though that will likely require significant additional investment in the US sales and marketing team to drive growth in that important market among gastroenterologists. We project revenues of £25.9m in 2021 and £28.4m in 2022 with net losses of £21.2m and £24.4m, respectively.

Exhibit 7: Financial summary

£'000s	2019	2020	2021e	2022e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	13	9,429	25,933	28,374
Cost of Sales	(9)	(5,394)	(13,506)	(14,797)
Gross Profit	5	4,035	12,427	13,577
Sales, General & Administrative and Research & Development Expenses	(18,365)	(25,525)	(33,693)	(36,550)
EBITDA	(18,234)	(21,441)	(21,216)	(22,922)
Operating Profit (before amort. and except.)	(18,875)	(23,037)	(22,813)	(24,518)
Intangible Amortisation	0	0	0	0
Other	127	49	50	51
Exceptionals	0	(447)	0	0
Operating Profit	(18,875)	(23,484)	(22,813)	(24,518)
Net Interest	260	22	138	143
Other	0	0	0	0
Profit Before Tax (norm)	(18,615)	(23,015)	(22,675)	(24,375)
Profit Before Tax (reported)	(18,615)	(23,462)	(22,675)	(24,375)
Tax	2,704	3,146	1,513	0
Deferred tax	(0)	(0)	(0)	(0)
Profit After Tax (norm)	(15,911)	(19,869)	(21,162)	(24,375)
Profit After Tax (reported)	(15,911)	(20,316)	(21,162)	(24,375)
Average Number of Shares Outstanding (m)	121.3	156.5	172.0	183.0
EPS - normalised (£)	(0.131)	(0.127)	(0.123)	(0.133)
EPS - Reported (£)	(0.13)	(0.13)	(0.12)	(0.13)
Dividend per share (£)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	2,169	32,994	32,587	32,851
Intangible Assets	865	28,529	27,594	27,366
Tangible Assets	1,296	3,378	3,851	4,343
Other	8	1,086	1,142	1,142
Current Assets	86,094	60,510	72,173	59,567
Stocks	727	6,812	6,911	6,911
Debtors	1,616	5,633	6,843	6,843
Cash	81,048	45,092	53,265	40,659
Other	2,702	2,973	5,154	5,154
Current Liabilities	(5,056)	(21,837)	(15,455)	(15,455)
Creditors	(4,883)	(16,024)	(15,455)	(15,455)
Short term borrowings	(173)	(5,813)	0	0
Long Term Liabilities	(544)	(8,861)	(8,764)	(18,764)
Long term borrowings	(544)	(6,542)	(6,566)	(16,566)
Other long term liabilities	0	(2,319)	(2,198)	(2,198)
Net Assets	82,663	62,806	80,541	58,199
CASH FLOW				
Operating Cash Flow	(11,674)	(15,815)	(22,340)	(21,991)
Net Interest	(51)	(173)	0	0
Tax	(127)	(291)	0	0
Capex	(1,118)	(576)	(596)	(616)
Acquisitions/disposals	0	(20,586)	0	0
Financing	49,306	159	36,320	0
Dividends	0	0	0	0
Other	124	0	0	0
Net Cash Flow	36,460	(37,282)	13,385	(22,606)
Opening net debt/(cash)	(44,155)	(80,331)	(32,737)	(46,699)
HP finance leases initiated	0	0	0	0
Exchange rate movements	0	36	0	0
Other	(284)	(10,348)	578	0
Closing net debt/(cash)	(80,331)	(32,737)	(46,699)	(24,093)

Source: company reports, Edison Investment Research

Contact details	Revenue by geography
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Management team

CEO: Craig Gulliford	CTO: Chris Hancock
Craig is a founding angel investor in Creo Medical and joined the company as CEO in 2012. Craig qualified with an MSc in electronic engineering from the University College of North Wales and has over 20 years' experience in building international businesses from early stage through to significant scale. Craig's early career developed in the Middle East working with large corporates delivering complex commercial projects. In January 1999, Craig joined a start-up software and hardware business where, as COO, he was part of a small team that grew the company both organically and through acquisition, from a loss-making start-up to a profitable business delivering significant shareholder returns and an exit in 2007.	Chris is the founder of Creo Medical with over 20 years' experience in medical device development including four years at Gyrus Group in his role as senior engineer. Chris holds a personal chair in the Medical Microwave Systems Research Group at Bangor University. Chris is a Fellow of the Institute of Physics, a chartered physicist, Fellow of the Institute of Engineering and Technology, a chartered engineer and a senior member of the IEEE. Chris is also a Royal Academy of Engineering Visiting Professor at UCL and was awarded Katherine Burr Blodgett Gold Medal and Prize in 2019 for work on Creo's CROMA Advanced Energy Platform technology. Chris is a named inventor and lead author on over 800 granted patents, patent applications and international journal publications.
Chief Commercial Officer: David Woods	**CFO: Richard Rees**
David is an industry veteran within the med-tech sector. His experience in the medical device market encompasses general and orthopaedic surgery, gastroenterology, pulmonology and ENT. David was previously the president and CEO of PENTAX Americas and M&A Director of HOYA Group PENTAX Medical. David was awarded the ASGE Presidents award in 2010 recognising exceptional contributions to the society and its mission.	Richard joined Creo Medical as CFO in July 2016. Prior to joining Creo, Richard was CFO of SPTS Technologies, a UK-based, global manufacturer of semiconductor capital equipment. In 2011, Richard was part of a management team at SPTS Technologies that, together with Bridgepoint Capital, acquired SPTS Technologies for $200m from Sumitomo Precision Products. In 2014, SPTS Technologies was acquired by Orbotech for more than $350m. Prior to joining SPTS Technologies, Richard spent seven years at KPMG in audit.

Principal shareholders	(%)
Canaccord Genuity Wealth	14.57
Baillie Gifford	8.43
Capital Research	7.16
M&G Investment Management	5.28
AXA Investment Managers	3.05
FIL Investment Advisors	2.95
BennBridge	2.85

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