EDISON

Paion

Headline trial results

Positive data in bronchoscopy Phase III

Pharma & biotech

Paion announced positive top-line results from the confirmatory Phase III trial of remimazolam for procedural sedation in bronchoscopy, adding to the positive results of a Phase III colonoscopy trial. It is currently conducting additional Phase I studies to further assess abuse potential as the final step of its US clinical development program. Paion is on track to file for approval in both the US (in procedural sedation via partner Cosmo Pharmaceuticals) and Japan (for general anaesthesia) by mid-2018. With the successful completion of the Phase III program for procedural sedation we increase our valuation to €240m (vs €214m) or €4.13 per share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/15	0.1	(34.0)	(55.7)	0.0	N/A	N/A
12/16	4.3	(24.3)	(36.4)	0.0	N/A	N/A
12/17e	5.9	(16.4)	(23.2)	0.0	N/A	N/A
12/18e	3.5	(12.9)	(18.6)	0.0	N/A	N/A

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

Positive top-line bronchoscopy data

The primary endpoint of successful completion of the bronchoscopy procedure without the need for rescue medication or more than five top-up doses was easily met: procedural success was 82.5% for remimazolam vs 3.4% for placebo ($p<0.0001$). Adverse events occurred less frequently with remimazolam compared to midazolam. The results in the secondary endpoints were in keeping with the Phase III colonoscopy study and the high-risk colonoscopy safety study, with induction and recovery from sedation faster with remimazolam than midazolam or placebo.

US filing for procedural sedation expected mid 2018

Paion has initiated additional Phase I studies to further assess abuse potential, ahead of a pre-NDA meeting planned for the end of 2017. A US filing by partner Cosmo is expected in mid-2018 (pending successful abuse potential studies).

Japan filing likely mid-2018, GA Phase I to start soon

Paion has begun to prepare a dossier for a potential mid-2018 filing for remimazolam for general anaesthesia (GA) in Japan, and is in ongoing discussions as it seeks to partner in the Japanese market. Paion will shortly commence a Phase I trial to collect data to aid the design of an EU Phase III study for GA in general surgery patients. The Phase III could start in 2018, subject to funding.

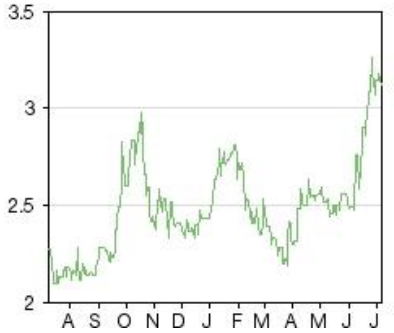
Valuation: Increased to €240m or €4.13 per share

We increase the probability of success in the US to 85%, which lifts our valuation to €240m or €4.13/share (vs €214m or €3.68/share). Paion's cash reach extends beyond end 2018, which would allow it to complete filings in the US (via partner Cosmo) and Japan. Paion has guided that it would need an additional ~€20-25m to restart development of remimazolam in Europe (we model the funds coming from Cosmo milestones, but a licence deal or capital raise could also contribute).

7 July 2017

Price	**€3.12**
Market cap	**€182m**
	US$1.10/€
Net cash (€m) at 31 March 2017	28.7
Shares in issue	58.2m
Free float	75%
Code	PA8
Primary exchange	Frankfurt (Xetra)
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	26.1	29.3	40.8
Rel (local)	29.2	27.7	6.6
52-week high/low		€3.3	€2.1

Business description

Paion is an emerging specialty pharma company developing anaesthesia products. Lead product remimazolam is undergoing US Phase III trials and is partnered with Cosmo (US), Yichang (China), Hana Pharma (South Korea), Pendopharm (Canada) and R-Pharm (CIS, Turkey, MENA).

Next events

Complete abuse potential studies	H217
Pre NDA meeting with FDA	Q417
FDA filing	mid 2018

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Edison profile page

Positive results in bronchoscopy Phase III trial

Paion reported positive results from the confirmatory US pivotal study of remimazolam in patients undergoing bronchoscopy; 83% of patients in the remimazolam arm achieved the composite primary outcome (completion of the bronchoscopy procedure without rescue medication) vs 3.4% on placebo (Exhibit 1). The time from start of medication to start of procedure (induction time) was 5 minutes for remimazolam vs 16 minutes for midazolam, while time from end of procedure to fully alert was 6 minutes for remimazolam vs 12 minutes for midazolam. There were also fewer instances of hypotension and bradycardia in the remimazolam arm. One patient in the remimazolam arm experienced two treatment related serious adverse events after being administered the opioid pain reliever fentanyl at twice the dose allowed by the study protocol.

Exhibit 1: Key results from Phase III colonoscopy procedural sedation trial

	Remimazolam	Placebo	Midazolam (open label)
Initial/top up dose (mg)	5/2.5		1.75/1.0*
Procedural success	82.5%	3.4%	34.8%
Use of rescue sedation	16.2%	96.6%	56.5%
Start of medication to start of procedure (median, minutes)	5.0	17.0	16.0
End of procedure to fully alert (mean, minutes)	6.0	14.0	12.0
Back to normal (min)	404	935	479

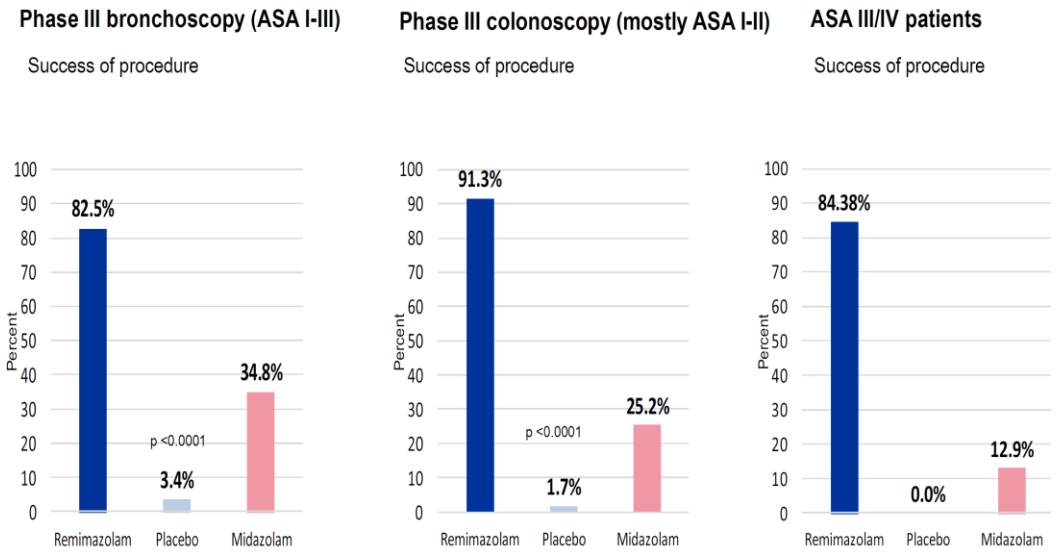
Source: Paion, Edison Investment Research. Note: *1.0/0.5 mg for elderly/debilitated/chronically ill.

The dosage protocols for remimazolam allow for top-up doses to be administered at one minute intervals to facilitate more rapid induction of sedation. The midazolam label specifies a two-minute interval between top-up doses, and midazolam was administered in accordance with the label in the trial protocol.

For this reason the criterion for procedural success in the composite primary outcome shown above was slightly different for the open-label midazolam arm than it was for the double-blind remimazolam and placebo arms. The definition of procedural success was: no need for rescue medication, completion of the procedure and no more than five doses within any 15-minute window for remimazolam/placebo and no more than three doses within any 12-minute window for midazolam.

Exhibit 2 shows that the relative treatment success rates for remimazolam compared to midazolam were similar across the different patient populations in the two pivotal studies and the high-risk colonoscopy study.

Exhibit 2: Comparable treatment success rates in the different patient populations



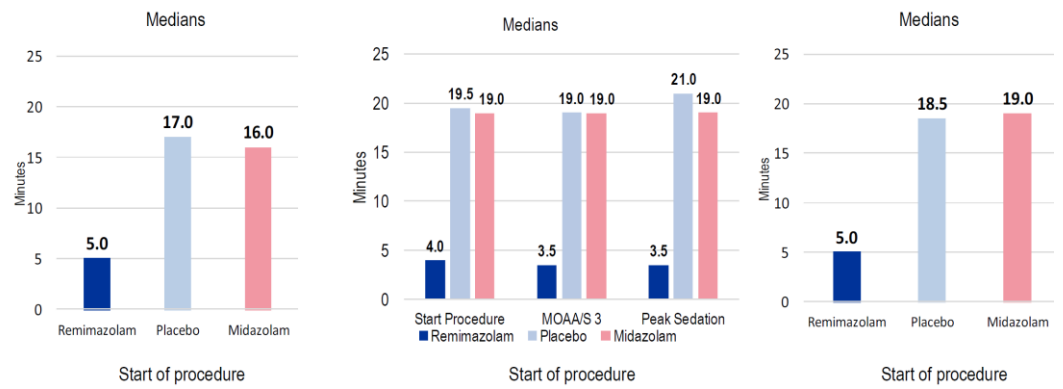
Source: Paion investor presentation. Note: ASA III/IV patients refers to the safety study in high-risk colonoscopy patients with severe systemic disease.

The patient populations in the three studies ranged from younger and mostly healthy individuals in the Phase III colonoscopy study to a selected group of high-risk patients undergoing colonoscopy. These high-risk patients were classified as American Society of Anaesthesiologists (ASA) class III (patients with severe systemic disease) or class IV (patients with severe systemic disease that is a constant threat to life). The subjects in the bronchoscopy Phase III were intermediate between these two groups, with 38% ASA of subjects in class III compared to 7% in the colonoscopy Phase III trial.

Exhibits 3 and 4 show that induction of and recovery from sedation was faster for remimazolam than midazolam in each of the three studies.

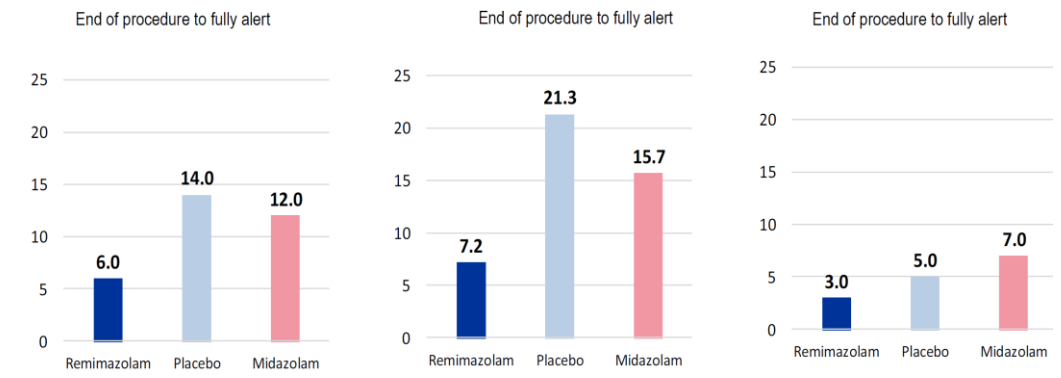
Exhibit 4 shows that for each of the treatments the absolute recovery times were shorter in the sicker patient populations where lower doses of sedation agents were use. However, in each study recovery was faster for remimazolam than midazolam.

Exhibit 3: Similar patterns of time to start of procedure for remimazolam and midazolam



Source: Paion investor presentation. Note: ASA III/IV patients refers to the safety study in high-risk colonoscopy patients with severe systemic disease.

Exhibit 4: Recovery faster with remimazolam in all three pivotal studies



Source: Paion investor presentation. Note: ASA III/IV patients refers to the safety study in high-risk colonoscopy patients with severe systemic disease.

Exhibit 5 summarises the sedation and recovery times for remimazolam and midazolam in the three studies. In each study the induction and recovery times were shorter for remimazolam than for midazolam, with total induction and recovery times between 17 and 23.5 minutes shorter for remimazolam than for midazolam (average 19.5 minutes).

As we previously noted in our report dated 21 November 2016, in the clinical setting midazolam is often administered at higher initial doses and with shorter intervals between top-ups than is recommended on the label. However, our review of published studies found that while this led to faster induction of sedation (6 minutes) the average recovery times were significantly longer (30 minutes), so the total induction and recovery time in the published studies averaged 36 minutes, similar to the 35 minutes total for midazolam in Paion's Phase III colonoscopy study. It is possible that the more rapid administration of midazolam results in higher total doses leading to slower recovery from sedation.

Exhibit 5: Induction and recovery times for the three pivotal studies

	Bronchoscopy Phase III		Colonoscopy Phase III		High-risk colonoscopy	
	Remimazolam	Midazolam	Remimazolam	Midazolam	Remimazolam	Midazolam
Time to start of procedure (min)	5.0	16.0	4.0	19.0	5.0	19.0
End of procedure to fully alert (min)	6.0	12.0	7.2	15.7	3.0	7.0
Total induction plus recovery time	11.0	28.0	11.2	34.7	8.0	26.0
Time saving with remimazolam	**17.0**		**23.5**		**18.0**	

Source: Edison Investment Research

The longer total induction and recovery times for midazolam compared to remimazolam are supportive of the business case that remimazolam will enable more colonoscopy procedures to be completed in a given time period and thus increase patient throughput. We expect this improved throughput to drive significant uptake of remimazolam in the addressable market of 35m procedures per year in the US.[1]

1 CDC procedural stats.

Sensitivities

The key sensitivity is the outcome of clinical trials with remimazolam, notably the outcome of abuse potential studies in the US. The Cosmo licence deal means that Paion should be fully funded until it begins to receive royalty income from US sales, but this is dependent on successful completion of the abuse potential studies and timely regulatory review and subsequent approval by the FDA.

Paion has sufficient cash to fund operations beyond the end of 2018, which would allow it to complete filings in the US (via partner Cosmo) and Japan. Management has guided that ~€20-25m of additional funds would be needed should it choose to restart development of remimazolam in Europe – while we model these funds coming from Cosmo milestone payments, we note that a licence deal or a capital raise are also potential sources.

Valuation

Our sum-of-the-parts DCF valuation increases to €240m, or €4.13 per share, from €214m or €3.68 per share. We have increased the likelihood of success in the US from 75% to 85% following the successful completion of the Phase III development program for remimazolam in procedural sedation, and have rolled forward the DCF model to the mid-year. Our other valuation assumptions are unchanged. Our financial forecasts are also unchanged except for a €0.4m increase in risk-adjusted milestone revenue in 2018 due to the increased probability of success in the US.

Exhibit 6 shows our key valuation assumptions and Exhibit 7 shows a breakdown of the contribution of the individual components of our valuation.

Exhibit 6: Valuation assumptions for pipeline

	Launch date	Peak sales US$m	Risk adjustment (%)	Market penetration (%)	Royalty (%)
Remimazolam EU	2021	175	50	15	20
Remimazolam US	2019	280	85	20	20
Remimazolam Japan	2019	75	60	15	20
Remimazolam RoW	2020	165	50	12	12
Remimazolam Canada	2020	42	60	20	15

Source: Edison Investment Research

The potential catalysts in H217 include completion of the Phase I abuse potential trials and the European Phase I trial in general anaesthesia, the pre-NDA meeting with the FDA, and an update on partnering options for Japan. Paion is evaluating its commercialisation options in unpartnered regions, which could lead us to adjust our royalty rate assumptions.

Exhibit 7: Summary valuation

	Value (€m)	Value per share (€)
Remimazolam EU	36.4	0.63
Remimazolam US	184.4	3.17
Remimazolam Japan	47.0	0.81
Remimazolam RoW	21.3	0.37
Remimazolam Canada	10.6	0.18
Risk-adjusted milestones	59.0	1.01
Expenses	(54.4)	(0.93)
Tax	(80.2)	(1.38)
Net cash FY17e	15.9	0.27
Total	**240.1**	**4.13**

Source: Edison Investment Research

Exhibit 8: Financial summary

€000s	2014	2015	2016	2017e	2018e
Year end 31 December					
PROFIT & LOSS					
Revenue	3,456	61	4,262	5,874	3,500
Cost of sales	(4)	0	0	0	0
Gross profit	3,452	61	4,262	5,874	3,500
R&D expenditure	(11,799)	(29,385)	(23,408)	(19,000)	(13,000)
General, administrative & selling	(3,702)	(5,729)	(5,129)	(3,800)	(3,914)
Other	411	965	(807)	51	51
Operating profit	(11,639)	(34,088)	(25,082)	(16,875)	(13,363)
Depreciation and amortisation	(93)	0	(759)	(500)	(400)
Share-based payments	0	0	0	0	0
Exceptionals	0	0	0	0	0
EBITDA	(11,546)	(34,088)	(24,323)	(16,375)	(12,963)
Operating profit (before GW and except)	(11,546)	(34,088)	(24,323)	(16,375)	(12,963)
Net interest	(66)	42	21	20	20
Profit before tax (norm)	(11,612)	(34,046)	(24,302)	(16,355)	(12,943)
Profit before tax (reported)	(11,704)	(34,046)	(25,061)	(16,855)	(13,343)
Tax	2,468	5,834	4,944	3,135	2,145
Profit after tax (norm)	(9,143)	(28,212)	(19,359)	(13,220)	(10,798)
Profit after tax (reported)	(9,236)	(28,212)	(20,118)	(13,720)	(11,198)
Average number of shares outstanding (m)	39.9	50.7	53.2	57.0	58.2
EPS - normalised (c)	(22.9)	(55.7)	(36.4)	(23.2)	(18.6)
EPS - reported (c)	(23.2)	(55.7)	(37.8)	(24.1)	(19.2)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Gross margin (%)	NA	NA	NA	NA	NA
EBITDA margin (%)	NA	NA	NA	NA	NA
Operating margin (before GW and except.) (%)	NA	NA	NA	NA	NA
BALANCE SHEET					
Fixed assets	3,516	3,417	2,855	2,355	1,955
Intangible assets	3,440	3,362	2,688	2,313	2,013
Tangible assets	76	56	167	42	-58
Refund from assumption of dev costs	0	0	0	0	0
Other	0	0	0	0	0
Current assets	63,032	40,051	35,128	20,925	10,127
Stocks	0	0	0	0	0
Debtors	467	0	0	25	25
Cash	58,912	32,680	30,111	15,883	5,085
Other	3,653	7,371	5,017	5,017	5,017
Current liabilities	(3,924)	(7,901)	(13,040)	(7,266)	(7,266)
Trade payables	(3,338)	(7,332)	(6,353)	(6,353)	(6,353)
Short-term borrowings	0	0	0	0	0
Provisions	(306)	(224)	(555)	(555)	(555)
Finance lease liabilities	0	0	0	0	0
Other current liabilities	(254)	(305)	(359)	(359)	(359)
Current deferred income	(26)	(39)	(5,774)	0	0
Long-term liabilities	(17)	(6)	0	0	0
Long-term borrowings	0	0	0	0	0
Provisions	0	0	0	0	0
Long-term deferred income	(17)	(6)	0	0	0
Deferred taxes	0	0	0	0	0
Other long-term liabilities	0	0	0	0	0
Net assets	62,607	35,562	24,943	16,014	4,816
CASH FLOW					
Operating cash flow	(12,044)	(28,212)	(17,135)	(22,174)	(12,963)
Net interest	(66)	43	19	20	20
Tax	0	2,575	5,529	3,135	2,145
Capex	0	0	7	0	0
Purchase of intangibles	(26)	(33)	0	0	0
Acquisitions/disposals	0	0	(199)	0	0
Equity Financing	57,618	22	9,212	4,790	0
Dividends	0	0	0	0	0
Other	0	0	0	0	0
Net cash flow	45,482	(25,605)	(2,567)	(14,229)	(10,798)
Opening net debt/(cash)	(13,292)	(58,912)	(32,680)	(30,111)	(15,883)
Effect of exchange rate changes	(72)	(66)	(2)	0	0
Other	210	(560)	0	0	0
Closing net debt/(cash)	(58,912)	(32,680)	(30,111)	(15,883)	(5,085)

Source: Edison Investment Research, Paion accounts

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