EDISON

Intec Pharma

Earnings report

Progress across ongoing and new clinical trials

Pharma & biotech

Intec Pharma has made significant progress, both with its current development programme and in new directions. The company is in a Phase III clinical trial of an accordion pill (AP) formulation of carbidopa and levodopa (AP-CDLD), and announced that it has reduced the target trial size to 328 patients (from 460) based on feedback from experts, and expects to be fully enrolled by Q417. Additionally, the company announced in March 2017 that it has started a Phase I trial expected to complete in Q317 of an AP formulation with cannabidiol and tetrahydrocannabinol (AP-CBD/THC), the two primary cannabinoids in Cannabis sativa.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/15	0.0	(7.2)	(0.92)	0.0	N/A	N/A
12/16	0.0	(13.4)	(1.17)	0.0	N/A	N/A
12/17e	0.0	(12.8)	(0.89)	0.0	N/A	N/A
12/18e	0.0	(13.6)	(0.89)	0.0	N/A	N/A

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

AP-CDLD trial size down on updated assumptions

The reduction in the target enrolment for the AP-CDLD Phase III trial was made following feedback from key opinion leaders and biostatisticians, which suggested that standard deviation would be lower than initial assumptions. The new design will require only a modest improvement in data (18% better resolution, power of 0.9, assuming similar standard deviations in the arms) than the previous design. The trial is targeting full enrolment at the end of 2017 and top-line data in mid-2018.

Cannabinoid programme initiated

The company initiated a Phase I clinical trial of AP-CBD/THC to examine the pharmacokinetics, safety and tolerability of the drug in comparison to the approved sublingual CBD/THC spray Sativex. The oral bioavailability of cannabinoids is low at approximately 6% and the pharmacokinetics are somewhat unpredictable due to low solubility, but the AP is a device that can potentially address these issues. Potential target indications include neuropathic low back pain and fibromyalgia, although it has not committed to either programme yet.

Reduced financial hurdles

The company performed a private placement of 2.3m shares at $4.40 on 10 March 2017, bringing estimated cash to $27.2m. We expect the company will only need a further $10m in additional financing before AP-CDLD approval in 2019.

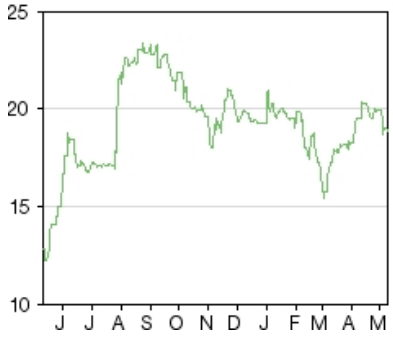
Valuation: Increased to NIS606m

We have increased our valuation to NIS606m (~$166m) from NIS540-582m, although the value per share has reduced to NIS44.02 (~$12.04) from NIS47-51. The majority of this increase is due to a reduction in the clinical trial costs for AP-CDLD, offset by an increase in shares from the offering. We expect to update our valuation following the completion of the AP-CBD/THC clinical trial in Q317.

22 May 2017

Price	**NIS18.80**
Market cap	**NIS258m**
	NIS3.65/US$
Estimated net cash ($m) at March 2017	27.2
Shares in issue	13.8m
Free float	83%
Code	NTEC
Primary exchange	TASE
Secondary exchange	NASDAQ

Share price performance



%	1m	3m	12m
Abs	(3.8)	(3.3)	42.5
Rel (local)	(6.1)	(6.7)	34.4
52-week high/low	NIS23.4		NIS12.2

Business description

Intec Pharma is a drug delivery company that has developed the accordion pill, a novel gastroretentive controlled release formulation. The company is currently using this technology to develop AP-CDLD for Parkinson's in Phase III, AP-ZP for insomnia completed Phase II, and AP-CBD/THC in Phase I for pain indications.

Next events

AP-ZP partnering discussions	Ongoing
AP-CBD/THC Phase I completion	Q317
AP-CDLD enrolment complete	Q417

Analysts

Maxim Jacobs	+1 646 653 7027
Nathaniel Calloway	+1 646 653 7036

healthcare@edisongroup.com

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AP-CDLD trial size down

In November 2016, Intec reported that it reduced the size of its Phase III clinical programme from 460 patients to 328, a reduction of 29%. The trial is measuring the improvement in off time between patients on AP-CDLD and patients on Sinemet, a formulation of immediate release carbidopa/levodopa. The reduction in trial size was made following feedback from key opinion leaders and biostatisticians, which suggested that the predicted standard deviation for the trial was too large. Based on the stated power of 0.9, we have calculated that the reduction in patient number will require data that is 18% better resolved than in the initial trial design (assuming similar standard deviations between arms) to be statistically significant. Resolution in this context refers to the separation between the arms (delta) over the standard deviation of the arms, which the experts suggested was be too large in the initial trial assumptions. This means that only a modest improvement in the standard deviation (15%) is required to justify using 132 fewer patients. The company stated that the trial should be fully enrolled in Q417, implying completion in mid-2018.

The cannabinoid programme

Intec announced in March 2017 that it has initiated a Phase I clinical trial of an AP formulation of the two primary cannabinoids in Cannabis sativa, cannabidiol (CBD) and tetrahydrocannabinol (THC), AP-CBD/THC. The company has announced that it intends to examine AP-CBD/THC for the treatment of "various indications, including low back pain and fibromyalgia". The current Phase I trial is in 21 healthy volunteers and is examining the pharmacokinetics, safety and tolerability of two Ap-CBD/THC formulations in comparison to Sativex. Sativex is a buccal formulation of CBD and THC developed by GW Pharmaceuticals for the treatment of spasticity associated with multiple sclerosis. Sativex is approved in 28 countries, although it is not approved in the US. The trial has a target completion date in Q317.

There are several aspects of cannabinoid pharmacology that could potentially be improved by the AP formulation. Cannabinoids have a low oral bioavailability measured at an average of 6% for THC[1] and CBD,[2] although with high levels of variability between individuals and doses even when administered under similar conditions. THC and CBD are very oily molecules that dissolve poorly in the aqueous gastric medium. The dissolution and absorption of the drug is aided in the gut by bile acids. One study showed a significant increase in THC bioavailability when it was co-administered with the bile acid glycocholate.[3] This dependence on bile acids for absorption also explains some of the variability in bioavailability. THC will sometimes have a peak concentration at two different times due to the enterohepatic circulation of bile acids and variable absorption rates depending on their presence.[4] The AP device is specifically designed to maximize the exposure of drugs to bile acids secreted in the upper gastrointestinal tract, and an AP-CBD/THC formulation may significantly improve the drug's oral profile. The goal of the Phase I study is to examine this profile and determine the applicability of the formulation to any future indications.

[1] Ohlsson A, et al (1980) Plasma delta-9 tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. *Clin. Pharmacol. Ther.* 28, 409-16.

[2] Agurell S, et al. (1981). Interaction of THC with cannabinol and cannabidiol following oral administration in man. Assay of cannabinol and cannabidiol by mass fragmentography. Experientia 37, 1090–2.

[3] Perez-Reyes M, et al. (1973) Pharmacology of orally administered Δ9-tetrahydrocannabinol. Clin. *Pharmacol. Ther.* 14, 48-55.

[4] Huestis MA, (2007) Human Cannabinoid Pharmacokinetics. *Chem. Biodivers.* 4, 1770-1804.

The two indications being pursued by the company were neuropathic low back pain and fibromyalgia, although they have made no commitments to study either. Although both of these indications can be described as pain disorders, their etiologies are significantly different. Low back pain can be mechanical in nature due to stress on the muscles or bones of the lower back, or neuropathic as in the case of sciatica, and the company has stated that it intends to focus on the neuropathic variety. Low back pain is an exceptionally common disorder, and approximately 10% of US adults have chronic low back pain (lasting over 12 weeks),[5] and approximately 17% of cases are predominantly neuropathic in origin.[6] Cannabinoids are well positioned for the treatment of neuropathic low back pain because there is evidence of their efficacy in neuropathic pain.[7]

Fibromyalgia is a poorly understood disorder characterized by chronic diffuse pain in multiple regions of the body. Although the cause of the disorder is not well understood, it has a high comorbidity with mood disorders and appears to be caused by a defect of the nervous system. This is evidenced by the drugs approved for the disorder, which include antidepressants such as Savella (milnacipran) or Cymbalta (duloxetine), as well as neuropathy drug Lyrica (pregabalin). The Centers for Disease Control (CDC) estimates that approximately four million adults are affected by the disorder in the US, although the prevalence of the disease varies dramatically based on the diagnostic criteria.[8] The synthetic cannabinoid nabilone has shown efficacy in reducing the symptoms of the disease ($p<0.02$ for pain, $p<0.02$ for impact, $p<0.02$ for anxiety).[9]

Valuation

We have increased our valuation to NIS606m (~$166m) from NIS540-582m, although the value per share has reduced to NIS44.02 (~$12.04) from NIS47-51. The company increased the total share count from 11.4m to 13.8m during the recent private placement. The biggest driving factor for the increase was the reduction in our AP-CDLD development costs and cash spent on the trial to date. This improved the negative NPV from NIS43m to NIS23m. The remaining increases were due to advancing our NPVs to year-end 2016. These were partially offset by an adjustment in the research timeline for AP-ZP to account for the lack of research spending or a partnership in H216.

We currently do not include the AP-CBD/THC programme in our valuation because the company has not announced a precise target indication for the programme. We expect to update our valuation following the release of more details. The current NPV for either of the proposed indications would be small at this time, as the clinical trial costs largely offset the commercial value at the requisite high-risk adjustment for a programme before completion of Phase I.

[5] Freburger JK, et al. (2009) The Rising Prevalence of Chronic Low Back Pain. *J. Am. Med. Assoc. Int. Med.* 169, 251-258.

[6] Torrance N, et al. (2006) The Epidemiology of Chronic Pain of Predominantly Neuropathic Origin. Results From a General Population Survey. *J. Pain* 7, 281-289.

[7] Lynch ME and Campbell F (2011) Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials. *Br. J. Pharmacol.* 72, 735-744.

[8] Jones GT, et al. (2015) The Prevalence of Fibromyalgia in the General Population: A Comparison of the American College of Rheumatology 1990, 2010, and Modified 2010 Classification Criteria. *Arthritis and Rheumatology* 67, 568-575.

[9] Skrabek RQ, et al. (2008) Nabilone for the Treatment of Pain in Fibromyalgia. *J. Pain* 9, 164-173.

Exhibit 1: Valuation of Intec Pharma

Development programme	Clinical stage	Prob. of success	Launch year	Launch pricing ($)	Peak sales ($m)	Patent/exclusivity protection	Royalty/ margin	rNPV (NISm)
AP-CDLD, US	Phase III	60%	2019	7,700	111	2029	47%	281
AP-CDLD, Europe	Phase III	60%	2019	4,600	85	2029	40%	180
AP-CDLD development costs	Phase III							-23
AP-ZP (US and Europe)	Phase III ready	40%	2020	700	155	2028	15%	60
AP-ZP Licensing upfront	Phase III ready	30-50%	2018					33
Unallocated costs (administrative costs, etc.)								-24
Total								507
Net cash and equivalents (YE16 + offering) ($m)								100
Total firm value (NISm)								606
Total basic shares (m)								13.8
Value per basic share (NIS)								44.02
Options (m)								0.1
Total diluted shares (m)								13.9
Value per diluted share (NIS)								43.58

Source: Intec reports, Edison Investment Research

Financials

Intec Pharma reported its FY16 results in April 2017. The company has changed accounting practices and now reports results in US dollars instead of NIS. Our forecasts now reflect this. The company reported an operating loss of $13.8m for the year, up from $7.6m in 2015. This increase was driven by R&D spending associated with the AP-CDLD Phase III clinical trial, with total R&D spending of $10.7m. We have slightly decreased our 2017 R&D spending to $9.9m (from $11.1m) to reflect the reduction in the AP-CDLD Phase III trial size. This is partially offset by spending on the new AP-CBD/THC Phase I. The company ended 2016 with $18.2m in cash and equivalents, which has subsequently been supplemented with a $10m (gross) private placement (2.3m shares at $4.40,). We expect that the company will need $10m in additional financing to bring it through approval of AP-CDLD and profitability in 2019. We include this as illustrative debt in 2018.

Exhibit 2: Financial summary

$'000s	2014	2015	2016	2017e	2018e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	0	0	0	0	0
Cost of Sales	0	0	0	0	0
Gross Profit	0	0	0	0	0
Research and development	(3,409)	(4,815)	(10,749)	(9,916)	(10,332)
Selling, general & administrative	(2,609)	(2,788)	(3,097)	(3,407)	(3,747)
EBITDA	(6,369)	(8,330)	(14,513)	(13,795)	(14,551)
Operating Profit (before GW and except.)	(5,784)	(7,584)	(13,812)	(13,289)	(14,045)
Intangible Amortisation	0	0	0	0	0
Exceptionals/Other	0	0	0	0	0
Operating Profit	(5,784)	(7,584)	(13,812)	(13,289)	(14,045)
Net Interest	91	404	450	450	450
Other (change in fair value of warrants)	0	0	0	0	0
Profit Before Tax (norm)	(5,693)	(7,180)	(13,362)	(12,839)	(13,595)
Profit Before Tax (IFRS)	(5,693)	(7,180)	(13,362)	(12,839)	(13,595)
Tax	0	0	0	0	0
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(5,693)	(7,180)	(13,362)	(12,839)	(13,595)
Profit After Tax (IFRS)	(5,693)	(7,180)	(13,362)	(12,839)	(13,595)
Average Number of Shares Outstanding (m)	4.8	7.8	11.4	14.5	15.2
EPS - normalised ($)	(1.18)	(0.92)	(1.17)	(0.89)	(0.89)
EPS - IFRS ($)	(1.18)	(0.92)	(1.17)	(0.89)	(0.89)
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	4,397	4,076	4,047	4,042	4,058
Intangible Assets	0	0	0	0	0
Tangible Assets	4,397	4,076	4,047	4,042	4,058
Other	0	0	0	0	0
Current Assets	8,105	33,096	20,674	18,849	15,941
Stocks	0	0	0	0	0
Debtors	288	2,361	2,384	2,384	2,384
Cash	7,742	30,673	18,228	16,403	13,495
Other	75	62	62	62	62
Current Liabilities	(184)	(614)	(1,152)	(1,076)	(1,137)
Creditors	(184)	(614)	(1,152)	(1,076)	(1,137)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(1,164)	(327)	(97)	(97)	(10,097)
Long term borrowings	0	0	0	0	(10,000)
Other long term liabilities	(1,164)	(327)	(97)	(97)	(97)
Net Assets	11,154	36,231	23,472	21,718	8,765
CASH FLOW					
Operating Cash Flow	(4,751)	(7,931)	(12,005)	(11,324)	(12,386)
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(76)	(1,384)	(482)	(501)	(521)
Acquisitions/disposals	2,865	0	206	0	0
Financing	4,682	32,452	0	10,000	0
Dividends	0	0	0	0	0
Other	(9)	13	0	0	0
Net Cash Flow	2,711	23,150	(12,281)	(1,825)	(12,908)
Opening net debt/(cash)	(5,400)	(7,742)	(30,673)	(18,228)	(16,403)
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	(369)	(232)	8	0	0
Other	0	13	(172)	(0)	0
Closing net debt/(cash)	(7,742)	(30,673)	(18,228)	(16,403)	(3,495)

Source: Intec reports, Edison Investment Research

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Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 8249 8342
Level 12, Office 1205, 95 Pitt Street,
Sydney , NSW 2000,
Australia

Tel Aviv +44 (0)20 3734 1007
Medinat Hayehudim 60,
Herzilya Pituach, 46766
Israel