EDISON

Acacia Pharma

Initiation of coverage

Raising the BAR in PONV

Pharma & biotech

Acacia Pharma is focused on bringing antiemetic drugs to the US hospital setting for unmet needs in post-operative nausea and vomiting (PONV) and chemotherapy-induced nausea and vomiting (CINV). We expect FDA approval of Acacia's lead product, BARHEMSYS (repurposed amisulpride), for the management of PONV by its 5 October 2018 PDUFA date. In the near term, Acacia will concentrate on the US commercial opportunity by expanding its sales and marketing infrastructure. We anticipate US launch of BARHEMSYS in Q219 for PONV 'rescue treatment' and expect broadening of use for PONV prophylaxis in subsequent years. We value Acacia Pharma at €579m or €10.9 per share.

Year end	Revenue (£m)	PBT* (£m)	EPS* (£)	DPS (£)	P/E (x)	Yield (%)
12/16	0.0	(16.3)	(5.06)	0.0	N/A	N/A
12/17	0.0	(6.5)	(2.32)	0.0	N/A	N/A
12/18e	0.0	(20.3)	(0.36)	0.0	N/A	N/A
12/19e	2.7	(45.6)	(0.82)	0.0	N/A	N/A

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

BARHEMSYS; rescue in PONV is an unmet need

BARHEMSYS, intravenously administered, low-dose amisulpride (dopamine antagonist) is in registration phase for the management of PONV. The NDA submission covers 'rescue treatment' (patients who are uncontrolled following prophylactic treatment with standard of care antiemetics) and prophylaxis of PONV as monotherapy and in combination with standard of care antiemetics. The total addressable US patient population is c 30 million patients, a sizable opportunity.

US commercialisation to maximise returns

Acacia will commercialise BARHEMSYS through a US salesforce (60-100 reps), which will focus on anaesthetists at ~1,600 US hospitals that account for ~80% of relevant surgical procedures. Inadequately treated PONV leads to prolonged stay in post-anaesthesia care unit (PACU) recovery rooms. BARHEMSYS use could reduce patient hospitalisation time and the associated costs. Despite the near-term increase in SG&A, we estimate that successful commercialisation could enable break-even in 2023 and long-term operating margins of more than 60%. Further funding in the near term will be required to build the required US organisation.

Second indication; CINV repurposed amisulpride

Acacia is developing APD403 (repurposed intravenous and oral amisulpride) for utility in CINV. The acute dose-ranging Phase II study is scheduled to start in 2019 and potential launch in the US in 2022 is feasible. Acacia will leverage its US infrastructure and estimates that it will need to hire ~40 additional reps to target community- and hospital-based oncologists for CINV.

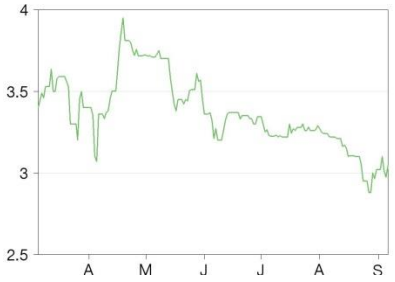
Valuation: €579m or €10.9per share

Our valuation of Acacia Pharma, at €579m or €10.9/share, is predominantly based on a risk-adjusted NPV model of BARHEMSYS for rescue treatment and prophylaxis of PONV, in addition to the CINV opportunity for the US market only.

7 September 2018

Price	**€3.04**
Market cap	**€161m**
	$1.29/£, $1.16/€, €1.11/£
Net cash (£m) at 30 June 2018	29.0
Shares in issue	53.1m
Free float	100%
Code	ACPH
Primary exchange	Euronext
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(5.5)	(5.2)	N/A
Rel (local)	0.1	(1.6)	N/A
52-week high/low		€3.95	€2.88

Business description

Acacia Pharma is a hospital pharmaceutical company focused on the development and commercialisation of new nausea and vomiting treatments for surgical and cancer patients. Its main product, BARHEMSYS, is for the treatment of PONV and is forecast to launch in 2019.

Next events

BARHEMSYS PDUFA date	5 October 2018
US launch as PONV 'rescue therapy'	2019

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Edison profile page

Acacia Pharma is a research client of Edison Investment Research Limited

Investment summary

Company description: Focus on BARHEMSYS

Acacia Pharma, a hospital pharmaceuticals group based in Cambridge, UK and Indianapolis, US, is focused on developing and commercialising treatments for nausea and vomiting. Lead product, BARHEMSYS, is a repurposed formulation of amisulpride (dopamine antagonist approved in high dose for the treatment of schizophrenia in Europe), which it has identified to serve an unmet need for the prophylaxis or rescue treatment of nausea and vomiting in surgical and oncology patients. Acacia will commercialise BARHEMSYS in the US to maximise its economic returns; the ex-US international opportunity will depend on partnering deals. Acacia Pharma's management team has extensive experience in the discovery, development and commercialisation of hospital pharmaceutical products and in drug repurposing. This experience will be critical to the product's success. The company was founded in 2007 and listed on Euronext Belgium in March 2018, raising £33.9m (c €37m) net. To date, the group has raised £78.2m in equity; in addition, it has a $30m debit facility with Hercules (drawn down $10m [c £7m]).

Valuation: €579m or €10.9 per share

Our valuation of Acacia Pharma, at €579m or €10.9/share, is exclusively based on a risk-adjusted NPV model of BARHEMSYS for rescue treatment and prophylaxis of PONV, in addition to the CINV opportunity for the US market only. We do not include any contribution from Europe or ROW opportunities as these will be dependent on out-licensing agreements with various future partners, on which we have no visibility. Our NPV calculation incorporates end-June net cash of €32.3m (£29.0m) and we utilise a 12.5% discount rate.

Financials: Further funding required for full commercialisation

Following the £33.9m net raise from the IPO in March and the drawdown of $10m from the $30m credit facility with Hercules Technology Growth Capital (Hercules), Acacia has £35.7m in cash as of 30 June. To fund ongoing operations, we forecast that an additional c £75m (in addition to the remaining $20m from Hercules) will need to be raised in 2019 and 2020. We forecast a significant increase in expenses from historic levels driven by the commercialisation of BARHEMSYS and the clinical trial programme for APD403. FY17 SG&A and R&D were £1.5m each. We forecast R&D costs of £2.9m in FY18, growing to £7.7m in FY19. We anticipate that SG&A costs will increase to £16.7m in FY18, growing to £37.8m in FY19. We forecast a net loss of £19.3m in FY18 and £43.6m in FY19. We forecast that Acacia will reach break-even in 2023.

Sensitivities: Strategic execution crucial to success

Acacia Pharma is subject to various sensitivities common to speciality pharmaceutical companies, including commercialisation (pricing, reimbursement, uptake and competition), manufacturing and financing risks. The key sensitivities for Acacia Pharma relate to execution risk; our sales forecasts and valuation are dependent on the successful US commercialisation of BARHEMSYS (subject to approval by the US FDA later this year). Furthermore, with the focus on one asset in the short term, the valuation is skewed to and dependent on BARHEMSYS. Therefore, if BARHEMSYS fails to obtain approval, it would have a serious and detrimental effect on Acacia's long-term strategy and our valuation. We note significant commercial risks, including the group's ability to recruit, train and retain adequate numbers of effective sales and marketing personnel; the ability of sales personnel to obtain access to or persuade adequate numbers of anaesthetists and/or physicians to prescribe any future products; the lack of complementary products offered by sales personnel, unforeseen costs and expenses associated with creating an independent sales and marketing organisation; and costs of marketing and promotion above those anticipated by the group and our forecasts, particularly any need to undertake additional, costly, real-world studies to further confirm BARHEMSYS's pharmacoeconomic benefit if uptake is slower than anticipated.

Evolving into a commercial entity

Acacia Pharma is at a major inflection point in its history. Its lead drug candidate, BARHEMSYS, has the potential to be the company's first internally developed asset to reach the market. Approval of BARHEMSYS for PONV (PDUFA date 5 October) would validate the company's R&D efforts, which are focused on repurposing approved drugs for unmet clinical needs. The rationale is not to identify novel molecules, but rather to identify approved drugs that may be modified (by changes in dosing or administration) for use in other indications than those in which they were originally approved. This approach lowers the typical drug development risks associated with developing new chemical entities (NCEs) as substantial clinical safety and efficacy data exist for approved therapies.

BARHEMSYS has been developed as a novel approach for treating PONV, a significant negative contributor to prolonged hospitalisation stays, and the associated costs and overall patient wellbeing. Current standard of care for medium or high-risk patients involves the prophylactic treatment with standard-of-care antiemetics, including 5-HT_3 receptor antagonist (eg ondansetron). If a patient develops PONV despite receiving prophylaxis antiemetic drugs, guidelines indicate that the patient should receive other antiemetics with a different mechanism of action (MOA) as rescue therapy. Currently there are limited options; patients can receive corticosteroids, an NK-1 receptor antagonist or butyrophenones, but all have limitations. BARHEMSYS is a dopamine receptor antagonist, a class of drugs that has historically had safety concerns. Droperidol, a butyrophenone that acts as a dopamine receptor antagonist was a commonly used effective antiemetic until the FDA issued a black box warning in 2001 that cited concerns about QT prolongation and Torsade de Pointes (which could result in sudden cardiac death). BARHEMSYS active ingredient amisulpride is a dopamine antagonist with a lower propensity for cardiac and neurological side effects compared to droperidol (see clinical trial information below). In four registration studies BARHEMSYS has demonstrated a tolerable safety profile. Importantly, no cardiac toxicity or neurological adverse events were reported. Generally, adverse events were lower with BARHEMSYS than placebo.

The regulatory submission of BARHEMSYS is based on four Phase III clinical trials that tested the drug candidate as a rescue treatment following either failed prior prophylaxis or no prior prophylaxis and as a prophylactic treatment in combination or alone. All four studies demonstrated that BARHEMSYS had a statistically significant improvement in treating PONV compared with placebo. If approved across these settings, BARHEMSYS will be the first antiemetic that can be used as a rescue treatment following failed prophylaxis or as a combination treatment when used as a prophylaxis.

With approval likely, Acacia Pharma has started to build its US marketing organisation with 21 senior hires in sales, marketing, managed markets and supply chain management in H118. If BARHEMSYS is approved, Acacia plans to continue hiring, notably sales representatives (60+), before its anticipated launch in Q219.

Our analysis reveals that through an aggregate investment in personnel of $160–180m over the 2018-21 period, Acacia could build up its commercial operations including the sizeable salesforce of 60-100 reps it needs to focus on the ~1,600 hospitals that account for ~80% of US surgical procedures. The modest need for R&D expense (to support the Phase II and Phase III clinical trials of amisulpride in CINV) over the same period, coupled with high gross margins, leads to our forecast that financial break-even in 2023 is feasible on BARHEMYSYS combined sales of c $110m. We note that significant risk remains around commercial execution, particularly as financial investment in the short to medium term will be high ($100m+).

Ramp-up of BARHEMSYS sales in the rescue and broader prophylactic settings has longer-term positive implications for gross margin and EBIT development, mainly through operational leverage. BARHEMSYS is a high gross margin product; gross margins of around 90-95% are not

unreasonable assumptions for this small molecule drug. Based on the assumptions discussed in more detail in the valuation section, we forecast peak net sales of BARHEMSYS of $314m in the rescue setting and $90m in the prophylactic setting. Furthermore, after initial infrastructure-related and launch period costs are met, we forecast that SG&A will grow at a much slower rate than sales growth. From 2023, we expect R&D expenses to reduce significantly as the CINV clinical programme will have likely completed. Successful commercial execution will be a critical driver of BARHEMSYS sales; we forecast that sales of $236m would lead to 51% operating margin in 2025.

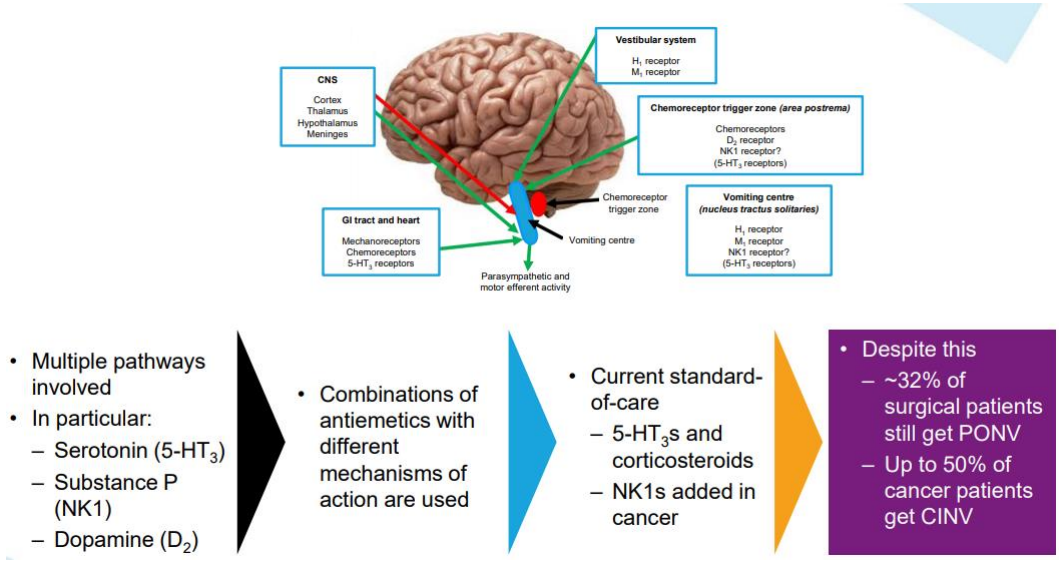
BARHEMSYS raising the bar in PONV

A new drug application (NDA) for BARHEMSYS (amisulpride/APD421) has been submitted to the FDA for the treatment of established PONV (including after prophylaxis antiemetic failure) with a 10mg single dose (so-called rescue therapy), and prophylaxis of PONV (as monotherapy or in combination) with a 5mg single dose. The NDA submitted to the FDA contains the full range of clinical data to support a broad prescribing label that encompasses rescue and prophylactic use as monotherapy or in combination with available antiemetics respectively.

Post-operative nausea and vomiting (PONV) is a complex and significant issue in anaesthesia practice. It affects 30-80% of surgical patients and is the second most common complaint from patients (pain being the first). While the current mainstay of antiemetic treatments (combinations of different classes of antiemetic drugs are given pre- or intra-operatively) provide relief, these drugs are not 100% effective when used as nausea and vomiting (N+V) prophylaxis, with an estimated 30% of patients still suffering from PONV. The outcome is a prolonged stay in a post-operative recovery room with delayed discharge and recovery, and increased medical costs. Better PONV management improves patient symptoms and can reduce hospitalisation costs, an important factor for drug coverage by payors. According to Acacia Pharma's market research, there are ~65m applicable invasive surgical procedures undertaken annually in the US, of which ~49 million patients receive prophylactic PONV treatments and ~32% fail on prophylaxis (~16 million patients pa are candidates for rescue therapy). Initially, Acacia Pharma will focus marketing efforts on (assuming approval on the 5 October PDUFA date) on patients who have failed prophylaxis before expanding to prophylaxis treatment for higher-risk surgical patients.

Current standard of care for medium to high-risk patients is use of one or more antiemetic drugs (5-HT_3, dopamine, and histamine antagonists and dexamethasone) as prophylactic agents. Prior to 2001, the dopamine antagonist (D_2) droperidol was widely used and the agent of first choice in international consensus guidelines. However, significant cardiac toxicity issues (QT interval prolongation) led to withdrawal/disuse of the drug in many countries. This has led to a void of efficacious and low side effect profile D2/3 antagonists. Acacia Pharma has identified amisulpride in low dose as a clinically effective treatment for N+V with an improved side effect profile vs available dopamine antagonists (very low tendency for QT interval prolongation and extrapyramidal signs and symptoms at the proposed nausea and vomiting dose treatment levels).

Exhibit 1: Multiple pathways involved in the pathophysiology of PONV



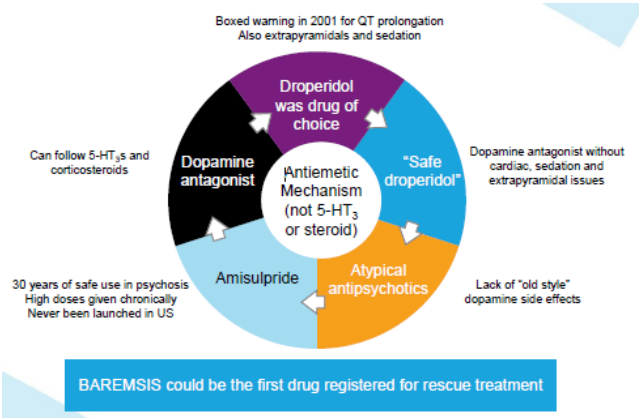
Source: Company presentations

BARHEMSYS IV: Repurposed amisulpride

Acacia Pharma has developed APD421 (amisulpride injection) branded as BARHEMSYS for its initial indication for PONV as rescue therapy and for prophylactic management. Data from four Phase III clinical trial studies have been submitted as part of the NDA to ascertain a broad prescribing label that encompasses rescue and prophylactic use as monotherapy or in combination with available antiemetics. The company plans initially to target patients whose N+V are uncontrolled on prior prophylaxis therapy, so-called rescue treatment, a high unmet need. In time, once the US commercialisation infrastructure is fully established, Acacia will look to exploit the broader label of prophylaxis for N+V (either used in place of or in addition to ondansetron and dexamethasone).

Amisulpride is a selective dopamine receptor antagonist with high affinity for mesolimbic D2 and D3 receptors (both have been implicated in the emetic response). In Europe it has been approved at doses of 400-800mg for the treatment of acute episodes of schizophrenia and at 50-300mg for maintenance therapy in schizophrenia. At these high treatment doses, amisulpride is associated with clinical side effects relating to the dopamine antagonist class such as sedation, restlessness and extrapyramidal side effects (EPS). Despite its efficacy as an antipsychotic agent, the drug was not developed for use in the US market. This decision appears to be a strategic one made by the drug's originator (Sanofi-Aventis) rather than a molecule specific efficacy or side effect issue. Acacia Pharma identified amisulpride (Exhibit 2) as a potential candidate for the treatment of N+V in surgical and oncology patients after screening a multitude of dopamine receptor antagonists for a predefined target profile (Exhibit 3), which included potency similar to droperidol, no major EPS effects and low drug interaction potential (enabling combination use).

Exhibit 2: BARHEMSYS designed to provide the solution for PONV



Source: Company presentations

Exhibit 3: Target profile for a D2 antagonist

Efficacy	Potency similar to droperidol
	Long plasma half life (≥ 6 hours)
Safety	Good pharmacological selectivity
	Low potency on HERG channels
	No major extrapyramidal side effects (EPS)
	Low drug interaction potential
	Wide range of approved clinical doses (safety margin)
Other	Physical chemistry to allow IV formulation
	Off-patent, but with potential for IP angle

Source: Company presentations

Four pivotal phase III trials form basis of the NDA

Acacia Pharma is targeting a broad and differentiated label for BAREMSYS for the treatment of established PONV, with or without prior prophylaxis and prophylaxis of PONV alone and in combination. The four Phase III pivotal clinical trials (DP10015, DP10017, DP10018 and DP10019) have completed and, alongside four additional supportive clinical trials, formed the NDA dossier submitted to the US FDA. DP10018 and DP10019 support the use of BARHEMSYS as rescue therapy, either as monotherapy or in combination with standard-of-care antiemetic drugs, respectively. DP10015 and DP10017 support the use of BARHEMSYS for the prophylaxis of PONV as monotherapy or in combination respectively. Importantly, there were no safety signals (extrapyramidal side effects or cardiac events) reported across any of the four trials. This is a critical differentiation factor for BARHEMSYS given the side effect profile, which has limited or led to the withdrawal of previous dopamine antagonists used to treat PONV.

DP10018: BARHEMSYS monotherapy in treatment (no prior antiemetic prophylaxis)

This double-blind study (ClinicalTrials.gov Identifier: NCT02449291) compared 5mg and 10mg of BARHEMSYS with placebo for the treatment of established PONV in patients who had not received any prophylactic antiemetics at the time of anaesthesia induction (n=560). The primary efficacy endpoint of the trial was complete response (CR) defined as no emesis in 30 minutes to 24 hours after treatment or use of rescue medication in 0-24 hours after treatment (Exhibit 4).

Exhibit 4: BARHEMSYS 5mg or 10mg in rescue treatment (no prior prophylaxis)

DP10018	Placebo		BARHEMSYS 5mg		p value	BARHEMSYS 10mg		p value
Number of subjects	181		191			188		
Complete Response (24hr) - primary endpoint	39	22%	60	31%	0.016	59	31%	0.016
Complete response (2h)	79	44%	112	59%	0.002	105	56%	0.010
Vomiting	62	34%	64	34%	0.440	57	30%	0.209
Rescue medication use	135	75%	121	63%	0.010	119	63%	0.010
Nausea AUC (0-2h)	5,645		4,513		0.007	4,863		0.022

Source: Company reports

DP10019: BARHEMSYS monotherapy for prophylactic use in PONV

DP10019 (ClinicalTrials.gov Identifier: NCT02646566) evaluated safety and efficacy for the treatment of established PONV, with or without prior prophylaxis. Data from Phase III study DP10019 support BARHEMSYS efficacy as PONV rescue therapy (Exhibit 5). 10mg IV led to an

absolute reduction of N+V of 13% at 24 hours and 21% at 2 hours vs placebo (n=702). Furthermore, the average stay in a PACU was 35 minutes less with 10mg BARHEMSYS vs placebo (141 minutes vs 176 minutes) and the average hospital stay was six hours shorter (50hrs vs 56hrs).

Exhibit 5: BARHEMSYS 10mg in rescue treatment (patients receiving prior prophylaxis)

Study DP10019	Placebo		10mg BARHEMSYS		p value
Number of subjects	235		230		
Complete response (24hrs), primary endpoint	67	29%	96	42%	0.003
Complete response (2hrs)	116	49%	160	70%	<0.001

Source: Company reports

DP10015: BARHEMSYS monotherapy for prophylactic use in PONV

This placebo-controlled Phase III study (ClinicalTrials.gov Identifier: NCT01991860) evaluated 5mg of BARHEMSYS monotherapy (IV) administered at the time of anaesthesia induction in 342 adult surgical patients with two or more risk factors for PONV. The primary efficacy endpoint of the trial was complete response (CR) defined as no episodes of vomiting or retching or requirement for antiemetic rescue medication in the 24 hours after the end of surgery. Patients who received BARHEMSYS reached CR of 44.3% vs 32.5% on the placebo arm (p=0.013). Secondary efficacy endpoints included incidence of rescue medication use, time to PONV and time to first use of rescue medication (Exhibit 6). Importantly, the incidence of rescue medication use decreased from 66.9% to 54.5% (p=0.010), median time to onset of PONV (failure of prophylaxis) increased from 341 minutes with placebo to 752 minutes with BARHEMSYS (p=0.004) and median time to first rescue medication use increased from 371 to 859 minutes (p=0.003). In terms of safety, BARHEMSYS was broadly comparable to placebo aside form a small and transient increase of serum prolactin levels in the BARHEMSYS group (class effect of dopamine antagonists).

Exhibit 6: mITT* analysis of 342 dosed patients in the DP10015 study

mITT population	Placebo		5mg BARHEMSYS		p value
Number of subjects	166		176		
Complete response*	54	32.5%	78	44.3%	0.013
Vomiting	37	22.3%	35	19.5%	0.293
Rescue medication use	111	66.9%	96	54.5%	0.010
Significant nausea	82	49.4%	69	39.2%	0.029
Any nausea	102	61.4%	94	53.4%	0.067

Source: Company reports. Note: *mITT = modified intent to treat.

DP10017 BARHEMSYS combination therapy for prophylactic use in PONV

This Phase III trial (Clinical trials identifier NCT02337062) assessed BARHEMSYS as part of combination prophylaxis in high-risk patients (as defined as three or four PONV risk factors) in 1,147 high-risk patients, of which 51% of surgical patients received ondansetron as combination antiemetic and 48% received a corticosteroid (dexamethasone or betamethasone) as combination (Exhibit 7). The average PACU stay was 17 minutes shorter on 5mg BARHEMSYS combination prophylaxis than placebo (145 minutes vs 162 minutes).

Exhibit 7: BARHEMSYS 5mg as part of combination prophylaxis in high-risk patients

Study DP10017	Placebo plus standard antiemetic		5mg BARHEMSYS plus standard antiemetic		p value
Number of subjects	575		572		
Complete response, primary endpoint	268	46.6%	330	57.7%	<0.001
Vomiting	115	20.0%	79	13.8%	0.003
Rescue medication use	284	49.4%	234	40.9%	0.002
Significant nausea	274	47.7%	212	37.1%	<0.001
Any nausea	335	58.3%	286	50.0%	0.002

Source: Company reports

Safety profile differentiation

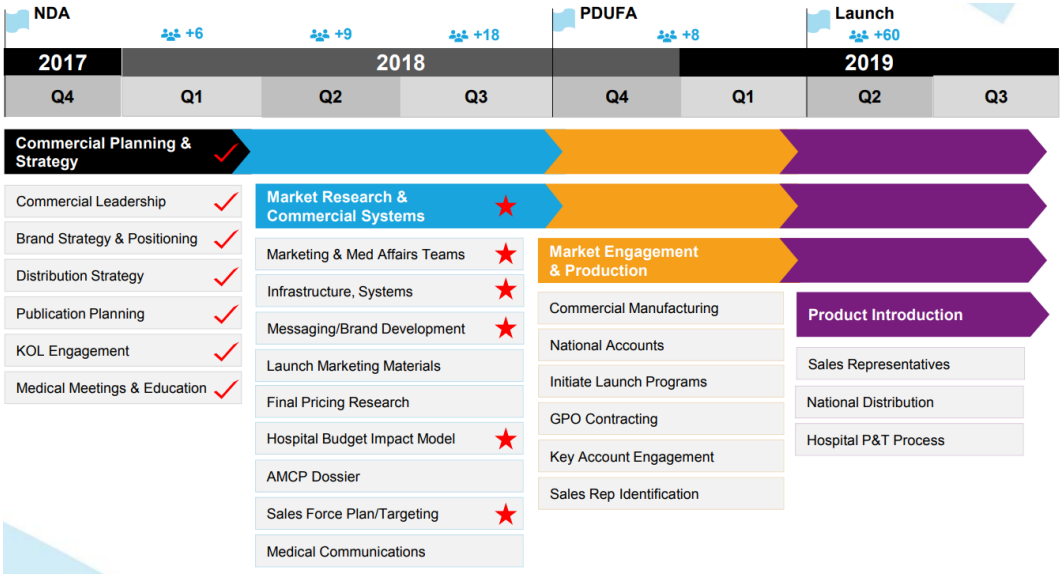
Across its Phase III trials BARHEMSYS has established an improved safety profile compared to other antiemetic classes (no cardiac toxicity, no EPS, no sedative effects and no anticholinergic effects). There was no increase over placebo in relation to anxiety, depression, blood sugar abnormalities, GI disturbances and headache. Importantly, discontinuation of droperidol for PONV historically was related to QT interval prolongation of 25± 8 millisecond (ms) (QT interval is measured by ECG; prolongation of the interval can lead to a ventricular arrhythmia known as Torsades de Pointes, which can result in sudden cardiac death). Drug-induced QT prolongation of less than 10ms is not considered significant and this is the threshold for regulatory concern; data up to 20ms are inconclusive and above 20ms raise concerns. The maximum impact of BARHEMSYS at a 5mg dose on QT prolongation was 5.0ms, and for 10mg was calculated under standard extrapolation to be 7.9ms. This is a critical differentiating factor.

The commercial opportunity in PONV

The company's business model centres on enhancing economic returns by commercialising BARHEMSYS in the US market through a targeted hospital-focused salesforce; outside the US the group will seek regional partnership deals.

In the more lucrative US market, Acacia Pharma will market and commercialise BARHEMSYS through its own sales and marketing infrastructure of 60 medical reps initially (rising to 100 reps over three years). These reps will target ~1,600 hospitals that conduct ~80% of surgical procedures in the US focusing on PONV rescue and PONV prophylaxis indications for BARHEMSYS. Acacia Pharma's management team has extensive experience in the discovery, development and commercialisation of hospital pharmaceutical products and in drug repurposing, which will be critical to product success. To date, Acacia has made 21 hires in its US subsidiary (total staff of 22 in the US, expected to rise to 40 by year-end) as it starts to build the US commercialisation team ahead of potential approval by its 5 October PDUFA date. Key suppliers have been appointed for product distribution, marketing and advertising. If BARHEMSYS is approved, Acacia plans to continue hiring according to the strategy it has presented (Exhibit 8).

Exhibit 8: BARHEMSYS launch plan



Source: Acacia Pharma. Note: Ticks refer to completed activity; stars are ongoing processes.

Complex US commercial market means execution is key

In the US, Acacia plans to focus its BARHEMSYS commercial sales team on hospital-based anaesthetists and surgical teams. Assuming BARHEMSYS is approved with the label Acacia seeks, we anticipate that the company will face three key challenges to the successful commercialisation of BARHEMSYS in the US: 1) salesforce effectiveness including marketing and education; 2) pricing and hospital formulary access; and 3) third-party payor reimbursement and potential contracting.

1. Using an initial salesforce of 60 reps, Acacia plans to focus on the ~1,600 hospitals that it estimates account for ~80% of applicable surgical procedures across the US. Acacia has based its account targeting on the previous experience of the senior sales teams, particularly CCO Mike Bolinder, who led the commercialisation of OFIRMEV (pain management, API is acetaminophen, commonly referred to as paracetamol outside the US) when he was head of hospital marketing at Mallinckrodt. Acacia is planning to focus on hiring experienced reps, which it believes will enable it to drive the uptake needed, albeit at an increased cost per rep. One of the core challenges will be the education about and marketing of BARHEMSYS; as the last treatment for PONV was approved in 2009 (Emend aprepitant, NK-1 receptor) some physicians may be unfamiliar with the medical need for a new antiemetic for these indications. An initial focus on educating and informing KOLs, particularly anaesthetists, will be important to drive uptake.
2. To be able to successfully commercialise BARHEMSYS, Acacia must ensure the product is accepted onto each hospital's formulary (a list of drugs that healthcare providers in the hospital can prescribe). This often requires the hospital's Pharmacy & Therapeutics (P&T) committee to be convinced of the clinical and economic benefits of the drug before approving it to be on formulary. Once on hospital formulary, treatment with BARHEMSYS would be provided under Diagnosis-Related Group (DRG) codes where the treatment costs would be included in the total cost of a surgery. Under the DRG system, hospitals will charge third-party payors a standard price for a procedure. The cost of the care the hospital provides under this code will be determined by the hospital. As such, the hospitals are incentivised to reduce costs. Acacia will need to demonstrate that BARHEMSYS can provide a pharmacoeconomic benefit at its specified price point (as evidenced by the reduction in PACU and hospitalisation stay overall (clinical trials DP10017 and DP10019). To date, research undertaken by Acacia Pharma has highlighted that a prophylaxis single-dose 5mg IV would likely be priced at approximately $40, with a rescue single-dose 10mg IV priced at approximately $80. Any significant deviation from that price could significantly alter Acacia's financial returns. We note that commonly utilised drugs like ondansetron and Emend (aprepitant) are typically priced between $10 and $130 per pill, with generically available ondansetron at the lower end of the range vs branded NK-1 antagonist Emend at the top end. Acacia believes that BARHEMSYS used as a rescue treatment results in a 35-minute reduction in PACU time and a 0.25-day reduction in overall hospital stay, which would generate a $670 net cost saving. We note that Acacia may need to undertake additional, costly, real-world studies to further confirm BARHEMSYS's pharmacoeconomic benefit if uptake is slower than anticipated.
3. BARHEMSYS use in the hospital setting and utilisation under DRG codes mean third-party reimbursement will not be as important as it is for many other drugs or treatments that are utilised outside the hospital setting. However, for certain treatment settings, like outpatient surgical settings, Acacia will still need to interact with and gain sufficient reimbursement from third-party payors and/or government agencies. Driven by political pressure, drug pricing and reimbursement continues to be subject to downward pressure and third-party payors are increasingly questioning the effectiveness of a therapy, its price and whether it is a necessity. These providers take many different forms, including government healthcare programmes like Medicaid and Medicare, private managed care providers like Blue Cross Blue Shield and

private insurers like UnitedHealth. We note that in CINV patients (who are treated in the outpatient setting), reimbursement will be a more important factor and will be key to the product's success.

Outside of commercial pressures in the US, Acacia faces a variety of operational challenges. Its active pharmaceutical ingredient (API) amisulpride is currently sourced from one manufacturer (Patheon, part of Thermo Fisher Scientific), with which Acacia has a commercial supply agreement. While the API is currently single sourced, it is available from multiple sources and we envision limited supply chain risk at this time, particularly as the finished product has a three-year lifespan and the low cost of the API would enable sufficient stocking. However, any swapping of suppliers or limitations in production capacity at the current supplier could have an effect on the pricing, quality and availability of BARHEMSYS.

In the long term Acacia plans to leverage its salesforce to sell APD421 (dependent on successful FDA approval) to treat CINV. Acacia predicts that this will require an additional 40 sales reps; however, we note the company will be targeting different specialists (oncologists) compared with BARHEMSYS and the ability to target this distinct patient population may require a higher number of reps and associated cost than currently anticipated.

Patent and exclusivity periods

Acacia's ability to protect its BARHEMSYS franchise will be vital to its long-term sales prospects. Acacia expects its key patents to remain valid until 2031 in the US, EU, Japan and China. The company currently has applications pending that aim to extend exclusivity periods to 2038. To date, Acacia has faced no patent challenges, but any future litigation could prove detrimental to its financial position in terms of both legal costs and lost sales. We would anticipate higher barrier to generic entry given the intravenous formulation of amisulpride and fact that the drug has never been available in the US market.

Exhibit 9: BARHEMSYS and APD403 patents

Patent description	Application number	Valid until	Valid countries
PONV	PCT/GB2011/050472	03/2031	Granted in the US, Australia, Mexico, New Zealand, South Korea, Israel, South Africa, Japan, China, Hong Kong, Canada and by the EPO. Pending in other countries where applications have been made.
PONV	PCT/GB2017/053288	11/2037	Pending
PONV	PCT/GB2018/050374	02/2038	Pending
PONV	GB1720607.9	12/2038	Pending
CINV	PCT/GB2011/050472	03/2031	Granted in the US, Australia, New Zealand, South Korea, Israel, South Africa, Japan, China, Hong Kong and by the EPO. Pending in other countries where applications have been made.
CINV	PCT/GB2016/050998	04/2036	Pending in all countries where applications have been made.

Source: Acacia Pharma, Edison Investment Research

PONV a common surgery-related issue

Post-operative nausea and vomiting (PONV) is the second most common complaint after pain in patients who have undergone surgery. PONV is associated with many different risk factors (Exhibit 10) and risk is assessed using a scoring system such as Apfel simplified scoring system (score 1 for gender, non-smoker, perioperative opioid use, prior history of PONV or motion sickness).

Exhibit 10: Risk factors for PONV

Risk factors	Notes
Patient factors	Gender (female), being a non-smoker, previous history of PONV, obesity increase risk
Perioperative factors	Use of perioperative opioid analgesia
Intraoperative factors	Type of surgery (abdominal surgery, cholecystectomy, gynaecological and laparoscopic surgery are associated with higher risk. Anaesthetic factors (eg drugs such as ether, ketamine and cyclopropane increase risk, regional anaesthesia lowers risk by 9x less than general anaesthesia). Anaesthesia: etomidate (used as an anaesthetic induction agent) increased risk of PONV vs other agents (sodium thiopental).
Post-operative factors	Pain, use of opioid analgesia

Source: Edison Investment Research

The pathophysiology of PONV is multiform, involving various pathways and receptors. Stimulation of five different afferent pathways leading to the vomiting centre, an ill-defined region in the brain, can activate N+V via various receptors. Neurotransmitters involved in the pathophysiology of N+V include serotonin (5-HT_3 receptor), dopamine, acetylcholine, histamine and substance P (NK-1 receptor). This complexity means that combination therapy for PONV prophylaxis is recommended, particularly in high-risk patients as blockade on one pathway or receptor is unlikely to alleviate symptoms in all patients. The incidence of PONV reduces from 52% when no antiemetics were used, to 37%, 28%, and 22% when one, two and three antiemetics, respectively, are administered. The American Society of Anaesthesiologists suggests that patients who have three or more risk factors (Apfel score) should receive at least two prophylactic antiemetic agents of different classes preoperatively or intraoperatively. Combinations include 5-HT_3 antagonist plus dexamethasone or droperidol or all three, or droperidol plus dexamethasone.

Exhibit 11 highlights the main drugs used in the management of PONV classified by the mode of action at the various receptors involved in the multiple pathways implicated in the pathophysiology.

Exhibit 11: Main antiemetic drug classes for PONV

Class	Examples	Notes
Serotonin (5-HT_3) antagonists	Ondansetron, dolasetron, granisetron,	Risk of QT prolongation; ondansetron FDA recommendation single dose limit does not exceed 16mg. FDA banned dolasteron for ~CINV due to concerns of QTc prolongation and Torsades de Pointes.
Corticosteroids	Dexamethasone	Relatively slow set of onset so is administered at the time of induction
Anticholinergics/antimuscarinics	Scopolamine	Transdermal scopolamine used in the setting of patient-controlled analgesia
Histamine (H1) antagonists	Cyclizine, Promethazine, diphenhydramine	Side effects limit use
Dopamine (D2) antagonists	Domperidone, metoclopramide, droperidol	Metoclopromide is a weak antiemetic and side effects include dyskinesia and extrapyramidal side effects. Droperidol use has greatly declined in the US from 2001 as a result of the FDA black box restriction due to significant cardiovascular (CV) events.
Neurokinin-1 antagonist	Aprepitant, cospitant, rolapitant	Aprepitant and rolapitant approved for CINV. Aprepitant is more effective than ondansetron in the 24-48 hour post-op period.

Source: Edison Investment Research

However, even prophylactic combination therapy given before or during the operation does not eliminate PONV in all patients, and those that continue to experience symptoms of PONV are candidates for rescue therapy. When rescue therapy is required, it is recommended that a different class of antiemetic is used to what was given prophylactically. Given that 90% of medium to high-risk patients receive a 5-HT_3 antagonist and around 50% will receive a corticosteroid as a second, drug options for rescue therapy remain limited.

CINV additional indication potential launch 2022

Acacia Pharma is developing APD403 (repurposed amisulpride, the active ingredient in BARHEMSYS in both an intravenous form for use alongside chemotherapy and an oral version for use at home in the subsequent days) for management of chemotherapy-induced nausea and vomiting (CINV) as a follow-on indication. Oncologists commonly prescribe CINV drugs alongside chemotherapy across a range of cancer types as N+V is a common and intolerable side effect of many of these agents.

According to the NIH National Cancer Institute, an estimated 1.7 million new cases of cancer are expected to be diagnosed in the US in 2018. In 2012 there were 14.1 million new cancer cases worldwide. The incidence of cancer is growing due to demographic factors, and the number of new cancer cases per year is expect to grow to 23.6 million by 2030. CINV is a common side effect of chemotherapy drug regimens in cancer treatment. Rates of developing CINV depend on the class of chemotherapy agency; the National Comprehensive Cancer Network (NCCN) classification is based on the level of emetogenicity. Level 5 – high emetic chemotherapy (HEC) risk is associated with 90% frequency of emesis and Level 3/4 moderate emetic chemotherapy (MEC) risk is associated with 30–90% frequency of emesis. Many standard-of-care chemotherapies (eg cisplatin, cyclophosphamide, oxaliplatin, carboplatin, doxorubicin, irinotecan) fall into Level 3, 4 or 5. Furthermore, combination chemotherapy agents can increase the risk of developing emesis, eg cyclophosphamide and doxorubicin are both classified as MEC but, when given together, the regimen is highly emetic. CINV can be defined as acute CINV (occurs within 24 hours or receiving chemotherapy infusion), delayed CINV (occurs after 24 hrs, 2–5 days) or anticipatory CINV.

Guidelines published by the American Society of Clinical Oncology (ASCO), the Oncology Nursing Society (ONS) and the National Comprehensive Cancer Network (NCCN) are similar. Current guidelines advocate the use of 'triple therapy', the combination of three different antiemetic classes consisting of a 5-HT_3 antagonist (eg ondansetron), corticosteroid (eg dexamethasone) and NK-1 antagonist (eg aprepitant, or its IV prodrug fosaprepitant) to target the various neuronal pathways implicated. All three drugs are given just prior to chemotherapy for prophylaxis of acute CINV, and oral dexamethasone is given two to four days afterwards to prevent delayed CINV.

Despite available treatment options, 30-50% of patients receiving HEC do not achieve adequate CINV control (despite 97% receiving a 5-HT_3 antagonist and 78% receiving a steroid), particularly with respect to delayed nausea (triple drug therapy can control acute CINV in 80-90% of patients on HEC). Guidelines recommend consideration of using a dopamine D2 receptor antagonist in patients, although side effects and cardiac events have limited use and only IV metoclopramide is actually approved for use in CINV. Given amisulpride's favourable efficacy and safety profile to date and assuming the Phase III programme replicates findings so far, it could be the only dopamine antagonist to receive approval for CINV combination use.

APD403 has completed two Phase II studies, one of which evaluated IV and oral drug versus placebo in HEC patients (cisplatin/anthracycline/cyclophosphamide) in delayed CINV. 46% of patients on the drug met the primary endpoint of delayed-phase complete response (no vomiting and no rescue medication for 24-120 hours after chemotherapy) vs 20% in the placebo arm (p=0.002), representing a relative risk reduction of 32%. Safety was no worse than placebo, showing that APD403 is a safe and efficacious treatment for CINV. Given amisulpride is a dopamine antagonist and therefore works with a different mechanism of action to approved antiemetic drugs for CINV, the rationale is for combination use to improve delayed-phase nausea.

Acacia plans to initiate an acute phase, dose-ranging Phase II/III study in H119. The Phase III programme is expected to start in 2020. The FDA has confirmed the requirement for two Phase III trials (in cisplatin patients, an HEC agent) plus additional safety and efficacy data in breast cancer patients receiving AC chemotherapy (Adriamycin plus cyclophosphamide). Safety will be paramount, particularly in terms of repeated dosing, on the basis that cancer patients are on a multitude of other drug treatments. Contingent on the filing of an NDA efficacy supplement in 2022, we forecast launch of APD403 for CINV in 2022. CINV is an important additional indication given the commercial opportunity in CINV. Successful operational execution in building the US sales and marketing infrastructure in 2019-21 will also lay important foundations for subsequent launch of the new CINV indication, enabling Acacia Pharma to build its speciality franchise. The company will need to increase the number of sales reps moderately to target hospital- and community-based oncologists for this indication.

Commercial opportunity

In 2017, the global CINV market was valued at $1.7bn (source: MarketInsights reports) and rising prevalence of cancer has led to increased rates of chemotherapy use. The most highly prescribed drugs in CINV are the 5-HT_3 receptor antagonist and Neurokinin-1 receptor antagonists. While volumes have been increasing, the market has been affected by availability of generic drugs, particularly in the 5-HT_3 receptor class. Acacia Pharma estimates that 6.6m cycles of chemotherapy in the US have CINV treatments prescribed alongside; ~3.9m HEC cycles are on triple therapy CINV, and an additional ~one million are on MEC cycles (triple therapy). Based on the encouraging Phase II data presented so far, we forecast peak sales potential of $108m. We assume pricing of $300 per chemotherapy cycle. We forecast peak penetration of 12.5% in 2021 and assume amisulpride use in the 50% of patients receiving HEC or MEC agents who do not achieve adequate CINV control.

Sensitivities

Acacia Pharma is subject to various sensitivities common to speciality pharmaceutical companies, including commercialisation (pricing, reimbursement, uptake and competition), manufacturing and financing risks. The key sensitivities for Acacia Pharma relate to execution risk. Our sales forecasts and valuation are dependent on the successful US commercialisation of BARHEMSYS (subject to approval by the US FDA later this year). Furthermore, with the focus on one asset in the short term, valuation is skewed to and dependent on BARHEMSYS. Therefore, if BARHEMSYS fails to obtain approval, it would have a serious and detrimental effect on Acacia's long-term strategy and our valuation. We note significant commercial risks including the group's ability to recruit, train and retain adequate numbers of effective sales and marketing personnel; the ability of sales personnel to obtain access to or persuade adequate numbers of anaesthetists and/or physicians to prescribe any future products; the lack of complementary products offered by sales personnel, which may put the group at a competitive disadvantage relative to companies with more extensive product portfolios; unforeseen costs and expenses associated with creating an independent sales and marketing organisation; and costs of marketing and promotion above those anticipated by the group.

Valuation

Our valuation of Acacia Pharma, at €579m or €10.9/share, is mainly based on a risk-adjusted NPV model of BARHEMSYS for rescue treatment and prophylaxis of PONV, in addition to the CINV opportunity for the US market only. We do not include any contribution from Europe or ROW opportunities as these will be dependent on out-licensing agreements with various future partners, on which we have no visibility. We include end-June net cash of €32.3m (£29.0m) in our valuation and use a 12.5% discount rate.

Exhibit 12: Valuation

Product	Indication	Launch	Peak sales ($)	Value (€)	Probability	rNPV (€m)	rNPV/share (€)
BARHEMSYS US only	PONV	2019	404.7	594.8	90%	533.7	10.1
APD403 US only	CINV	2024	107.9	71.9	30%	12.9	0.2
Net cash at 30 June 2018				32.3	100%	32.3	0.6
Valuation				698.9		578.9	10.9

Source: Edison Investment Research

For the US PONV market, we have valued the opportunity in both high-risk prophylaxis patients and rescue treatment patients. For high-risk prophylaxis, we assume 65 million patients have surgical procedures pa, of which 49 million receive antiemetic treatment and 18 million of those are high risk. We assume a peak penetration of 10% for BARHEMSYS and an initial price of $40 per 5mg dose with a gross to net discount of 20%.

For rescue treatment patients, we assume that 32% of those who receive prophylaxis fail treatment (approximately 16 million) are eligible to receive rescue treatment. Of these patients, we forecast a peak penetration for BARHEMSYS of 10%. We assume an initial price of $80 per 10mg dose with a gross to net discount of 20% and forecast that each patient receives two doses.

We assume no R&D costs for BARHEMSYS, although future pharmacoeconomic studies may have to be undertaken to drive sales. For S&M we assume that 60 sales reps are hired initially (as per company guidance) at a cost of $250k per rep, with the total number of reps growing to 100 in the first four years of launch. We forecast additional costs in the region of $150-200m in the first five years of commercialisation that relate to the wider US commercial team including marketing, managed markets, commercial operations and back office. We assume initial COGS of 5% for the 10mg vial and 6% for the 5mg vial.

For APD403 in CINV we forecast a smaller opportunity then PONV due to a smaller market size. Of the approximately five million moderate to high emetogenic patients, 50% will require rescue treatment. We forecast a peak penetration of 12.5%, the hire of an additional 40 sales reps (as per company guidance), COGS of 5% and the price of a 200mg oral treatment at $300 per cycle.

Below we include sensitivity analyses on how pricing and penetration assumptions for BARHEMSYS for PONV prophylaxis and rescue treatment, and APD403 for CINV could impact on our valuation of Acacia Pharma.

Exhibit 13: BARHEMSYS PONV prophylaxis

		Price, $				
		30	35	40	45	50
Penetration	5.0%	445	459	472	485	499
	7.5%	485	505	525	546	566
	10.0%	525	552	579	606	632
	12.5%	566	599	632	666	699
	15.0%	606	646	686	726	766

Source: Edison Investment Research

Exhibit 14: BARHEMSYS PONV rescue treatment

		Price, $				
		70	75	80	85	90
Penetration	5.0%	176	200	223	246	270
	7.5%	332	367	402	436	471
	10.0%	487	533	579	625	671
	12.5%	641	699	756	814	871
	15.0%	795	864	933	1002	1071

Source: Edison Investment Research

Exhibit 15: APD403 CINV

		Price, $				
		250	275	300	325	350
Penetration	7.5%	560	561	563	565	567
	10.0%	566	569	571	574	576
	12.5%	572	576	579	582	585
	15.0%	579	583	587	590	594
	17.5%	585	590	594	599	603

Source: Edison Investment Research

Financials

Following the £33.9m net raise from the IPO in March and the drawdown of $10m from the $30m credit facility with Hercules, Acacia has £35.7m in cash as of 30 June. £34.4m is held in US dollars to meet expected dollar expenses. In June, Acacia repaid £3.7m of outstanding debt on the Silicon Valley debt facility.

To fund operations we forecast that an additional c £75m (in addition to the remaining $20m from Hercules) will need to be raised in 2019 and 2020. We note that, for simplicity, in our model we currently illustrate this as a debt raise. However, Acacia management has stated that it plans to finance the company by a combination of equity and debt.

In the short term, revenues remain wholly dependent on the success of BARHEMSYS. We forecast no revenue generated in FY18 and FY19 revenues of £2.7m as the company expects to start rolling out the product.

We forecast a significant increase in expenses from historic levels driven by the commercialisation of BARHEMSYS and the clinical trial programme for APD403. FY17 SG&A and R&D were £1.5m each. We forecast R&D costs of £2.9m in FY18, growing to £7.7m in FY19. We anticipate that SG&A costs will increase to £16.7m in FY18, growing to £37.8m in FY19 driven by the investment in personnel.

Acacia reported a net loss of £5.7m in H118 (H117: net loss of £2.7m) driven in core by activities around the NDA filing. We forecast a net loss of £19.3m in FY18 and £43.6m in FY19. Based on the operational and price assumptions outlined above, we forecast that Acacia will reach break-even in 2023 and, in the longer term, operating margins could reach some 55%.

Exhibit 16: Financial summary

Accounts: IFRS, Year-end: December, £m	2015	2016	2017	2018e	2019e	2020e
PROFIT & LOSS						
Revenue	0.0	0.0	0.0	0.0	2.7	13.7
Operating revenues	0.0	0.0	0.0	0.0	2.7	13.7
Cost of sales	0.0	0.0	0.0	0.0	(0.2)	(0.9)
Gross profit	0.0	0.0	0.0	0.0	2.5	12.9
Gross margin %	N/A	N/A	N/A	N/A	0.9	0.9
SG&A (expenses)	(2.4)	(0.8)	(1.5)	(16.7)	(37.8)	(42.7)
R&D costs	(10.1)	(13.6)	(1.5)	(2.9)	(7.7)	(10.1)
Other income/(expense)	0.0	0.0	0.0	0.0	0.0	0.0
EBITDA (reported)	(12.5)	(14.4)	(3.0)	(19.6)	(43.0)	(39.9)
Depreciation and amortisation	0.0	0.0	0.0	0.0	0.0	0.0
Reported Operating Income	(12.5)	(14.4)	(3.0)	(19.6)	(43.0)	(39.9)
Operating Margin %	N/A	N/A	N/A	N/A	N/A	N/A
Finance income/(expense)	(2.6)	(1.8)	(3.5)	(0.7)	(2.5)	(2.6)
Exceptionals and adjustments	0.0	0.0	0.0	0.0	0.0	0.0
Reported PBT	(15.1)	(16.3)	(6.5)	(20.3)	(45.6)	(42.4)
Income tax expense (includes exceptionals)	2.2	2.8	0.3	1.0	2.0	1.6
Reported net income	(12.9)	(13.5)	(6.2)	(19.3)	(43.6)	(40.8)
Basic average number of shares, m	2.7	2.7	2.7	53.1	53.1	53.1
Basic EPS (£)	(4.83)	(5.06)	(2.32)	(0.36)	(0.82)	(0.77)
Adjusted EPS (£)	(4.83)	(5.06)	(2.32)	(0.36)	(0.82)	(0.77)
Dividend per share (£)	0.00	0.00	0.00	0.00	0.00	0.00
BALANCE SHEET						
Property, plant and equipment	0.0	0.0	0.0	0.0	0.1	0.8
Goodwill	0.0	0.0	0.0	0.0	0.0	0.0
Intangible assets	0.0	0.0	0.0	0.0	0.0	0.0
Other non-current assets	0.0	0.0	0.0	0.0	0.0	0.0
Total non-current assets	0.0	0.0	0.0	0.0	0.1	0.8
Cash and equivalents	5.5	6.9	3.1	12.7	14.0	11.1
Inventories	0.0	0.0	0.0	0.0	0.1	0.5
Trade and other receivables	0.3	0.5	0.2	0.0	0.5	2.3
Other current assets	2.1	2.8	0.3	0.3	0.3	0.3
Total current assets	7.9	10.2	3.6	13.0	15.0	14.2
Non-current loans and borrowings	0.0	5.0	0.0	6.7	56.7	96.7
Other non-current liabilities	0.0	0.0	0.0	0.0	0.0	0.0
Total non-current liabilities	0.0	5.0	0.0	6.7	56.7	96.7
Trade and other payables	2.9	5.1	1.0	9.1	5.2	5.8
Current loans and borrowings	0.0	2.7	5.2	0.4	0.0	0.0
Other current liabilities	7.8	9.1	15.2	0.0	0.0	0.0
Total current liabilities	10.8	17.0	21.4	9.5	5.2	5.8
Equity attributable to company	(2.8)	(11.7)	(17.8)	(3.2)	(46.8)	(87.6)
CASH FLOW STATEMENT						
Operating Profit	(15.1)	(16.3)	(6.5)	(20.3)	(45.6)	(42.4)
Depreciation and amortisation	0.0	0.0	0.0	0.0	0.0	0.0
Share based payments	0.0	0.0	0.0	0.0	0.0	0.0
Other adjustments	2.7	1.9	3.7	0.7	2.5	2.6
Movements in working capital	1.6	2.0	(3.8)	(6.9)	(4.5)	(1.5)
Interest paid / received	0.0	0.0	0.0	(0.7)	(2.5)	(2.6)
Income taxes paid	1.1	2.2	2.8	1.0	2.0	1.6
Cash from operations (CFO)	(9.7)	(10.2)	(3.7)	(26.3)	(48.2)	(42.4)
Capex	0.0	0.0	0.0	0.0	(0.1)	(0.7)
Acquisitions & disposals net	0.0	0.0	0.0	0.0	0.0	0.0
Other investing activities	0.0	0.0	0.0	0.1	0.1	0.1
Cash used in investing activities (CFIA)	0.0	0.0	0.0	0.1	0.0	(0.6)
Net proceeds from issue of shares	12.5	4.5	3.4	33.9	0.0	0.0
Movements in debt	0.0	7.1	(3.4)	1.9	49.6	40.0
Other financing activities	0.0	0.0	0.0	0.0	0.0	0.0
Cash from financing activities (CFF)	12.5	11.7	0.0	35.8	49.6	40.0
Cash and equivalents at beginning of period	2.6	5.5	6.9	3.1	12.7	14.0
Increase/(decrease) in cash and equivalents	2.8	1.4	(3.8)	9.6	1.4	(3.0)
Cash and equivalents at end of period	5.5	6.9	3.1	12.7	14.0	11.1

Source: Company accounts, Edison Investment Research

Contact details	Revenue by geography
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Management team

CEO: Dr Julian Gilbert	CFO: Christine Soden
Julian is chief executive officer and co-founder of Acacia Pharma. He has more than 30 years of commercial and technical experience in the pharmaceutical industry gained at a number of companies including Chiroscience, Mundipharma, British Technology Group (BTG) and Smith Kline & French (now GlaxoSmithKline). Prior to co-founding Acacia, he was co-founder and commercial director of Arakis. He has a degree in pharmacy and a PhD in pharmaceutics, both from the University of Nottingham.	Christine joined Acacia Pharma in February 2015, and is chief financial officer and company secretary. She is a chartered accountant and has substantial experience in technology and commercialisation-stage companies. Most recently, Christine served as CFO of AIM-listed medical device company, Electrical Geodesics. Previously she was CFO of UK-listed companies Optos, BTG and Celltech-Chiroscience, each of which had significant US operations. She also held senior finance roles with Oxagen and Medeva and is a non-executive director of e-Therapeutics, Fertility Focus and Futurenova.
CMO: Gabriel Fox	**CCO: Mike Bolinder**
Gabriel joined Acacia Pharma in 2008 from Hoffmann-La Roche, where he was head of global oncology marketing. Previously, he held various roles in development and medical marketing in Roche's market-leading oncology franchise. Prior to that, Gabriel was medical director for NeXstar Pharmaceuticals and Gilead Sciences, and subsequently acted as a consultant in both clinical development and commercial areas for a number of large and small pharma/biotech companies. Gabriel undertook his medical training at Cambridge University.	Mike joined Acacia Pharma in August 2015 as VP of marketing and was subsequently promoted to chief commercial officer. He has more than 15 years' experience in the pharmaceutical industry. Prior to Acacia, Mike served as head of marketing and commercial strategy for the Hospital division at Mallinckrodt Pharmaceuticals (via the Cadence Pharmaceuticals. acquisition), which commercialised Ofirmev, a post-operative pain control product promoted to anaesthetists and surgical teams. Prior to joining Cadence, he worked at Eli Lilly for 11 years in various sales and marketing roles of increasing responsibility across multiple therapeutic areas and successful product launches.

Principal shareholders	(%)
Gilde	32.0%
Lundbeckfond	23.6%
Novo A/S	14.4%
F-Prime	9.3%
AXA Investment Managers	5.1%

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