EDISON

Skyepharma

Company update

flutiform continues to impress

Pharma & biotech

Following the successful April 2014 £112m capital raise and early repayment of the bonds, Skyepharma's investment case now rests on the success of recent product launches. H114 results highlight the improving operational performance, especially the encouraging uptake for flutiform. The strengthened balance sheet enables a renewed emphasis on pipeline replenishment, with the licensing of a COPD technology platform notably promising. We raise our valuation from 260p a share to 326p.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/12	49.9	(14.2)	(27.8)	0.0	N/A	N/A
12/13	62.6	(0.1)	3.7	0.0	82.8	N/A
12/14e	78.9	15.4	16.4	0.0	18.7	N/A
12/15e	104.4	29.9	27.1	0.0	11.3	N/A

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

H114 results highlight improving operating outlook

H114 revenues rose by 10% to £34.4m, with the contributions from the recently launched products, including flutiform, Exparel and the new GSK respiratory products, comfortably offsetting the declines in the mature portfolio. Operating profit rose from £4.6m to £13.2m, with EBITDA up from £6.6m to £14.6m. The £25.5m exceptional finance charge means the reported loss per share widened from 3.6p to 27.0p. Net debt was £2.9m, versus £84.2m at December 2013.

flutiform uptake is ahead of our expectations

flutiform is an inhaled combination of fluticasone and formoterol for treating asthma, and its progress is rightly the focus of investor attention. In-market sales continue to track ahead of our, admittedly conservative, expectations. flutiform has been launched in 23 countries (including France in Q114, which triggered a €3m milestone), with further launches in other markets (including Spain, which will trigger a circa €2m milestone) expected during the year.

New product development back on the agenda

The successful restructuring of the balance sheet was a precursor to focusing on operating functions once more, with rebuilding of the pipeline a key objective. Skyepharma has acquired the rights to a novel inhaled therapy platform from Pulmagen Therapeutics. The first product, SKP-2075 for COPD, should complete a Phase II proof of concept trial by 2017. Further such deals, for both inhaled and oral delivery, are expected and should underpin the next phases of growth.

Valuation: Increased from 260p to 326p a share

We value Skyepharma using a DCF model based on detailed revenue projections through to 2027 (up from 2024), followed by a terminal value. Factoring in the revised new product revenue profiles results in an equity value of £342m, or 326p a share. This compares to our previous equity valuation of £273m, or 260p per share.

1 September 2014

Price	**306.25p**
Market cap	**£321m**
	$1.65/£, €1.21/£
Net debt at June 2014 (£m)	2.9
Shares in issue	104.8m
Free float	100%
Code	SKP
Primary exchange	LSE
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	24.9	22.8	311.3
Rel (local)	24.4	23.6	289.4
52-week high/low		315p	69.5p

Business description

Skyepharma is an expert oral and inhalation drug-delivery company. It combines proven scientific expertise with validated proprietary drug-delivery technologies to develop innovative oral and inhalation pharmaceutical products.

Next events

IMS	October 2014
FY14 update	December 2014
FY14 results	March 2015

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Edison profile page

flutiform effect beginning to show through

Over the last 18 months there has been a progressive and material reduction in Skyepharma's risk profile, which arguably is not yet fully reflected in the share price. It was the approval of flutiform (especially in Europe but to an extent in Japan too) that set the scene for the early repayment of the bonds in April 2014 and effectively removed the major uncertainty affecting the company's future. This means the company's outlook is now largely dependent on operational factors and no longer on its ability to service its previous debt burden.

The H114 results highlight the continuing progress across the board, with revenues arising from royalties on 15 products; however, despite this broad portfolio, the investment case rests on the success of the recently launched products, including flutiform, Exparel and the new generation of GSK inhalers. fluitiform in particular (in multiple territories) is expected to contribute over half of Skyepharma's royalty income, as well as profit from manufacturing and supply, with the market uptake continuing to suggest the sales trajectory could exceed our conservative expectations.

H114 sales were up 10% from £31.3m to £34.4m, driven by the contribution from the seven products approved since March 2012. These generated £21.8m of sales (up from £15.1m in H113), with a further £11.0m in milestones and contract development revenue (up from £6.3m H113), and more than offset the decline in certain older products. Although flutiform will be the main contributor over the medium term, the half-year performance was due principally to the strong growth of Exparel (a long-acting bupivacaine injection), with only minimal royalties from the new generation of GSK inhaled products (Relvar/Breo Ellipta, Anoro Ellipta and Incruse) during the period.

Following the divestment of the Injectable Business (now Pacira Pharmaceuticals) in 2007, Skyepharma receives a 3% share of net sales (until patents expire in September 2018) and contingent milestones that are not patent dependent. A milestone of $8m (£4.7m) was recognised in the period since cumulative annual sales exceeded $100m, although the cash will be received during H214. Further milestones of $8m and $32m are payable when annual sales reach $250m and $500m respectively, with an additional payment of $4m on the first commercial sale in a major European market.

flutiform, a combination of the inhaled corticosteroid (ICS) fluticasone and the rapid onset but long-acting bronchodilator (LABA) formoterol, is now launched in 23 markets, including 18 European countries and Japan (where it is partnered with Mundipharma and Kyorin respectively). The French launch triggered a €3m (£2.5m) milestone, with a further €2m milestone due with the launch in Spain (possibly H214). Royalties are paid on sales to wholesalers, which are distorted by launch stocks as flutiform continues its roll-out across Europe and so are not representative of prescribing patterns. Exhibit 1 shows the in-market sales (ie sales to pharmacies), which show the encouraging prescription trend seen so far is continuing.

Exhibit 1: flutiform in-market sales trends

€m	2012	Q113	Q213	Q313	Q413	Q114	Q214
EU/RoW (excluding Americas and Japan)	0.8	2.0	3.2	4.7	8.0	10.5	13.4
Japan	-	-	-	-	1.5	1.6	2.9
Total	**0.8**	**2.0**	**3.2**	**4.7**	**9.5**	**12.1**	**16.3**
Quarter on quarter total growth %		151%	58%	45%	103%	28%	34%

Source: IMS Health Data Q214, based on pharmacy sales excluding Cyprus, Iceland and Belgium hospitals

The Japanese uptake is particularly impressive given the market for inhaled treatments is still developing in Japan (oral treatment is still the preferred option, but GlaxoSmithKline and AstraZeneca are educating the market on the benefits of inhaled therapies) and that the full dose (120-puff) inhaler has yet to be launched. Since flutiform is a new inhaled drug, the maximum prescription is limited to 14 days (a 56-puff only inhaler) until 30 November 2014.

In Latin America, the first approval has been received in Argentina, with a review of the NDA ongoing in Columbia. These local filings use the EU data package, with small milestones for each major country approval and high single-digit royalties on net sales. Sanofi is the largest multinational pharmaceutical company in the region and is the partner for flutiform here. The continuing weakness of the local currencies, notably in Argentina and Brazil, is a cause for concern since the majority of the production costs are in Euros. Sanofi and Skyepharma are jointly reviewing the impact of the local currency movements.

Exhibit 2: Edison forecasts for flutiform-based revenue in Europe

	2013	2014e	2015e	2016e	2017e	2018e
EU asthma ICS/LABA market (£m)	3,288	3,433	3,598	3,785	3,928	3,972
flutiform market share	0.5%	1.8%	2.4%	3.2%	4.8%	5.2%
flutiform in-market sales (£m)	16.4	61.8	84.5	121.1	188.6	206.5
Skyepharma royalty (£m)	1.6	4.3	6.8	10.9	18.9	20.7
Skyepharma milestones (£m)	1.7	4.2	0.0	0.0	0.0	0.0

Source: Edison Investment Research. Note: Excludes €25m Mundipharma claw-back.

The European market is a particularly important sensitivity, with flutiform's commercial success here a key determinant of Skyepharma's outlook. The ICS/LABA combination segment is currently dominated by GlaxoSmithKline's (GSK) Seretide, followed by AstraZeneca's Symbicort, with Chiesi/UCB's Fostair/Foster trailing in a very distant third position. The market dynamics are set to change as new compounds, such as GSK's Relvar/Breo Ellipta and Anoro Ellipta, and generic competitors, such as Sandoz/Vectura's AirFluSal Forspiro (a copy of Seretide), enter the scene.

Exhibit 2 details our current expectations, updated for currency and market movements. Currently flutiform is indicated for the treatment of asthma[1] but Mundipharma initiated a 1,530-patient clinical programme in September 2013 to support a COPD indication, an important segment for ICS/LABA combinations. In July 2014 Mundipharma entered into a co-marketing agreement with Zambon for Italy, with launch of its version of flutiform, known as Abriff, due before end-2014. Mundipharma is also developing a breath-activated version of flutiform, which uses the standard canister in a novel breath-actuated device.

Exhibit 3: Edison's forecasts for Flutiform-based revenue in Japan

	2013	2014e	2015e	2016e	2017e	2018e
Japan asthma ICS/LABA market (£m)	756	794	833	875	919	965
Flutiform market share	0.2%	0.9%	1.8%	4.0%	6.0%	6.0%
Flutiform in-market sales (£m)	1.2	7.1	15.0	35.0	55.1	57.9
Skyepharma royalty (£m)	0.1	0.5	1.1	2.5	3.9	4.1
Skyepharma milestones (£m)	2.6	0.0	0.0	0.0	0.0	0.0

Source: Edison Investment Research

flutiform was launched in Japan by Kyorin in November 2013. Skyepharma receives high/mid-single-digit royalties on net sales. Our assumptions are summarised in Exhibit 3, along with a breakdown of the royalties and milestones.

New inhaled therapy platform being developed

In August 2014 Skyepharma acquired the rights to a novel inhaled therapy platform from Pulmagen Therapeutics (a private UK-based company). The principle is that an ultra-low dose of theophylline can be used to potentiate the anti-inflammatory effect of an inhaled corticosteroid (ICS). Skyepharma will use its inhaled drug development expertise to initially explore one combination product, SKP-2075, using theophylline with an undisclosed but well-characterised steroid

[1] flutiform is currently indicated for the regular treatment of asthma in patients aged 12 years and over (50/5µg and 125/5µg strengths), in adults (250/10µg strength) whose symptoms are not adequately controlled on an ICS and an as-required inhaled short-acting β2-agonist (SABA), and in those patients who are already receiving treatment with both an ICS and LABA.

(presumably fluticasone) for use in COPD. This will be progressed to a proof-of-concept (PoF) stage Phase II trial. This study will be powered to produce robust clinical data, so should involve several hundred patients being examined for a treatment duration of several months. The intention is to then partner the product to a major player in the respiratory area, which can fund and progress the larger-scale study programmes that would be required for approvals.

Skyepharma is responsible for the development programme, which is expected to start in H2 2014, with preliminary results due in 2017. The investment required to formulate a suitable inhaled dosage form and complete the Phase II PoF trial is estimated at c £14m and will be funded from internal cash generation. The deal involves no upfront or fixed fee, with Pulmagen receiving launch milestones (in specified but undisclosed markets) and a share of Skyepharma's licensing income from any eventual deal. The proportion of this share will reflect the amount of work that has had to be performed in developing SKP-2075.

The use of theophylline in asthma and COPD is not new, having been used in the treatment of respiratory diseases for more than 70 years. It is still in common use in some markets but its narrow therapeutic index (when used orally as a broncholdilator), coupled with the improved efficacy of inhaled beta-agonists as bronchodilators and, in asthma, inhaled corticosteroids as anti-inflammatories, means it is now relegated to third-line therapy. Theophylline's bronchodilator activity is thought to work through selective PDE (phosphodiesterase) inhibition, with the therapeutic dose equivalent to plasma levels in the 10-20mg/L range. Efforts to improve on theophylline's efficacy and minimising adverse effects have led to a number of selective PDEs inhibitors being developed, albeit with mixed results.

Around a decade ago it became clear that COPD patients on combination therapy (ICS plus SABA/LABA) fared better than expected with theophylline in their treatment regimen. The effect is thought to be an activation of histone deacetylases (HDAC), where impaired HDAC activity is associated not only with increased inflammatory activity but with a resistance to the anti-inflammatory responses normally seen with corticosteroids. The effect was particularly noticeable during exacerbations of COPD, with the addition of low dose theophylline improving the anti-inflammatory effects of the inhaled steroids. These effects were seen at plasma levels of 5-10mg/L, which are sufficiently low to effectively avoid the adverse effects that have limited theophylline's appeal. The understanding of these anti-inflammatory effects at such low doses has rekindled interest in theophylline, with the primary hope being it could overcome the resistance to corticosteroids that limits the usefulness of ICS agents in COPD.

Pulmagen undertook a small Phase II study to examine the effect of ultra-low dose theophylline (equivalent to plasma levels of 0.4mg/L) co-administered with budesonide on inflammatory markers and lung function in COPD. A total of 91 patients with moderate-severe COPD were treated for four weeks with nebulised budesonide (1mg twice daily) and 12.5mg of theophylline or placebo. The active arm contained 47 patients, with the results (presented at the American Thoracic Society annual conference 2010) suggesting such low doses of theophylline did restore the anti-inflammatory effects of ICS in COPD patients.

If the potentiating effect of low-dose theophylline on ICS therapy is confirmed in larger and more robust trials then it could find a useful role in treating all stages of COPD, with a possible role as an integral part of the widening range of inhaled combinations that are being employed. From a commercial perspective, such combination products would benefit not only from additional patent protection but would offer greater differentiation in what is becoming an increasingly complex and crowded therapeutic segment. Despite the attraction of this therapy platform, we will not include any value for SKP-2075 in our DCF model until the proposed Phase II trial has initiated.

Valuation

We currently value Skyepharma using a DCF model, although as meaningful profits begin to show through we will adopt an earnings-based approach too. Our DCF is now based on detailed forecasts through to 2027 (extended from 2024), discounted back at 10%, and employs a terminal value to reflect the expected cash flows after that. Although obviously based on somewhat subjective assumptions, these do help capture major effects, such as patent expiries and expected product competition. This approach effectively reduces the effect of the terminal value on our valuation and is, arguably, more reflective of Skyepharma's prospects.

Our expectations are based on conservative assumptions, notably for the flutiform contributions, and we will review these as the complex competitive situation (especially in Europe) unfolds. The repayment of the bonds in April 2014 has transformed our valuation, with the reduced finance charges materially improving shareholder value. Following the solid performance from the newer products, notably Exparel, we have revisited our forecasts. Exparel sales have materially exceeded market forecasts, with the result that the milestones, especially the $32m payable when annual sales reach $500m, appear achievable (as a result we now include this $32m payment in our 2017 forecast). Our DCF model currently results in an equity value of £342m, or 326p per share, which compares to our previous £281m, or 260p a share.

The most important sensitivity is, understandably, the degree of uptake for flutiform and its eventual peak sales. This reflects not just the effect on the royalty stream, but also the fact that the manufacturing income benefits disproportionately from the associated higher volumes. We have re-profiled our flutiform model slightly to reflect the current rate of market adoption but retained peak sales for flutiform in Europe of around £200m pa. This continues to reflect our conservative stance, especially ahead of an expected increase in competition both from the launch of new product combinations, as well as the introduction of generic versions of existing blockbuster products. To put this into perspective, a simple 10% increase/decrease in our flutiform sales assumptions currently results in our valuation increasing/decreasing by 8%.

Financials

Skyepharma has successfully restructured its balance sheet through a £112m (£104m net) equity raise to repay its bonds early. The repayment costs £95.6m, which represents a £25.2m discount to total forecast cash payments, with the balance, after transaction costs, (£8.2m) retained for general corporate purposes. The bond repayment has removed a large element of uncertainty that had been overhanging Skyepharma and now the focus is on operational, rather than financial, factors.

H114 results showed revenues up 10% from £31.3m to £34.4m, with gross profit up 74% from £12.2m to £21.2m as the reduced Lyon manufacturing volumes (which do not impact margin) and improving economies of scale with flutiform showed through. R&D spend was £5.3m, in line with H113, with net investment (excluding contract R&D) up from £0.4m to £1.8m with the additional spend reflecting the increased focus on new oral technologies. During H214 we expect a further increase as initial formulation work on SKP-2075 begins, but overall net R&D investment is likely to fall towards the higher end of the £3m to £6m guidance range. The slight increase in corporate costs, from £1.2m to £1.5m, meant operating profit (ex-exceptionals) rose from £4.6m to £13.2m. Similarly, EBITDA (ex-exceptionals) increased from £6.6m to £14.6m.

The reported net loss leapt from a £1.7m loss to a £17.7m loss due to the exceptional £25.5m finance charge (£25.1m of which related to the loss on extinguishing the bonds and £0.4m for the costs of the bond repayment), with reported loss per share similarly rising from 3.6p to 27.0p. Excluding the exceptional charge EPS would have been 11.8p. Operating cash flow rose from

£5.5m to £8.8m, but was largely consumed by debt repayment, interest and capex. Following the £112m capital raise to repay the bonds, net debt at June 2014 was £2.9m (down from £84.2m at December 2013).

Exhibit 4: Summary of changes to our forecasts

	2014e previous	2014e new	2015e previous	2015e new
Revenues (£m)	72.6	78.9	93.3	104.4
Operating profit (before GW and except.) (£m)	20.6	22.0	22.7	32.3
PBT (£m)	14.0	15.4	20.2	29.9
Net income (£m)	13.7	14.0	19.9	28.4
EPS (p)	16.0	16.4	19.0	27.1

Source: Edison Investment Research

Our changes to our forecasts for Skyepharma's key items are shown in Exhibit 4. As before, we have only included the known milestones and licensing fees (with the phasing of the c €2m milestone for the launch in Spain brought forward to 2014, the $8m Exparel milestone brought forward to 2015 and the first time inclusion of the $32m Exparel milestone in 2017). flutiform is expected to make the greatest contribution to the incremental growth, resulting in the generation of over half Skyepharma's royalties and the bulk of the manufacturing and supply income by 2018. Our expectations are based on conservative assumptions, notably for the flutiform contributions, and we will review these as the complexities of the ICS/LABA market become clearer. The GSK royalty payments are also an important consideration (the reduced market expectations for the rate of uptake of these products are still within our original forecasts) with virtually all the payments made flowing straight through to the bottom line.

Exhibit 5: Financial summary

£'000s	2012	2013	2014e	2015e	2016e
Year end 31 December					
PROFIT & LOSS					
Revenue	49,900	62,600	78,943	104,417	109,340
Cost of sales	(21,900)	(33,200)	(38,410)	(52,832)	(55,634)
Gross profit	28,000	29,400	40,534	51,585	53,706
Selling, marketing & distribution	(1,500)	(1,500)	(1,575)	(1,654)	(1,736)
R&D expenditure	(11,900)	(10,800)	(13,795)	(14,280)	(14,887)
Administrative costs & other	(2,000)	(3,500)	(3,765)	(3,940)	(4,125)
Operating profit	17,100	13,600	(5,101)	31,711	32,958
Goodwill amortisation	(700)	(900)	(600)	(600)	(600)
Exceptionals	4,500	0	(26,500)	0	0
Share-based payment	0	0	0	0	0
EBITDA	15,600	17,900	24,499	34,811	36,058
Operating profit (before GW and except.)	13,300	14,500	21,999	32,311	33,558
Net interest	(27,500)	(14,600)	(6,609)	(2,405)	(617)
Profit before tax (norm)	(14,200)	(100)	15,390	29,905	32,941
Profit before tax (FRS 3)	(10,400)	(1,000)	(11,710)	29,305	32,341
Tax	(200)	1,800	(1,400)	(1,500)	(4,253)
Profit after tax (norm)	(14,400)	1,700	13,990	28,405	28,688
Profit from discontinued operations	6,200	0	0	0	0
Profit after tax (FRS3)	(4,400)	800	(13,110)	27,805	28,088
Average number of shares outstanding (m)	29.5	46.1	85.2	104.8	104.8
EPS - normalised (p)	(27.8)	3.7	16.4	27.1	27.4
EPS - FRS 3 (p)	(14.9)	1.8	(15.4)	26.5	26.8
Gross margin (%)	56.1%	47.0%	51.3%	49.4%	49.1%
EBITDA margin (%)	31.3%	28.6%	31.0%	33.3%	33.0%
Operating margin (before GW and except.) (%)	26.7%	23.2%	27.9%	30.9%	30.7%
BALANCE SHEET					
Fixed assets	37,000	33,800	33,446	33,216	31,306
Intangible assets	5,100	5,300	5,000	4,800	4,600
Tangible assets	31,900	28,500	28,446	28,416	26,706
Investment in associates	0	0	0	0	0
Available-for-sale financial assets	0	0	0	0	0
Current assets	35,500	40,800	62,770	90,075	99,917
Stocks	5,800	8,800	11,097	14,678	15,370
Debtors	13,300	13,500	17,025	22,518	23,580
Cash	16,400	16,500	34,648	52,879	60,967
Other	0	2,000	0	0	0
Current liabilities	(34,300)	(33,500)	(35,241)	(51,640)	(39,658)
Creditors	(20,400)	(19,900)	(25,095)	(33,193)	(34,758)
Other creditors	(2,500)	(2,500)	(2,500)	(2,500)	(2,500)
Short-term borrowings	(10,100)	(9,800)	(6,646)	(14,947)	(1,400)
Deferred income	(1,300)	(1,300)	(1,000)	(1,000)	(1,000)
Long-term liabilities	(104,200)	(105,700)	(33,347)	(18,800)	(17,800)
Long-term borrowings	(87,000)	(90,900)	(18,647)	(5,100)	(5,100)
Deferred income	(11,900)	(10,600)	(9,600)	(8,600)	(7,600)
Provisions and other long-term liabilities	(5,300)	(4,200)	(5,100)	(5,100)	(5,100)
Associated with assets held for sale	0	0	0	0	0
Net assets	(66,000)	(64,600)	27,627	52,851	73,765
CASH FLOW					
Operating cash flow	18,500	14,400	21,709	30,453	27,695
Net interest	(7,300)	(3,600)	(2,909)	(2,405)	(617)
Tax	(200)	(200)	(1,400)	(1,500)	(4,253)
Capex	(900)	(2,400)	(2,446)	(2,470)	(790)
Purchase of intangibles	(200)	(1,100)	(300)	(400)	(400)
Acquisitions/disposals	0	0	0	0	0
Financing	0	0	105,000	0	0
Dividends	0	0	0	0	0
Other	4,000	100	(26,100)	(200)	0
Net cash flow	13,900	7,200	93,555	23,477	21,635
Opening net debt/(cash)	99,000	80,700	84,200	(9,355)	(32,832)
HP finance leases initiated	0	0	0	0	0
Other	4400	(10,700)	0	0	0
Closing net debt/(cash)	80,700	84,200	(9,355)	(32,832)	(54,467)

Source: Skyepharma, Edison Investment Research. Note: 2014 £25.5m of the exceptional item relates to early bond repayment.

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