

Alliance Pharma (APH)



Alliance has successfully built the base for a speciality pharma business – LBO style. With development milestones in 2006/7 it is poised for a significant earnings inflexion in 2008.

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I certify that this report represents my own opinions.

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Key Points

3 August, 2006
Price: 13.75p

Alliance Pharma is a Speciality Pharma company, which has built a solid marketing platform based on the debt funded acquisition of mature and growth products on to which higher value, development based products can be grafted. With development milestones in 2006/7, Alliance is poised for a significant earnings inflexion in 2008 which will transform the Company.

- **Alliance Pharma: a misunderstood European Specialty Pharma company**

As evidenced by its £42 million valuation, Alliance appears to be significantly underestimated by the financial community. While biotech companies with uncertain market prospects, no earnings and pouring cash down an R&D black hole command phantasmagoric valuations based on the next billion dollar therapeutic, Alliance is quietly building a profitable business with significant growth prospects.

- **Blackjack biotech vs. 'barbequed steak with some sizzle'**

It is granted that Alliance is unlikely to become a £1 billion company anytime soon but then, it is just as unlikely that most biotech's will become billion pound entities either. Alliance is also unlikely to be acquired at the kind of valuations that Big Pharma are paying to acquire potentially valuable products to fill their pipelines. Yet, the risk reward profile of Alliance versus biotech is lopsidedly in favour of Alliance. It may seem that this is a 'plodding' way to get to a significant return but how one gets there is not really the point is it?

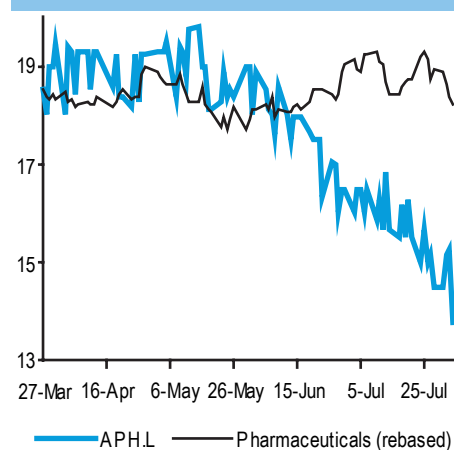
- **In pure baseball parlance, it's singles & doubles, which side steps the home runs**

Alliance is building a carefully crafted portfolio, intelligently financed and aimed at creating a platform where the level of risk can be ratcheted up somewhat in return for a much higher reward. Strict hurdle rates are applied and only products that meet this draconian profile are allowed into the portfolio.

- **An inexorable drive to reach an earnings inflexion point**

This should occur in 2008 when the higher return products overwhelm the core financial structure and product platform - a significant earnings breakout will be the result.

Price chart



Value of Equity

Core Scenario	£42m
Optimistic Scenario	£80m
Value per share:	26p - 50p

Company details

Quote	
Shares	
-London AIM	APH.L
-Berlin	ALP1.BE
Convertibles	
-London AIM	APHA.L
Hi-Lo last 12-mos. (p)	13.75 - 21.00
Shares issued (m)	162.10
Fully diluted (m)	198.89
Market Cap'n (£m)	21.90
Management ownership (%)	43.00
Stockbroker:	Numis Securities www.NumisCorp.com
Financial PR:	Buchanan Communciations www.buchanan.uk.com
Website:	www.alliancepharma.co.uk

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- ***It's not the debt stupid...focus on the underlying growth engine!***

In the short run, Alliance may look like an over-indebted company where the debt servicing is overwhelming the earnings from product revenue. However, in the medium term, Alliance is creating the critical mass that enables it to go up the value chain and accelerate its attainment of its earnings inflexion point.

- ***This business model has the ability to fine tune and modulate growth***

Alliance intends to balance its acquisitions between the three types of products that it already has in the portfolio: core unmanaged, core managed, and development products. It will also continue to balance the building of equity and debt.

- ***The result should be a significantly larger Company than today***

Alliance should sport a valuation that is at least significantly higher than the current one (rather than single digit multiples in biotech). So Caveat Emptor for the short-term investor and Ave to the patient, plodding, medium to longer term one!

- ***Isprelor the sure bet and Posidorm: the sleeping giant?***

Melatonin-induced sleep is a tricky area but the odds are favourable in the elderly market given past clinical work. If the Phase III trial is successful, Posidorm has the potential to change the dynamics of Alliance. If not, Plan B is not as exciting but it ain't that bad either!

- ***Alliance Pharma is a modified GARP¹ story***

Investors are being asked to look at the debt in a non-traditional fashion and look towards an earnings inflexion point and acceleration post 2007. In the meantime, the price does seem reasonable as the rest of the Company is not being valued at all! To be sure, biotech investors might have greater opportunities to make (and lose money) but in the end, with Alliance they probably have a surer bet.

¹ GARP - Growth at Reasonable Price

Alliance Pharma is a European-style 'Specialty' Pharma Company. It has a comparable profile and development path to that successfully trodden by a number of US companies in the past. The main difference is that it operates in the European arena where the preponderance of national healthcare systems, with effective price controls and strict hospital formularies, presents limitations. Adapting to this situation, Alliance has focused predominantly on hospital-orientated products where it can tap into stable or potentially stable products where physician-prescribing habits die hard creating a base of equally stable cash flow. It follows a disciplined business strategy and has assembled a diversified and stable core portfolio.

A portfolio approach with a twist: the LBO model

Alliance has crafted a portfolio using an unadulterated LBO model. Each product acquisition is looked at as if it is a private equity transaction and measured against its propensity to be financed by debt versus equity; all within the context of a target hurdle rate of return. Embodied in this approach, are three acquisition models. The Core Brand model, which consists of financing an acquisition almost entirely with debt, a Growth Brand model which blends in a percentage of equity into the mix and the Development product model, which is almost entirely financed by equity.

Core Brands: critical mass builder

Representing around 56% of the current sales mix, these brands require no promotion and tend to be demand driven. The attractiveness of these brands relies on their perceived efficacy by physicians and consistent prescription patterns. They build critical mass for the Company, generate excess cash flow beyond servicing their debt and help to build commercial channels, which need to be there when higher value Alliance products hit the market.

Growth Brands: a further stepping stone to future growth

Representing the balance of Alliance revenues, these brands are acquired because they have either been abandoned, poorly managed or are simply not core to their owner's business anymore. They require promotional effort to grow them to full potential and a focused commitment to making that happen. Since they are partially funded with equity, they tend to throw off more cash once they are back on track and add considerably to the improvement in profit margins that have been witnessed of late. They are also selected for their propensity to join the ranks of Core brands over time, adding to the excess cash flow derived from the latter and accelerating the Company's ability to pay down the debt taken on to acquire these products.

Development products: the ultimate target for growth and profitability

In the final analysis, Pharmaceutical companies are all about growth, profitability and excess cash flow to fund more growth, higher profitability and so on. They are not about LBO models and debt equity ratios. By contrast, Alliance has chosen a unique path to finance its ability to attain the proverbial Pharma endgame but its focus is firmly on the same target as any other Specialty Pharma. Posidorm and Isprelor are evidence that there is a profitable endgame in this unusual strategy. Financed by equity these products are the 'sizzle' that hold the potential to transform the Company's profile into one more easily recognizable as a traditional Specialty Pharma.

Financial platform, product mix and earnings inflexion points

The expected progressive shift from the leveraged Core and promoted Growth Brand model products towards higher margin equity-funded Development products and increasing international distribution is moving the P&L towards an inflexion point. As the percentage that debt-servicing represents in the mix shifts, this will allow a greater percentage of earnings to drop to the bottom line.

Debt and earnings momentum management and investor expectations

As guidance to the investment community, Alliance has indicated that it will continue to build its business in the way that it has historically done so. This translates into further acquisitions of core and growth brands while keeping an eye out for opportunities to add on new Development projects. An analyst once remarked that Pfizer was the 'largest massage parlour' on 42nd Street' in New York for the way that it 'managed' its earnings. In fact, American Home Products (now called Wyeth) was a much more astute practitioner of the art! Alliance's earnings management will not come from holding back earnings to smooth growth but rather by fine-tuning its debt/equity ratio in the face of rising revenues from Development products. This sort of 'earnings management' is aimed at maximizing the build of critical mass and a platform for future growth, while enabling the kind of earnings momentum that investors would like to see.

Isprelor is a shoo-in!

The only question with Isprelor is not whether, but rather when and how much! The Company has projected that this product could garner a 25%-30% share of the market. Given its effectiveness profile versus its competitor and the fact that it is already widely used off label, we think that this projection is rather conservative. We assume that Alliance will roll out the appropriate degree of marketing power to fully push the product in its own market (UK/Eire). We further believe that its EU distribution partner will aggressively move to garner market share. Ergo, we believe that the net result would be a market share closer to 60%.

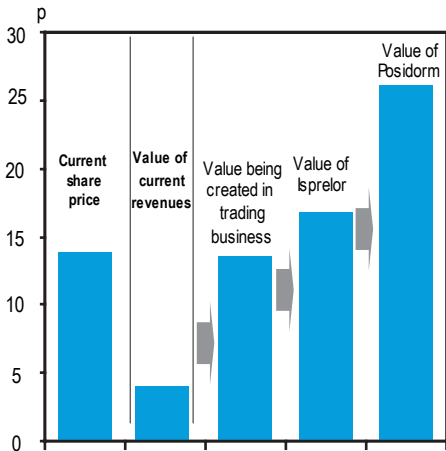
Posidorm: the great white hope!

The dynamics of Alliance will alter inexorably should the melatonin trials being run in the elderly achieve a successful outcome. This is controversial stuff but there is sufficient historical clinical data to justify the risk. The elderly sleep disorder market looks the most promising and has a potential value ranging from £16-£40 million all the way to a potential market of circa £200 million. Only a successful Phase III is required to get there!

Valuation

Alliance Pharma has successfully constructed a marketing “platform” on a model of largely, debt-funded acquisitions of mature and growth brands. In this model, products are mature, specialised, non-generic in nature, and tend to be rather stable. They are cash generative and can therefore be leveraged upon acquisition and de-leveraged in a progressive fashion.

Current Value (p)



Source: Objective Capital

Like all speciality pharma models there are immediate benefits from costs savings and more focused marketing in acquisitions but the real value comes from grafting-on pharmaceutical products, acquired or developed, that are of increasingly greater value.

Our model reflects the dual nature of the business where the core trading business, which consists of a core and growth portfolio, is valued in the traditional way one might value a speciality pharma business of this kind. We have then valued Alliance’s Development portfolio separately based on their economic potential and stage of clinical development.

Alliance’s Development portfolio has been valued taking into consideration all costs to be incurred until launch and assuming incremental costs beyond the SG&A reflected in the core trading business. We have valued the royalty streams to be expected from marketing partners assuming a global licensing number of 30% including all upfront and milestone payments that could be expected in any negotiated deal. It is possible that Alliance will go for a lower royalty rate of say 20-25% but exact upfront and royalty payments from its partners. Given the cashflow projections we have made, the latter is a likely scenario.

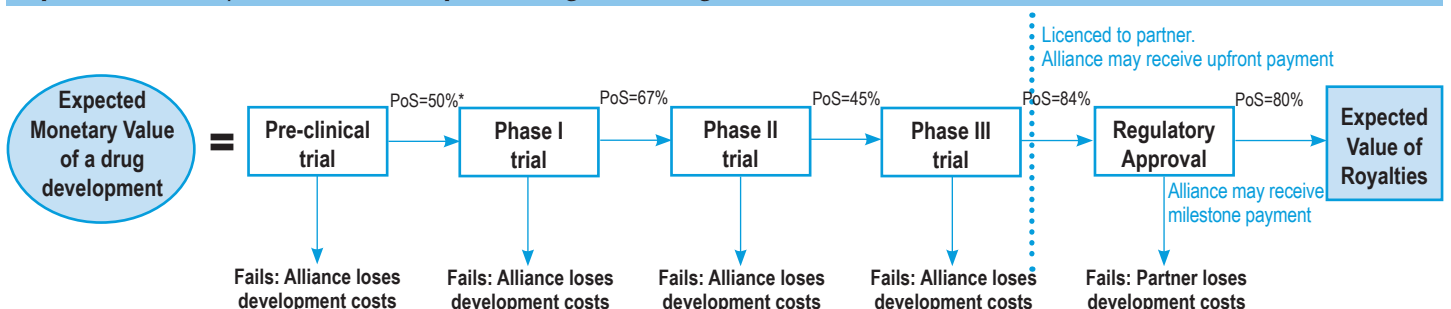
We are more optimistic than the Company’s guidance on three major issues:

1. the degree to which Periostat can attain market share in the UK;
2. the extent to which it might make inroads in international markets;
3. the market share that Isprelor might be able to achieve both in the UK and the EU.

The assumptions that we have made appear reasonable and are backed up by increased SG&A costs where appropriate.

When developing new drugs, it is always difficult to predict the extent to which a company might be able to garner market share. The temptation to be too optimistic is very alluring indeed and in the basic model, we have craftily staked out a position somewhere in-between where the company sees the world and where a more aggressive reality might lie. Just in case, for reference, we are presenting a second model that is a tad more optimistic than the base case scenario. This still only reflects a relatively modest market penetration and given the size of the Posidorm market even more optimistic scenarios are possible.

Expected Monetary Value of a development drug – licencing model

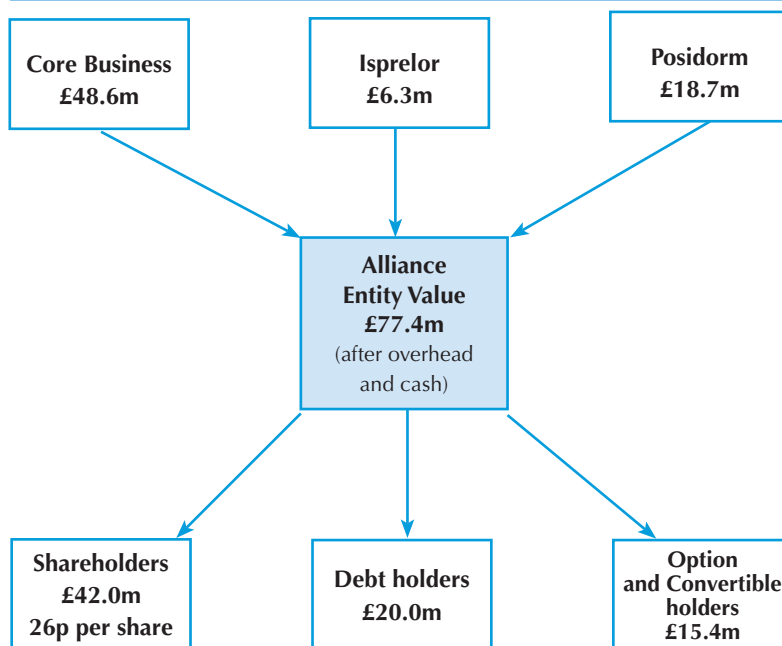


* industry averages

Valuation Summary (£m)

	Scenario	
	Core	Optimistic
Trading business	48.6	53.6
Development drugs		
- Isprelor	6.3	10.0
- Posidorm	18.7	48.3
Total Expected Operating Value	73.6	112.0
Add: Tax Benefits	1.3	1.3
Add: Starting cash & new funds	2.5	2.5
Total Current Value for Firm	77.4	115.8
Less: Convertibles' Debt Component	7.5	7.5
Less: Bank & Other Debt	20.1	20.1
Less: Minorities	0.0	0.0
Total Value to Equity Claims	49.9	88.2
Less: Alternative Equity Claims		
- Warrants + Options	0.4	0.8
- Convertibles (warrant element)	7.5	15.1
Total Value Attributable to Equity Holders	42.0	72.4
Value per share (£)	0.26	0.45
Value per convertible (£)	1.98	3.01

Components of Alliance Pharma's Entity Value



Trading Business Assumptions

£ millions	2006F	2007F	2008F	2009F
Revenue				
- Core brands	8.2	9.0	10.1	11.3
- Growth brands	8.8	11.9	15.9	20.2
Total	16.9	21.0	26.0	31.5
Gross Profit	9.3	11.5	14.3	17.3
Proforma EBIT*	2.7	4.2	5.9	8.2
Gross Margin	55%	55%	55%	55%
EBIT Margin	16%	20%	23%	26%

* before capitalised expenses

See page 18-19 for details

Expected Value of Isprelor

Scenario (£m)	Core	Optimistic
EV of Royalties	14.6	24.2
Likelihood of success (PoS)	77%	77%
EMV of Royalties	11.2	18.6
Add: EMV of upfront payments	0.0	0.0
Add: EMV of milestone payments	0.0	0.0
less: EMV of dev costs	2.2	2.2
EMV of Isprelor	9.1	16.5
per share (£)	0.06	0.10

See page 23 & 25 for details

Expected Value of Posidorm

Scenario (£m)	Core	Optimistic
EV of Royalties	48.3	118.1
Likelihood of success (PoS)	67%	67%
EMV of Royalties	32.3	79.1
Add: EMV of upfront payments	0.0	0.0
Add: EMV of milestone payments	0.0	0.0
less: EMV of dev costs	5.3	5.3
EMV of Posidorm	27.1	73.9
per share (£)	0.17	0.46

See page 23 & 26 for details

Sensitivity to change in ...

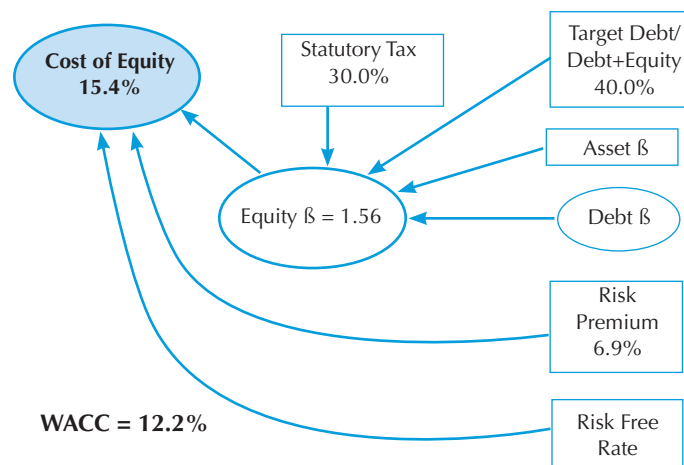
Increase in cost of capital (+%)	-1.0%	-0.5%	0.0%	+0.5%	+1.0%
Value (£m)	0.31	0.28	0.26	0.24	0.22
Change in Value	18%	9%	0%	-8%	-15%

Sensitivity to change in development drug assumptions ...*

Impact of generics (+% price decline)	-20%	-10%	+0%	+10%	+20%
Value (£m)	0.30	0.28	0.26	0.25	0.24
Change in Value	13%	7%	0%	-4%	-8%
Increase in licensing royalty (+%)	-10%	-5%	0%	5%	10%
Value (£m)	0.22	0.24	0.26	0.28	0.30
Change in Value	-14%	-7%	0%	7%	14%
Increase in margin on marketed revenues (+%)	-10%	-5%	0%	5%	10%
Value (£m)	0.25	0.26	0.26	0.27	0.27
Change in Value	-5%	-2%	0%	3%	3%

*consistent change across both Isprelor and Posidorm

Weighted Cost of Capital



Key Risks

Clinical efficacy and regulatory risks

As with all pharmaceutical companies, the risk that a clinical trial fails (i.e., fails to show statistical significance in achieving its primary endpoint) remains. Furthermore, the risk that a regulatory authority refuses to approve a product is also a risk that the Company must confront.

Longer term chronic use of melatonin

The efficacy of melatonin used for an extended period of time is unknown. There is some *in vitro* data in the scientific literature that points to the de-sensitisation of melatonin receptors when exposed to sustained high plasma levels of melatonin. The Company believes that its formulation does not elevate brain levels of melatonin beyond a normal level, an assertion which we find reasonable. Nevertheless, this could be a risk.

The inability to accede a hospital formulary

This remains a hurdle that Alliance must face for its development stage products. While the Core and Growth products do not face such a hurdle, any Development stage product will. Additionally, Alliance's local distributors face the same hurdles in their respective countries. Therefore, there can be no assurances that these products will achieve their full potential.

Pricing uncertainties related to Government-dictated pricing

Countries such as the UK will often mandate price reductions over time. While such price mandates can confer stability for a period of time there can be some degree of uncertainty as to the timing and degree of price decreases over the life of a drug.

Financial "structure" risks remain a factor

If a prolonged severe dislocation in interest rates were to occur, the Company's capital structure could become vulnerable to higher interest costs in the long term (e.g., the return of high inflation leading to high interest rates which the Company cannot offset with higher income due to the regulated market in which it operates). In the medium term, these risks have largely been mitigated by the use of financial swaps.

Ability to acquire further products that fit Alliance's model

The world of Speciality Pharma is a highly competitive one with many players vying for available product properties. This may limit the Company's ability to acquire products that fit its hurdle rates of return other than in non-competitive situations.

Non-performance by foreign distributors

While it is in both parties interest that a foreign distribution deal should work, Alliance has not yet proven that it can manage such relationships successfully. There can therefore be no assurances that these emerging relationships related to selected products where Alliance has rights over various foreign territories will be successful.

Alliance Pharma – the company

Originally founded in 1998 and floated on AIM at an effective price of 16p in December 2003, Alliance Pharma has built, through the acquisition of 33 brands (including recent acquisitions), a profitable, European Speciality Pharma Company with around £15 million of annualised sales. While historically, the vast majority of revenues have been in the UK and Eire, it now has the opportunity with both its Growth brands and its products in Development, to create an international distribution network. Under the leadership of Michael Gatenby, the Chairman (ex-Charterhouse Bank Vice Chairman) and John Dawson (ex Ciba and Sandoz), the Company's CEO and principal shareholder, Alliance has assembled a highly experienced team of individuals to execute an unusual, financially driven, business development model. The result is a Company with the makings of a significant Speciality Pharma platform, growing revenues, increasing gross margins and a path to significant internationalization and profitability over the next 2-3 years.

Business Strategy

Business model over the last 30 years

There are a number of pharma start-up business models that have been created and executed on over the past 30 years. These strategies are distinct from the classical model on which Big Pharma has been built where most started out as chemical companies using chemical synthesis and screening to develop therapeutically relevant drugs. With the emergence of Biotechnology in the mid-late 70's, a new model emerged, which is based on the high risk/high return development of biologically relevant molecules. Much of the actual development of such drugs is driven by similar parameters to any pharmaceutical product (toxicology, dose ranging studies, blinded randomised clinical trials...etc), but the process is leveraged by partnerships with big Pharma. This in turn serves to fund the pathway of such drugs to market and to fund marketing/sales infrastructure in selected regions or even globally (e.g. Genentech, Amgen and the like) for the longer term development of the Company.

As the Pharma business grew in size, the need to market products with significantly greater market potential was based on the cost of maintaining a costly development and marketing infrastructure but mainly to perpetuate the kind of growth expected by investors in these companies. As a result, a third model emerged, primarily in the US, during the late 70's and early 80s. This consisted of cobbling together a portfolio of drugs either based on novel formulations of old drugs...or those orphaned by the drive of big Pharma to focus on the larger 'home run' drugs. Enter the 'Speciality' Pharma model, which spawned an entirely new sub-sector of companies focused on carving out a larger market share for these effective drugs through highly motivated and focused marketing/sales organisations. Alliance is one of those companies.

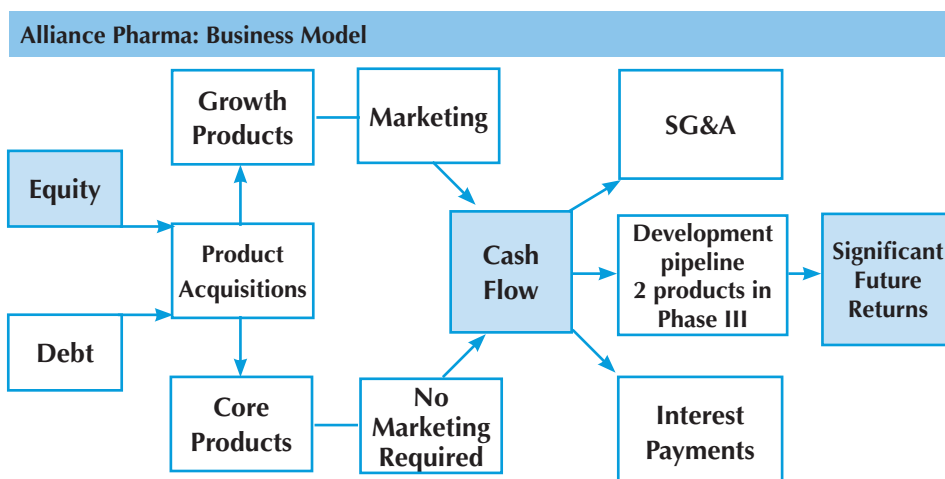
A long term business model: reaching the earnings inflection point

The model developed by the Company, is a phased one which consists of:

- creating a critical mass of stable, profitable products, acquired with an optimized mix of debt and equity to create cash flow and a distribution infrastructure platform on which other products can be grafted;
- then acquiring a second layer of products in need of marketing support. These products are either absent or under-represented in markets and have either failed to achieve their potential or represent an untapped opportunity. All of which leads to the creation of a marketing/detailing capability as well as a platform for international distribution.
- finally to seek out and acquire products with known functionality and therapeutic targets that are either absent from selected markets consistent with the Company's capabilities and where regulatory approval can be sought with a good chance of being granted.

The result is that the leveraged portion of the portfolio sets the stage for less levered products to be funneled through the platform. The Company is then engaged on a dynamic growth path where progressively more valuable members of the pipeline can be added at a marginal cost. As revenues and margins expand, the inherent profitability of the higher value products begins to overwhelm the levered structure creating an earnings inflection point leading to further margin gains and accelerated growth.

While Alliance can manage and modulate this growth path to some degree, this will only serve to delay the point at which this inflection occurs. Ultimately though, the dynamics lead to an inevitable climax unless the Company can find some way to pile on debt (associated with the acquisition of further products) to prevent it from happening. Any way you look at it, the shareholder is likely to be the winner!



Source: Alliance Pharma

Shareholders

Institutions

Morley Fund Management	9.2%
Fidelity	5.1%
Artemis Fund Managers	3.5%
Henderson Global Investors	3.0%
RAB Capital	1.7%
Majedie Investment PLC	1.7%
Cavendish Asset Management	1.2%
Seymour Pierce Ellis	1.3%
BNP Paribas	1.2%
NCL Smith & Williamson Investments	1.2%
Others (9)	9.4%
Total	38.5%

Large Private Holding (N Wray) 6.8%

Private Client Brokers/Retail 11.7%

Directors

John/Stella Dawson	38.4%
Others	4.6%
Total	43.0%

Total **100.0%**

Source: Alliance Pharma

The building of a diversified Specialty Pharma portfolio...LBO style

The management of Alliance has developed a series of parameters, which together form the analytical platform used to determine whether a product is worthy of acquisition at a price, or not. These parameters include amongst others:

- a benchmark IRR;
- the potential for margin improvement for Core and Growth brands;
- relative sensitivities to promotion/detailing or lack thereof;
- its relevance to the profile of the Alliance's current portfolio;
- any marketing synergies or potential for line extensions;
- the intrinsic international potential of a product;
- the potential to migrate regulatory approval from the region/country of origin to the UK/EU or other potential jurisdictions;
- the validation of mode of action/therapy validation for development;
- marketing exclusivity where relevant.

Once the basic commercial/financial rationale for a product has been determined, the Company then analyses each opportunity for its 'financeability':

- if it is a Core product, what would underline its propensity to attract full bank financing;
- if it is a Growth product, the level of equity that the Company and its investors would need to provide to attract appropriate debt financing;
- and finally, if the potential candidate falls in the 'Development' category, the ability to sell its risk profile to equity investors is assessed.

This process is akin to an LBO analysis with an assessment of risk levels in anticipation of creating an optimal credit structure that is consistent with the business profile of the drug and takes into account its full potential as a Core or Growth brand. With Development products, Alliance does not appear to be driven to 're-invent the wheel'. Its current product portfolio consists of rather safe bets where the therapeutic target, the indications for the drug and the clinical path are all crystal clear resulting in a significant de-risking of the projects. While mishaps still occur (as with all products in Phase III), the potential for failure is either minimal as in the case of Isprelor/misoprostol (used off-label by obstetricians for years) or relatively low as in the case of Posidorm/melatonin which is OTC in the US and has well defined pharmacokinetics and therapeutic effects. We would anticipate that any new projects in the 'Development' category would follow similar profiles.

Competitive Profile and Sales and Marketing platform

Sales & distribution

Alliance Pharma, by virtue of its business model and focus, does not require a large marketing and sales infrastructure in order to achieve successful marketing and penetration for its products. Through a combination of a small hospital orientated sales force (currently 9 people), rented specialist salesforces (as in the case of Periostat for the periodontal specialist) and distributors, it is possible to achieve targeted market penetrations without the expenditure of significant financial resources.

The Core portfolio requires little in the way of sales and marketing (pharmaceutical detailing) relying mainly on distribution and pharmacy pipeline filling through pharmaceutical distribution and fulfillment companies. (e.g., AAH, Unichem, etc.).

The Growth portfolio products require marketing/detailing to increase their usage and establish their reputation for efficacy. For example, in the case of Periostat, Alliance has contracted with OralDent, a specialist dental product marketing company to detail Periostat to periodontal specialists while Alliance's own salesforce focuses on hospital sales. It has recruited its own specialist dental head and has trained up the OralDent salesforce on Periostat.

For 'Development' products, Alliance will have to (and has already) incurred significant investment in marketing (conferences, seminars, etc) to achieve market success. With Isprelor, the task will be simplified by the fact that many obstetricians already use misoprostol (where the tablet is cut by the pharmacist) for the induction of labour so the switch to a convenient legally prescribable dosage form should be relatively straightforward. In the case of Posidorm, the task will be much more complex as it will involve a significant amount of doctor education, detailing and convincing. Substitution from the newer or older hypnotics (whether Benzodiazepenes or the newer GABA A receptor agonists) to Posidorm will require some convincing although with a clean side-effect profile, and good Phase III data this process has the potential to carry with it a significant degree of success.

International marketing is carried out through local companies in each country except in Eire where Alliance maintains its own presence. Alliance already has a significant number of distributors with whom it works in countries such as Israel, UAE, Malta, Cyprus, Spain, Switzerland, Austria and Italy in what might be termed developed countries. In developing countries, it has achieved a presence through distributors in Mauritius, Nigeria, Sri Lanka, Sudan and Guyana. The main effort internationally is adding distributors in Finland, Turkey, Australia, New Zealand and the Benelux in 2006 and then to begin to roll out in the more significant markets such as Germany and France and other Scandinavian markets over the 2007-2008 period. This applies to the marketing of Forceval, Hydromol, Uniflu and Periostat to a lesser or greater degree (there are some limitations here and there). For Posidorm and Isprelor, the addition of significant local marketing partners is a plan that Alliance Pharma wish to pursue.

Competition in this arena, while prevalent tends not to be as much a factor as in other pharmaceutical companies given the specialist nature of the products. We do not want to give the impression that there is no competition as we have already outlined for both Isprelor and Posidorm that there are alternatives. But what is distinctive in Alliance's case are that the profile of the products are such that although there are competitive approaches, the one that Alliance has taken guarantees some degree of market penetration with intelligent positioning, pricing and marketing. To what degree these products can penetrate the chosen markets and achieve the kind of market shares that we believe are possible will depend, amongst other things, on the strength of the clinical data generated by the respective trials for these products.

For the Core or Growth products, as these tend to be mature specialist markets, the nature of competition is not a particularly important factor. In the case of Periostat, as we have said above, Alliance is not fighting against any particular product but rather against periodontal specialist practices and habits. In the case of Uniflu, Forceval and Hydromol, competition is more on a brand recognition and price basis rather than product efficacy. In some cases, it is just uniqueness that wins the day!

Possible Candidates for Licencing Posidorm				
Company	Status	Country/Region	Comment	Current Products
Boeinger Ingelheim	Private	Germany/Europe	Broad based company	Depression/ Parkinsons
Servier	Private	France/Southern Europe	France & Italy but also Eastern Europe and other territories	CNS specialist
UCB	Public	Belgium/Europe	Europe and more	CNS specialist
Mundipharma/Purdue	Private	UK/Europe	Europe and more	CNS specialist
Leo	Public	Northern Europe/Europe	Northern Europe & more Europe	CNS specialist
Merz	Public	Germany/Europe	Northern Europe & more Europe	CNS specialist
Norgine	Private	UK/Europe	Europe and more	Some CNS/ salesforce provision

Source: Objective Capital

Product portfolio and revenue development

Alliance has developed a pharmaceutical platform, which consists of three separate portfolios of drugs with distinct characteristics.

Core portfolio

The 'Core' portfolio consists of a series of pharmaceutical products requiring no expenditure for either marketing or detailing. While these products have benefited from improved margins based on better logistics and better production costs they rely mostly on the relative inertia in prescribing habits that physicians display. As embodied in that wonderful expression 'when it ain't broke then don't fix it', a relatively large group of physicians who have had good success with certain products in their practice are reluctant to replace them.

Also, in European systems where physicians tend to operate under a lean budget system, those inexpensive drugs 'that work' tend to be workhorses that are not easily abandoned for new, snazzy and more expensive replacements. Add to that, better brand management, improved logistics, lower cost of manufacturing and use of other margin improvement tools and we have reached the central aim – maximise cash flow, whilst assisting in building a pharmaceutical platform where higher growth and higher margin products can be grafted over time. In this regard, the Alliance story has been largely successful.

In this category, the Core portfolio grows for the most part at modest rates. Growth comes almost exclusively from the international roll out of **Forceval** and **Uniflu**. Forceval is the only prescription multi-vitamin product in the UK and is favoured by physicians in the UK for conditions where suspected vitamin or mineral deficiencies are one of the causes of a diseased condition. This could be due to increased nutritional requirements, poor absorption or simply lack of nutritional intake. It can be taken as a pill (in capsule form) or a flavoured drink (powdered form particularly aimed at children and for geriatric use). The product was acquired (along with Uniflu, the domestic part of which was subsequently disposed of) from Unigreg Ltd in November 2004. While this NHS-reimbursed prescription product displayed stable growth in the UK, its international distribution had been poorly exploited which left room for Alliance to capture some additional growth. It represented about 18% of 2005 revenues. We forecast that Forceval will grow to £1.8m in international revenues out of a total of £3.0m through 2009.

Proforma Trading Business Forecast

£ millions	2006F	2007F	2008F	2009F
Revenue				
- Core brands	8.2	9.0	10.1	11.3
- Growth brands	8.8	11.9	15.9	20.2
Total	16.9	21.0	26.0	31.5
Gross Profit	9.3	11.5	14.3	17.3
Proforma EBIT*	2.7	4.2	5.9	8.2
Gross Margin	55%	55%	55%	55%
EBIT Margin	16%	20%	23%	26%

* before capitalised expenses

Source: Objective Capital

Syntocinon and **Syntometrine** represent another large part of the portfolio. Both are Obstetric products which are used to facilitate the childbirth process when required. Syntocinon is a synthetic version of the natural hormone oxytocin. Late in pregnancy, oxytocin is released by the pituitary gland to stimulate smooth muscle in the uterus (womb). The resultant contractions can then help to push out the baby. Syntometrine is also used either alone or in combination with ergometrine (an ergot alkaloid with a similar effect on smooth muscle but through a different pathway) to induce contractions post-partum to facilitate the delivery of the placenta out of the uterus and also to reduce bleeding. This product, which represented about 15% of 2005 revenues, has also served to generate the platform from which the marketing and sales of **Isprelor** can be launched.

The rest of this portfolio consists of low growth products in the Cardiovascular, CNS and anti-infective areas all of which serve as platforms for future 'growth' or development type products.

Portfolio of Core Brands

Revenue (31 Dec; £m)	2004/5	2005 ^(*)	2006F	2007F	2008F	2009F	CAGR
Syntocinon/Syntometrine	2.0	1.8	2.2	2.2	2.2	2.2	2%
Forceval	1.7	2.2	2.7	2.8	2.9	3.0	12%
Deltacortril	—	—	0.5	1.8	1.8	1.8	60%
Other	2.4	2.6	3.7	4.3	4.9	5.7	17%
Acquisitions	—	—	0.1	0.3	0.6	1.0	115%
Total	6.0	6.6	8.2	9.0	10.1	11.3	14%

^(*) 10 months only

Source: Objective Capital estimates

Growth portfolio

The products acquired in this portfolio tend towards the orphaned, mis- or unmanaged type. These are products that were not strategic to their former owners or were simply poorly managed both domestically and in some cases, internationally.

We estimate that this portfolio should grow by around 30% per annum through 2009 largely driven by both the dermatology and dental products. We have also constructed a more aggressive model, which takes into account a more optimistic view of the effect of starting up new international markets in both Periostat as well as the Dermatology range. Under this scenario we could see growth pushed up to perhaps 40% per annum through 2009.

Portfolio of Growth Brands

Revenue (31 Dec; £m)	2004/5	2005 ^(*)	2006F	2007F	2008F	2009F	CAGR
NuSeals	2.27	2.52	3.40	3.84	4.23	4.44	14%
Symmetrel	1.09	1.33	1.73	1.93	2.11	2.21	15%
Dermatology Range							
Hydromol Total			1.00	1.50	1.80	2.03	27%
Atarax			0.25	0.50	0.65	0.72	42%
Other Dermatology	1.46	1.50	1.51	1.74	1.88	2.03	2%
Total Dermatology	1.46	1.50	2.76	3.74	4.33	4.78	25%
Periostat		0.25	0.57	1.53	3.52	6.03	123%
Acquisitions	0.00	0.00	0.30	0.90	1.70	2.70	108%
Total	4.82	5.59	8.75	11.90	15.90	20.20	33%

^(*) 10 months only

Source: Objective Capital estimates

Nu-Seals

Currently, the largest product in this category (representing about 20% of 2005 revenues) is an enteric-coated version of low-dose aspirin called **Nu-Seals**, which is used as a secondary preventive measure in patients with vascular disease at risk of myocardial infarction, ischemic stroke and other vascular conditions. Its anti platelet action is thought to prevent the formation of vascular plaques and clotting, which can trigger these events. It has also been considered as a first line preventive measure for patients at risk of cardiovascular disease.

While low dose aspirin (75mg-162mg) increases the incidence of cerebral haemorrhagic stroke and gastrointestinal bleeding, it does not appear to have an effect on overall mortality. The literature related to the use of low-dose aspirin is complex and sometimes confusing but in the UK, low dose aspirin (75mg) is recommended as a secondary prevention for patients with occlusive vascular disease at risk of further vascular events. It is also recommended for patients without occlusive disease but considered to be at risk (patients over 50 with a 10 year risk greater than 20%, diabetics and those with hypertension related organ damage).

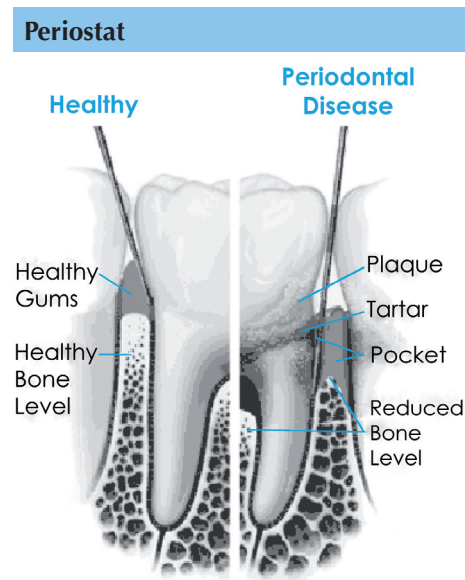
Enteric-coated low dose aspirin, as exemplified by Nu-Seals, reduces the incidence of gastrointestinal bleeding, which is one of the 2 serious complications of this therapy (the other being extracranial bleeding). While enteric-coated aspirin is available over the counter in the US, it is a prescription medicine in the UK and Eire for cardiovascular protection. Its usage tends to be driven by prescription or doctor recommendation. While Nu-Seals grew 17% for the 10 month period of 2005 (versus a full year in 2004/5) it is expected to continue to experience stable to low mid teens growth through 2009. However, this is an area where one could reasonably expect Alliance to seek further acquisitions given the platform that is in place.

Periostat: the near term growth driver

Driving the growth of this category are two product areas: Dental and Dermatology. The featured product in Dental is Periostat, a product acquired from the US company CollaGenex in early 2005. Periostat is an oral prescription product containing sub-antimicrobial doses of the tetracycline antibiotic doxycycline, a broad-spectrum antibiotic which appears to inhibit the enzyme collagenase. It is thought that the latter is responsible for the breakdown of collagen-containing connective tissue in the gum. There is evidence that in periodontal disease, an inflammation caused by food residue-induced bacterial accumulation, increases the levels of collagenase, which results in the breakdown of gingival connective tissue. This in turn creates the pocket in which dental plaque can accumulate. Periostat appears to inhibit the collagenase that is secreted by both accumulated bacteria and the immune cells (neutrophils, macrophage, fibroblasts...etc) that accumulate during the inflammatory process. It is prescribed as part of a 2-pronged approach to reduce bacterial load (through scaling and root planing or SRP and increased brushing and dental floss usage) and adjunctive inhibition of collagenase (to prevent the breakdown of gingival connective tissue).

In the UK, Alliance has a target of about 100k patients with severe periodontal disease out of a total of 3.2 million patients. Current treatment is physical in nature with the anti-microbial chlorhexidine (GSK's Corsodyl) prescribed as an adjunct therapy. Periostat usage would add an additional layer of therapeutic power if Alliance is able to convince periodontal specialists to use it. The difficulty lies in the fact that the latter (particularly the older ones) tend to view physical methods of SRP and increased cleaning and use of dental floss as adequate.

The evidence for Periostat's efficacy is based on a double blind randomised Phase III clinical trial conducted by CollaGenex on 190 patients that demonstrated SRP plus Periostat resulted in a 52% increase in clinical attachment of the gum to the tooth and a 62% decrease in pocket depth versus SRP and placebo². A more recent trial conducted in the UK, found in a double blind randomized, placebo-controlled multicentre clinical study in 210 subjects (over 9 months) that submicrobial doses of doxycycline (at 20mg B.I.D or orally twice daily), in combination with SRP, resulted in a statistically significant gain in clinical attachment levels (CAL) and a concomitant reduction in probing depth (PD) **'over and above those achieved by scaling and root planing with placebo'**³.



Source: Alliance Pharma

² Caton JG et al, *J Periodontol*, 2000 Apr; 71(4): 521-32.

³ Preshaw PM et al, *J Periodontol*, 2004 Aug; 75(8): 1068-76

On that basis, it should be possible to convince some if not most periodontal specialists to use Periostat in severe cases even alongside Corsodyl antibacterial treatment. It is clear to us that the market penetration that the Company is seeking is commensurate with the resources that it has available to develop this market.

Alliance estimates a £7m market in the UK alone. In addition, Alliance also acquired the worldwide rights ex-US for the product. The Company has been busy building an international network of distributors and will be registering the product in as many countries as possible over the next few years. Periostat is already available in Portugal, Israel, Austria and Switzerland. Alliance has just announced the appointment of a major distributor in Italy and is working on introducing Periostat in Finland, the Netherlands and Luxembourg in 2007. It is also aiming to introduce the product in Australia, New Zealand, Lebanon and generally across the Gulf areas in the near future. The development of international sales has the potential to be a major growth driver for Alliance over the next 3-4 years. We estimate that international sales will add an additional £3m of revenue (or 40% of the total) to Periostat by 2009. It is possible though that the latter number could be as high as £4-7m and that the level of penetration in the UK market could be higher than expected. Evidently, there is room for upside surprise here, which we have incorporated into our more aggressive valuation scenario.

Emerging dermatology platform: Hydromol

In early 2006, Alliance acquired a range of dermatological products under the brand name Hydromol. These products, which consist of an occlusive ointment, bath oil and a cream, are aimed at the treatment of dry skin and eczema. This product line is to be added to the core dermatology range, which includes a wide range of treatments for various skin disorders. The Company also recently added a product called Dermamist, a spray for dry skin, which will complement the existing dermatology range.

On June 6, Alliance further added to its dermatological platform with the acquisition of the UK rights from Pfizer of three products: AtaraxTM (an oral antihistamine), DeltacortrilTM (oral steroid) and TerracortrilTM (a topical combination steroid).

Although it is too early to say what this business is capable of producing in the way of revenues and growth, clearly Alliance believes that both Dermatology and this product line has significant potential. The base case scenario we have built calls for compounded growth of 25% per annum through 2009 with sales reaching £4.37 million (versus an estimated sales level of £2.78 million for 2006). However, international sales development could be viewed more aggressively leading to a scenario where compound growth would be closer to 33% per annum, hence sales reaching about £6 million in 2009.

Development portfolio

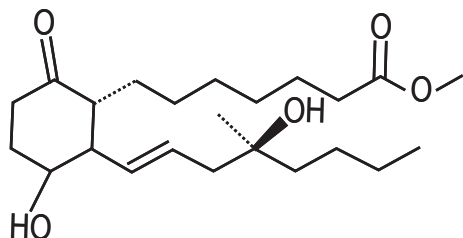
This is what its all about! If earnings are to accelerate post 2007, it will be based on the development of Isprelor and Posidorm. The latter two development stage drugs are part of what the Alliance model is all about. The ultimate goal is to construct a platform upon which development products of this type can be grafted with relative ease. The trick is to find late stage products where the Phase III risks, while always present, are minimized, while the development costs themselves are, from a financial point of view, within the realms of feasibility (through cash flow and equity financing primarily in this case). Isprelor and Posidorm are perfect examples of this.

Alliance is now in a position to add products of this nature in Phase II and III where the cost to market can be financed by equity. However, before Alliance adds more of these (currently none are planned) they need to successfully steer both Isprelor and Posidorm through the product development process and onto the market. We believe that it is only when demonstrable success has been delivered on this front that equity investors will be prepared to consider financing further acquisitions of this type. Although this might depend on the nature of the project.

Portfolio of Development Drugs						
Revenue (31 Dec; £m)	2007F	2008F	2009F	2010F	2011F	2012F
Isprelor						
UK & Eire	0.4	1.0	1.7	2.2	2.5	2.8
EU		0.6	1.5	2.3	2.7	3.0
Total	0.4	1.6	3.2	4.5	5.2	5.8
Posidorm						
UK & Eire	0.4	1.6	4.0	8.0	12.0	15.6
EU		1.0	4.0	10.0	20.0	30.0
Total	0.4	2.6	8.0	18.0	32.0	45.6
Total	0.8	4.2	11.2	22.5	37.2	51.4
YoY Growth	2007F	2008F	2009F	2010F	2011F	2012F
Isprelor						
UK & Eire		150%	70%	30%	15%	10%
EU			150%	50%	20%	10%
Total		200%	100%	39%	18%	10%
Posidorm						
UK & Eire		300%	150%	100%	50%	30%
EU			300%	150%	100%	50%
Total			208%	125%	78%	43%

Source: Objective Capital estimates

Isprelor



Source: Alliance Pharma

Isprelor (misoprostol)

Isprelor is a Prostaglandin E1 synthetic analogue. It was developed originally as a primary treatment for stomach ulcers as well as an adjunct to NSAID (Non-Steroidal Anti-Arthritic) therapy. In this indication, misoprostol increases the secretion of the protective mucus that lines the gastrointestinal tract. However, as misoprostol also has uterine properties, an off-label use in the induction of labour was developed based on misoprostol's contractile effect on smooth muscle in the female uterus.

This is the basis for pursuing the development of Isprelor. While other prostaglandins with very similar properties to Isprelor have been approved for the induction of labour, misoprostol has been extensively used around the world because it is highly effective. The problem lies in the formulation that is used and the delivery of the drug (intravaginal versus oral). The dosage for the anti-ulcer formulation is much higher (100-200 µg tablets) than that required for the induction of labour (25-50µg dose). Currently, obstetricians get the pharmacy to divide the tablet, which is then inserted in the posterior fornix (located between the posterior wall of the vagina and the cervix). The most common dose used has been 50 µg and the Company is testing both doses in a Phase III 'open design' double blind trial against dinoprostone tablets (currently the EU market leader approved for this indication).

In a meta-analysis of eight randomized studies comprised of 966 patients which compared the use of intravaginal misoprostol for cervical ripening and labour induction with that of dinoprostone, oxytocin or placebo, misoprostol was associated with a significantly lower rate of caesarian section, a higher incidence of vaginal delivery within 24 hours of application and a reduced need for oxytocin augmentation. Spontaneous labour occurred in nearly 85% of the women studied⁴.

From the data, assuming a robust trial design, it is highly likely that Isprelor will make it to market and it is equally likely that it will achieve market success. In its Spring 2005 list of essential drugs, the WHO included misoprostol so we leave the conclusions for the reader to ponder.

The market for **Isprelor** is estimated by Alliance to be roughly £13 million EU wide. The drug will be submitted for UK/Eire registration in late 2006 and is slated for launch in mid 2007 and pan European approval and launch in 2008. Alliance is estimating a conservative 25-30% penetration of the market. From our discussions with various obstetricians, we feel that this could be an ultraconservative estimate, which has a high probability of being beaten and feel that a market penetration of 60% could be achieved. While Alliance will not benefit from any period of market exclusivity, competitors would have to complete a bio-equivalence study which we believe they are unlikely to do given the small size of the market.

⁴ Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL., *Misoprostol for cervical ripening and labor induction: a meta-analysis*, *Obstet Gynecol* 1997; 89:633-42.

Expected Value of Isprelor

Summary of Valuation (pre-corp tax)

Scenario (£m)	Core	Optimistic
EV of Royalties	14.6	24.2
Likelihood of success (PoS)	77%	77%
EMV of Royalties	11.2	18.6
Add: EMV of upfront payments	0.0	0.0
Add: EMV of milestone payments	0.0	0.0
less: EMV of dev costs	2.2	2.2
EMV of Isprelor	9.1	16.5
per share (£)	0.06	0.10

Key Market & Licence Assumptions

Indication/ Market	Route to Market	Royalty Rate/ Effective Margin		Impact of Generics	
				Approx Date	Price Impact
UK& Eire	Marketed	70%		2017	-10%
EU	Licensed	30%		2017	-10%

Sensitivity to change in ...

Impact of generics (+ % price decline)	Royalty Rate/ Effective Margin				
	-20.0%	-10.0%	+0.0%	+10.0%	+20.0%
Value (£m)	9.8	9.8	9.1	8.3	7.6
Change in Value	8%	8%	0%	-8%	-17%

Increase in royalty/margin (+%)

Value (£m)	Royalty Rate/ Effective Margin				
	-10%	-5%	0%	5%	10%
Value (£m)	7.7	8.4	9.1	9.8	10.5
Change in Value	-15%	-8%	0%	7%	15%

Components of core valuation* (pre-corp tax)

Core scenario

Expected Value of Royalties/Revenue (£ millions)					
Indication/Market	EV of cashflow	Current Stage of Dev	PoS	EMV	% of Val.
UK & Eire	9.3	Phase 3	77%	7.1	49%
EU	5.3	Phase 3	77%	4.1	28%
Total	14.6		77%	11.2	

Opimistic view: higher market penetration

Expected Value of Royalties/Revenue (£ millions)					
Indication/Market	EV of cashflow	Current Stage of Dev	PoS	EMV	% of Val.
- Sales UK & Eire	12.6	Phase 3	77%	9.7	45%
- Sales EU	8.8	Phase 3	77%	6.8	32%
Total	21.4		77%	16.5	

Expected Monetary Value of Isprelor
£9.1m - £16.5m
6p - 10p per share

EMV of Upfront payments
£0m

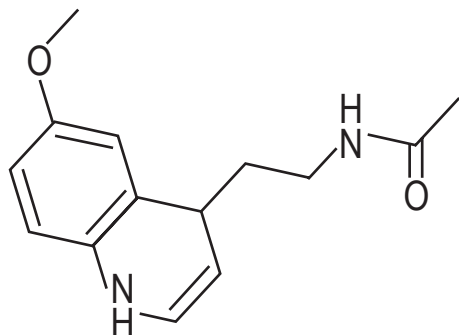
EMV of Milestone Payments
£0m

*See page 23 for forecast revenue

While the data cited above is based on a meta-analysis and is not anywhere near as robust as the trial being conducted by Alliance, it gives a very strong anecdotal indication of the kind of results to expect. There is much experience with misoprostol for this indication and although surprises are always possible, the odds point to a favourable outcome. Assuming that this is the case, we would posit a strong launch for the product and a rapid penetration of the market as indicated in our rapid ramp up of product sales.

Alliance is in the process of setting up a distributor network to handle the European roll out of the product and expansion into other territories may be possible. In any case we will stick to our peak market forecast of £6 million (based on a 45% penetration of the EU market) until the potential for penetration of markets beyond the EU becomes evident.

Posidorm



Source: Alliance Pharma

Posidorm: the sleeping giant rearing to emerge!

Who would have thought that someone would try and make a pharmaceutical product out of melatonin? Why on earth would anyone take an over the counter nutritional supplement in the US and turn it into an ethical pharmaceutical product in the EU? Well it might happen as soon as 2008 and Alliance is attempting that feat. The literature is full of studies on the use of melatonin as a sleeping aid and the bottom line on this literature is that it is confusing and controversial. Part of this may be due to the multitude of dosages used and the variability in patient selection.

Nevertheless, a portion of the trials conclusively point to the potential for melatonin as a facilitator for sleep and the attempt to turn that into an ethical pharmaceutical, although risky, seems like a worthwhile venture. As per the old adage, 'nothing ventured, nothing gained'!!!

Expected Value of Posidorm

Summary of Valuation (pre-corp tax)

Scenario (£m)	Core	Optimistic
EV of Royalties	48.3	118.1
Likelihood of success (PoS)	67%	67%
EMV of Royalties	32.3	79.1
Add: EMV of upfront payments	0.0	0.0
Add: EMV of milestone payments	0.0	0.0
less: EMV of dev costs	5.3	5.3
EMV of Posidorm	27.1	73.9
per share (£)	0.17	0.46

Key Market & Licence Assumptions

Indication/Market	Route to Market	Royalty Rate/ Effective Margin	Impact of Generics	
			Approx Date	Price Impact
UK& Eire	Marketed	39%	2017	-50%
EU	Licensed	30%	2017	-50%

Sensitivity to change in ...

Impact of generics (+ % price decline)

	-20.0%	-10.0%	+0.0%	+10.0%	+20.0%
Value (£m)	36.6	31.7	27.1	24.9	22.7
Change in Value	35%	17%	0%	-8%	-16%

Increase in royalty/margin (+%)

	-10%	-5%	0%	5%	10%
Value (£m)	17.8	22.4	27.1	31.7	36.4
Change in Value	-34%	-17%	0%	17%	34%

Components of core valuation* (pre-corp tax)

Core scenario

Expected Value of Royalties/Revenue (£ millions)					
Indication/Market	EV of cashflow	Current Stage of Dev	PoS	EMV	% of Val.
UK & Eire	6.6	Phase 3	67%	4.4	9%
EU	41.7	Phase 3	67%	27.9	58%
Total	48.3		67%	32.3	

Opimistic view: higher market penetration

Expected Value of Royalties/Revenue (£ millions)					
Indication/Market	EV of cashflow	Current Stage of Dev	PoS	EMV	% of Val.
- Sales UK & Eire	49.0	Phase 3	67%	32.8	30%
- Sales EU	61.9	Phase 3	67%	41.5	37%
Total	110.9		67%	74.3	

Expected Monetary Value of Posidorm
£27.1m - £73.9m
17p - 46p per share

EMV of Upfront payments
£0m

EMV of Milestone Payments
£0m

*See page 23 for forecast revenue

Overview

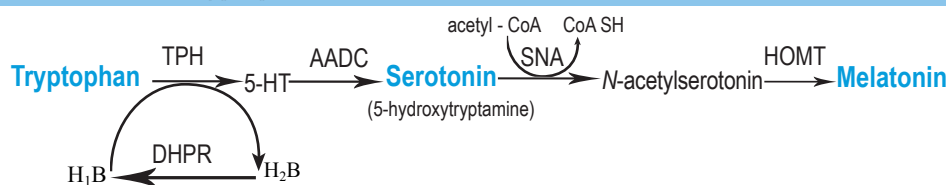
Melatonin is a product of the metabolism of tryptophan, an essential amino acid that must be part of the human diet. It is synthesized and secreted in the pineal gland in response to the onset of darkness and appears to be involved in the regulation of the sleep cycle through what is called the 'circadian rhythm'. During a 24-hour cycle, melatonin is secreted to its highest level during the night and then tails off during the day.

As seen in the accompanying Figure, the amino acid tryptophan is converted into serotonin (whose re-uptake drugs such as Prozac inhibits) and then converted after acetylation to N-acetylserotonin, which is then converted to melatonin.

There is a considerable body of data that points to lower levels of melatonin in the blood of the elderly. However, based on the variability of melatonin levels in the elderly and the fact that some elderly subjects with low melatonin levels are able to display normal sleep patterns, it is thought that melatonin levels may not be fully correlated to the quantity or quality of sleep. Nevertheless, several double blind randomized clinical trials of melatonin conducted in the elderly with disrupted or poor sleep patterns have been able to show significant improvements in the onset of sleep and its quality. While there is a considerable degree of conflicting data in this area, the variability in dosing and formulations and the target patient populations used could all have contributed to the variability in outcomes observed. Enter Alliance Pharma and the development of Posidorm.

Historically, melatonin has been (and still is) available as an over the counter (OTC) nutritional supplement in the US (it has anti-oxidant properties amongst other beneficial effects). In Europe it was withdrawn because its impact on sleep was deemed to be a pharmacological effect and hence classified as a medicine by the regulatory authorities. Conflicting clinical data, its widespread availability in the US and the need for a GMP formulation and clinical trials in Europe, have all been factors in the lack of motivation for international pharmaceutical companies to develop melatonin as a drug in the European arena. Although it is not available in Europe through conventional channels, doctors throughout Europe use melatonin in needy cases. In the UK alone, Alliance estimates that the sale of GMP grade melatonin is in excess of £6 million on a named patient basis⁵. Hence, the market potential is there and ready to be seized.

Metabolism of tryptophan into melatonin



Source: Alliance Pharma

⁵ "Named patients" are special dispensations obtained by doctors to treat a patient on a compassionate or as needed basis for a medication not approved in the UK

The opportunity to develop this market depends on the ability of Alliance to demonstrate a statistically significant result on the onset, quality and quantity of sleep in targeted populations. Under European directives, the clinical trials that Alliance is conducting would trigger a 10-year period of market exclusivity upon marketing. The Company is conducting Phase III clinical trials in the elderly and night shift workers to test its efficacy in helping to regularise sleep patterns for these targeted patient groups.

The 2 studies are designed in the way that most melatonin trials have been conducted as a double-blind randomized crossover trial where each patient is tested at one or two doses against placebo for a defined period of time with a 1 week washout in between.

Formulation and trial design

The studies being conducted derive from a considerable body of evidence that melatonin is efficacious in promoting the onset and maintenance of sleep without any 'hangover' effects the next day. Work carried out by Zhadanova in Richard Wurtman's lab at MIT⁶ has shown that physiological, low-dose melatonin (of 0.1 or 0.3mg) was sufficient to promote this effect in a double-blind, randomised, placebo-controlled crossover study. The formulation developed for Alliance takes into consideration the body of literature that shows that the elevation of melatonin plasma levels at the onset of darkness, which triggers sleep and maintenance of physiologic levels during the night time, in order to maintain sleep, might be the best combination to go for in a commercial preparation. The formulation derived in this way consists of an outer core that delivers a burst of drug upon oral delivery followed by sustained slow release of melatonin at a more physiological dose from an inner core over the 7-8 hours of night time where sleep occurs. The resulting formulation has been tested in a phase I study in human volunteers and exhibits the desired pharmacokinetic properties.

Elderly patients

The trial consists of a drug arm versus placebo in a double blind crossover trial of around 300 patients. The trial is a series of 4-week treatment periods, with a 1 week washout period in-between (where no drug is given). There is a 2-week run-in to determine suitability of the patient and there is a 4-week follow-up period to study the ease of withdrawal. The study is double blinded (so no one knows what is given) and the sequence of doses and placebo are randomised. The primary endpoint of the trial will be any statistically significant changes in the total amount of sleep as measured by sleep diaries and wrist actigraphs. Secondary endpoints will be the:

- time to sleep onset;
- number of night awakenings;
- sleep quality;
- results of the standard Leeds Sleep Evaluation Questionnaire.

⁶ Zhadanova IV et al, *J.Clin.Endocr. & Met.*, 86(10):4727-4730

Night shift workers

Around 15-20% of the workforces in industrialized countries are involved in jobs that either require night shifts or require rotation into them. This type of work has the ability to disrupt sleep patterns in these individuals with nefarious consequences both in terms of quality of life as well as morbidity.

Alliance is conducting a Phase III clinical trial to determine whether workers in 'shift pattern' jobs (12 hour shifts of 3-4 days followed by 4 days off and a repeat of this) who report a current reduction in sleep (that reduction must be at least 1/3 of normal sleep patterns) during the night shift section of the cycle, can benefit from Posidorm.

This trial involves active dose and placebo and follows the double blind, randomised, crossover pattern described above. The data in this area is not as clear as in the elderly but the trial is using GMP materials and is statistically powered to show significance if there is an effect.

The primary objective of the study is to determine whether 1.5 mg of Posidorm can increase daytime sleep following a night shift.

The secondary endpoints are to determine whether the administration of Posidorm can:

- increase the maintenance of daytime sleep;
- reduce sleep latency;
- reduce the number of episodes of disturbed sleep following a night shift;
- detect any 'hangover' effects during night shift after Posidorm intake;
- compare adverse events between Posidorm and placebo.

While success in this arena is a possibility, given the previous body of work and the lack of efficacy seen, we remain to be convinced that this trial will achieve a successful outcome. As we will see below, success would add a significant dimension to the potential of Posidorm.

Other target indications

Insomnia comes in different forms and the indications for a drug like Posidorm are not limited to the elderly and night shift workers. There are primary and secondary forms of insomnia. Secondary forms of insomnia tend to be associated with other conditions and are not the focus of a drug like Posidorm. Primary insomnia is where the causality is indeterminate and the disease is due to endogenous sleep factors such as melatonin or other sleep cycle related hormones or substances. In this category there are other potential indications that Alliance could pursue where there is already some evidence that a drug like Posidorm might have an effect.

In **Blindness**, a significant proportion of the population (as many as 50% of the blind population⁷) suffers from sleep disorder. This is thought to be due to the inability of the brain to process the daily shifts in sleep time onset, resulting in an 'out of synch' circadian rhythm. It has been shown that melatonin can be used to readjust the sleep clock, thereby alleviating these sleep disturbances, which would result in a significant improvement in the quality of life.

Jet Lag is a phenomenon well known to travellers when traversing time zones. A period of adjustment is required to, as we say, adjust the clock and melatonin could have a beneficial respect in this regard. With a diffuse market of this kind, it is very difficult to estimate the size of this market and even harder to run clinical trials!!

Neurodisabilities

It is also thought that the disturbed sleep patterns observed in a variety of neurodisabilities in children could also benefit from supplemental melatonin. ADHD and Alzheimers are potential opportunities which may be investigated.

The Market

As seen in the attached table, the European market for selected sleep disorders is estimated at around 25.6 million.

European market size for Posidorm				
Markets	Target population* (m)	Sleep disorders (m)	Treated (%)	Target market (m)
Elderly population	73.60	18.40	20	3.68
Night shift workers	9.20	6.44	10	0.64
Blind	0.78	0.39	10	0.04
Neurodisabilities (e.g., ADHD)	1.32	0.36	10	0.04
Total				4.40

* Based on 460m population in Europe incl UK

Source: Alliance Pharma, UN population statistics and various sources

⁷ WHO Data in *Br J. Ophthamol* 2002; 86:716-722

The prescription drug market for sleep disorders is dominated by hypnotics and anxiolytics, which include benzodiazepenes and derivatives (e.g., Valium) and non-benzodiazepenes or z-drugs (because they all start with a Z!) such as the GABA A receptor agonists. The market leader of late is Ambien (Sanofi Aventis, a GABA A receptor agonist) that achieved sales of US\$1.85bn in 2005 in the US in what is roughly a US\$3bn market worldwide. Evaluate Pharma estimates that this market should grow 5.26% per annum until 2010. The European market for hypnotics and anxiolytics is estimated to be around US\$700-US\$800 million (Company data and Evaluate Pharma). The recently introduced GABA A receptor agonist Lunesta (eszopiclone, Sepracor) has already clocked up around US\$329 million of sales in 2005 in the US and is expected to grow to around US\$1.35bn worldwide by 2010 (Evaluate Pharma). This would make it the new market leader. In this kind of market, it is not hard to see the potential for a successful product to rapidly fill its market niche!

Current hypnotics and anxiolytics carry a number of serious problems and side effects, which make their use problematic. Side effects and issues include:

- dependency and withdrawal;
- triggering bouts of hostility and aggression;
- impairment of judgment.

All of which would leave one to believe that the possibility of a treatment relatively clear of any serious side effects that is effective for sleep in these various indications would be welcome. Add to that a relatively modest pricing strategy and one could imagine Posidorm capturing a not insignificant market position. However, it is important not to get too carried away as the degree of suspicion that prescribing doctors will have for a treatment such as Posidorm should not be discounted. Doctors often tend towards the scientifically snazzy and might choose to ignore a melatonin-based formulation unless the data is absolutely compelling.

Estimated peak sales for Posidorm

Indication	Patient population (millions) (est.)	Estimated time	Cost per treatment course***	Total market (£m)	Market penetration (est.)	Est. peak mkt sales (£m)
Elderly*	3.7	6 months	£90.00	331	10%	33
Elderly**	18.4	6 months	£90.00	1656	10%	166
Night Shift	9.2	30 days	£24.00	221	10%	22

* Treated only

** All elderly with sleep disorders

*** At an estimated cost of £0.80 per diem. Average of 3-6 months

Source: Alliance Pharma and OC estimates

Assuming a cost of around £0.80 a day and a treatment for 6 months (£90 per treatment course), the European market for the elderly with a target population of treated patients of 3.7 million patients is somewhere in the neighbourhood of £331 million. If one assumes a market penetration of say 10%, the value of peak sales for the treated elderly market indication alone could be somewhere in the region of £33 million.

For night shift workers with an estimated potential market of 9 million workers for say 10 days a month for 3 months (£24 per treatment course) the market would be in the range of £220 million. At a 10% penetration rate this equates to an additional £22 million of peak sales.

Hence for these two indications alone, we can easily reach peak market sales in the range of £50m – £75m. And this assumes that the elderly market does not expand and that only patients that are currently treated would be potential market targets. The overall market for the elderly with sleep disorders is estimated to be somewhere in the range of 18 million patients. That would bring our elderly market value range to £1.66bn and a potential peak market at a 10% penetration to around £165 million.

These numbers are obviously very far from the £50 million estimate given by Alliance to the financial community. Assuming that compelling Phase III data is generated, it is possible to forecast a considerable shift towards this type of medication particularly in countries like France, Germany and in Scandinavia, where physicians are more open to natural remedies than say the UK or Italy. The only caveat for the UK would be if the NHS perceived the treatment as effective and low cost and promoted it as a good way to resolve sleep disorders. That would be a bonanza indeed!!!

The bottom line is whether the potential is the £50 million estimated by Alliance or the potential circa £200 million market for the elderly that we can reasonably estimate. Success here, along with the development of Isprelor could result in an explosion in earnings from 2008 on.

Overview

- Earnings in 2006 and 2007 will be relatively flat due to the front end loading of both development and pre-market launch costs
- We see a clear inflection point post 2007 with earnings exploding with the shift to Growth products along with the introduction of both Isprelor and Posidorm in late 2007 in the UK and Eire, and in the rest of Europe in 2008 and 2009
- In 2008 the significant ramp up in earnings should be driven by growth products (Periostat, International and Dermatology) but in 2009 the development portfolio should start to pitch in
- Clearly, as seen in the cashflow projections, the company will need to raise further capital to launch the Development portfolio

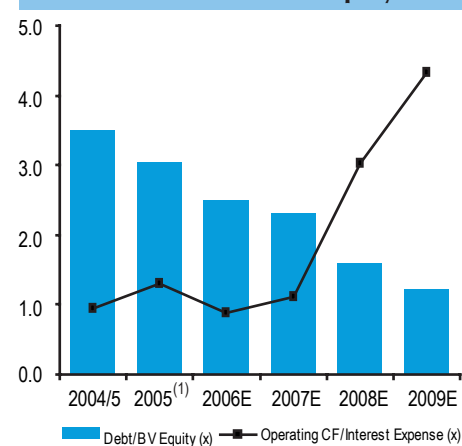
Debt structure and cashflow utilization

As of the end of 2005, Alliance had around £21.96 million in long-term debt of which £7.5 million is a convertible loan at a fixed rate of 8%. The conversion price works out to 21p any time up to 2013. Current liabilities at the end of 2005 were £933,000.

Generally, Alliance splits the use of its trading profit and cash flow into three uses: payment of interest, repayment of debt capital and development funding. Out of £3.08 million in actual trading profit (from the Core and Growth portfolio revenues) booked in 2005, interest paid was £1.426 million and £1.115 million of debt (capital) was repaid. Development costs were capitalized on the balance sheet and reflected £1.85 million plus £1.14 million of pre-marketing costs (which are expensed) related to launch of development products (Isprelor in particular). In cashflow terms, about £500,000 was contributed directly out of trading cashflow and the rest through financing. This is summarized below

Cash flows from trading activities	£ 3.08 million
Interest Paid & Similar Charges	(£1.426 million)
Repayment of Borrowings	(£1.115 million)
Contribution to Development Costs	(£500,000)

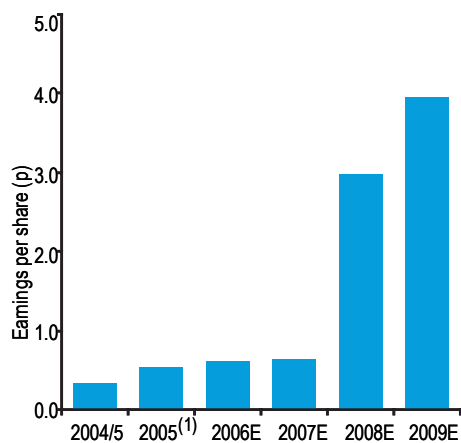
Interest Cover and Debt/Equity



⁽¹⁾ 10 months grossed up for 12 months

Source: Objective Capital

Earnings inflexion point post 2007



⁽¹⁾ 10 months grossed up to 12

Source: Objective Capital

Going forward, we are projecting increased interest payments as further acquisition-fuelled debt accumulates as well as a continued and sustained contribution to development costs and debt repayment wherever cashflow allows it. However, as we are unable to predict the size of acquisitions to be made post 2006, we are simply predicting that Alliance will make 'Core' and 'Growth' acquisitions at a flat rate in line with what we have seen in 2006 with debt increasing accordingly. In the final analysis, the rate of acquisition and debt take-up could be higher or lower depending on the nature of these activities.

As earnings are increasingly driven by the growth portfolio, international and the development drugs, we project a significant increase in operating cashflow in 2008 and 2009. The result will be progressive declines in the Debt:Equity ratio and Alliance's first dividend. The former assumes a slowdown in acquisitions as per our model, which may or may not turn out to be the case. How Alliance will fine tune this model is anybody's guess and is hardly predictable by the Company or ourselves. We anticipate that Development products will be a drain on cashflow in the initial 2-3 years but the losses incurred should be masked by the strong operating cashflow generated by the Growth products and International development in full swing post 2007. All of this contributes to our anticipation of an earnings inflexion followed by earnings acceleration in 2008 and beyond.

Profit and Loss Statement

YE 31 Dec., £m

(except per share data)

	2004/5	2005 ⁽¹⁾	2006F	2007F	2008F	2009F	CAGR
Total Revenues	11.8	12.3	16.9	21.8	30.2	42.7	29%
Cost of Sales	5.6	5.6	7.6	9.5	11.8	14.4	
Gross Profits	6.2	6.7	9.3	12.3	18.4	28.2	35%
Depreciation	0.1	0.1	0.1	0.2	0.2	0.2	
Amortisation	0.0	0.1	0.0	0.0	0.0	0.0	
SG&A	3.7	4.5	6.4	9.1	10.7	15.9	
Share-based Employee Remuneration	0.0	0.0	0.0	0.0	0.0	0.0	
Operating Profits before Non-Recurring Items	2.4	1.9	2.7	2.9	7.4	12.1	
Non Recurring Items	-0.1	0.2	0.00	0.0	0.0	0.0	
Earnings before Financing Costs	2.3	2.2	2.7	2.9	7.4	12.1	
Interest Paid	1.7	1.4	1.7	1.9	1.8	1.6	
Other finance Costs	0.2	0.1	0.0	0.0	0.0	0.0	
Change in the value of Derivative Instruments	0.0	0.1					
Pretax Profit (Loss)	0.4	0.7	1.0	1.0	5.6	10.5	91%
Taxes(credit)	0.0	0.0	0.0	0.0	0.6	3.1	
Net Income (Loss)	0.4	0.7	1.0	1.0	4.9	7.3	
- Dividends						0.7	
Net retained income	0.4	0.7	1.0	1.0	4.9	6.6	
Average Shares outst.	124.2	146.9	161.4	163.5	165.5	167.6	
Earnings per Share (in Pence)	0.33	0.45	0.61	0.63	2.98	3.94	65%
Grossed up for full year	0.33	0.54	0.61	0.63	2.98	3.94	

Margin and Line item Analysis	2004/5	2005 ⁽¹⁾	2006F	2007F	2008F	2009F
Gross Margin	52%	54%	55%	56%	61%	66%
SG&A	31%	37%	38%	42%	36%	37%
EBIT Margin	19%	18%	16%	14%	25%	28%
Taxes	0%	0%	0%	0%	12%	30%
Dividend Yield	—	—	—	—	—	10%
Net Margin	3%	5%	6%	5%	16%	17%

Growth Analysis	2005 ⁽¹⁾	2006F	2007F	2008F	2009F
Revenues	4%	38%	29%	39%	41%
SG&A	21%	43%	42%	17%	48%
Net Income	62%	50%	4%	377%	34%
EPS	37%	37%	3%	371%	33%

⁽¹⁾ 10 months only

Summary Balance Sheet

YE 31 Dec., £m	2004/5	2005 ⁽¹⁾	2006F	2007F	2008F	2009F
Fixed Assets						
Goodwill	1.1	1.1	1.1	1.1	1.1	1.1
Intangible						
Product Licenses	25.6	25.5	30.2	31.4	32.6	33.8
Development Costs	1.3	3.1	5.6	8.1	9.1	9.1
Property, Plant & Equipment	<u>0.3</u>	<u>0.3</u>	<u>0.4</u>	<u>0.5</u>	<u>0.5</u>	<u>0.6</u>
Total Fixed Assets	28.4	30.0	37.3	41.1	43.4	44.6
Current Assets						
Inventories	2.5	2.7	3.7	5.0	6.9	9.7
Trade and other Receivables	2.1	3.0	4.2	5.4	7.5	10.6
Cash and Cash Equivalents	<u>1.3</u>	<u>0.0</u>	<u>0.0</u>	<u>0.0</u>	<u>0.0</u>	<u>0.0</u>
Total Current Assets	5.9	5.8	7.9	10.5	14.5	20.5
Current Liabilities						
Cash and Equivalents	0.0	0.9	1.2	3.5	2.2	-2.9
Short term Notes	2.5	0.9	2.0	2.3	1.2	2.0
Accounts Payable	3.4	4.3	5.1	6.5	9.0	12.7
Total Current Liabilities	5.9	6.1	8.3	12.3	12.5	11.9
Net Current Assets	0.0	-0.3	-0.3	-1.9	2.0	8.6
Total Assets - Current liabilities	28.4	29.6	37.0	39.2	45.4	53.2
Long Term Financial Liabilities	14.3	14.8	18.1	18.9	19.8	20.6
Convertible Debt	7.1	7.2	7.5	7.5	7.5	7.5
Other Liabilities	0.2	0.2	0.4	0.4	0.4	0.4
Total Long Term Liabilities	21.6	22.1	26.0	26.8	27.6	28.5
Net Assets	6.8	7.5	11.0	12.4	17.7	24.7
Shareholders Equity						
Common Stock	1.5	1.5	1.6	1.6	1.7	1.7
Share Premium Account	9.0	9.0	11.4	11.7	12.1	12.4
Share Option Reserve	0.0	0.0	0.1	0.1	0.1	0.1
Reverse Takeover Reserve	-0.3	-0.3	-0.3	-0.3	-0.3	-0.3
Retained Earnings (Loss)	-3.4	-2.7	-1.7	-0.7	4.2	10.9
Total	6.8	7.5	11.0	12.4	17.7	24.7

⁽¹⁾ 10 months only

Cash Flow Analysis						
YE 31 Dec., £m	2004/5	2005 ⁽¹⁾	2006F	2007F	2008F	2009F
From Operating Activity						
Net Income (loss) from						
Continuing Operations	2.3	2.2	2.7	2.9	7.4	12.1
Depreciation	0.1	0.1	0.1	0.2	0.2	0.2
Inventories	-0.7	-0.3	-1.0	-1.3	-1.9	-2.9
Accounts Receivable	-0.2	-0.9	-1.2	-1.2	-2.1	-3.1
Accounts Payable	0.1	0.9	0.8	1.5	2.5	3.8
Working Capital	-0.8	-0.3	-1.4	-1.0	-1.5	-2.3
Intangible assets amortisation	—	0.1				
Gain on divestment of Uniflu	—	-0.3				
Share option Charges	0.0	0.0	0.0	0.0	0.0	0.0
Cash From Operations	1.6	1.8	1.5	2.1	6.1	10.1
Tax Paid	0.0				-0.6	-3.1
Cash Flow from						
Operating Activities	1.6	1.8	1.5	2.1	5.5	7.0
From Investing Activities						
Capex	-0.2	-0.1	-0.3	-0.3	-0.3	-0.3
Purchase of other						
Intangible assets	-9.2	0.0	-4.7	-1.2	-1.2	-1.2
Proceeds from the disposal						
of Uniflu		0.5				
Transaction costs on disposal						
of Uniflu		0.0				
Payment of Deferred						
Consideration	-0.1		0.0	0.0	0.0	0.0
Development Costs capitalised	-0.9	-1.8	-2.5	-2.5	-1.0	0.0
Net Interest Received	0.2	0.1	0.0	0.0	0.0	0.0
Net Inflow (outflow)						
from Investments	-10.3	-1.4	-7.5	-4.0	-2.5	-1.5
From Financing Activities						
Issue of Ordinary Shares	4.2	—	2.5	0.4	0.4	0.4
Interest Paid & Similar Charges	-1.8	-1.4	-1.7	-1.9	-1.8	-1.6
Other Finance Charges	0.0	0.0	0.0	0.0	0.0	0.0
Dividend's paid	0.0	0.0	0.0	0.0	0.0	-0.7
Receipt from Borrowings	6.9					
Repayment of Borrowings	-3.8	-1.1				
Net Receipt from borrowings	3.1	-1.1	4.9	1.2	-0.3	1.7
Finance lease Payments	0.0	0.0	0.0	0.0	0.0	0.0
Net Cash Provided for (used in)						
Financing Activities	5.4	-2.6	5.7	-0.4	-1.8	-0.3
Net Change in Cash	-3.3	-2.2	-0.3	-2.2	1.2	5.2

⁽¹⁾ 10 months only

Appendix: Management

Key Management Team

Michael Gatenby, Non-executive Chairman: ex-Vice Chairman of Charterhouse Bank and non-executive Director of Porvair and Cobra

John Dawson, CEO: Pharmacist and MSc in Finance. Ex Ciba and Sandoz

Maddy Scott, CFO, Company Secretary ACCA: Serco, Nokia and McCann Erickson

John Barber, Director, Scientific Affairs: ex Roche, Glaxo Wellcome (now GSK) and ICI (now AstraZeneca)

Sam Madden, Director, Acquisitions & Integration: ex Sandoz and Abbott Laboratories

Tony Booley, Director, Sales & Marketing: Ex Leo Pharma and Glaxo Wellcome (now GSK)

Non-Executive Directors

Paul Ranson

Lawyer with 26 years of experience in Pharmaceutical legal practice in-Company (MSD and SmithKline French) and as a lawyer (Simmons & Simmons) where he set up the Pharma practice. Currently a consultant to Saul Stringers Pharamlaw.

Andrew Leonard Smith

Ex-SmithKline Beecham (various senior positions, now GSK), Cerebrus (CEO until sale to what is now Vernalis) and Parexel International (President, International Medical Marketing Services)

We are pleased to bring you this report on **Alliance Pharma**.



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As always, I welcome your comments and feedback on our research!

Gabriel Didham, CFA
Objective Capital

Steven Zimmer, M. Sc. (Molecular Biology)
Steven has more than 25 years experience in analysis, corporate finance and as a portfolio manager in biotech and pharma including working for DLJ, CSFB and Robert Fleming in London, NY and Switzerland.

About our relationship with Alliance Pharma

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