

14 September 2009

Merrion Pharmaceuticals

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/07	0.5	(12.1)	(1.6)	0.0	N/A	N/A
12/08	1.3	(5.1)	(0.3)	0.0	N/A	N/A
12/09e	4.7	(3.6)	(0.2)	0.0	N/A	N/A
12/10e	5.5	(4.2)	(0.2)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding goodwill amortisation and exceptional items.

Investment summary: Nil by needle

Merrion transforms injected drugs into oral pharmaceuticals, offering relatively low development risk with minimal regulatory and marketing uncertainty. Recent Phase II data on Orazol could enable a 2010 major partnering deal with a possible 2013 launch into a \$1.4bn market. Merrion is also developing oral therapies to reshape the diabetes market in a \$116m licensing deal with Novo Nordisk.

Orazol – expanding the bone cancer market

Orazol is an oral version of Novartis's Zometa (zoledronic acid), which, assuming the regulatory strategy works, could be marketed by 2013. Oral delivery would expand the market and potentially enable development of a new indication in early-stage breast cancer. A partner needs to be signed by 2010; a large fee can be expected.

Oral diabetes treatments: Novo validates GIPET

Merrion has collaborations worth \$116m to develop oral insulin and oral GLP-1. Oral insulin could be a disruptive \$1bn+ product, but the royalty is modest; oral GLP-1 will enter a competitive market. Clinical development could start Q4 FY09 with possible data and milestones in mid-2010. Novo funds development to about €3.5m per year.

Regulators, partners and patents

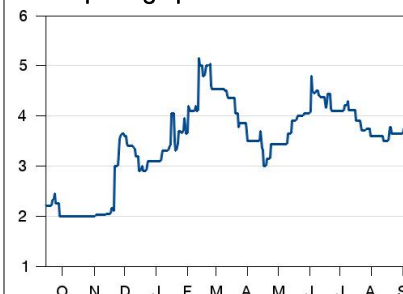
Merrion aims to use the FDA's 505(b)2 regulations to minimise Phase III clinical studies. Partners need to be signed for to progress generic reformulation projects. Patents on the core GIPET technology are strong but not fully secure in the US.

Valuation: Potential for rapid value growth on partnering

Merrion's value rests on the potential of Orazol in cancer and in oral insulin and GLP for diabetes. The reformulated generic products need partners to progress development and this is an important risk aspect. Using risk-adjusted DCF methodology based on 2020 sales projections, a 12.5% discount rate and a prospective P/E multiple of 8x, we have calculated an indicative value of €100m or €5.50 per share fully diluted. We expect rapid value progression on Orazol, perhaps to €8.80 per share when a deal occurs. Insulin clinical data could also add value.

Price **€3.78**
Market cap **€64m**

Share price graph



Share details

Code 3MP
Listing IEX
Sector Pharmaceuticals
Shares in issue 16.9m

Price

52-week High Low
€5.05 €2.00

Balance sheet as at 31 December 2008

Debt/equity (%) N/A
NAV per share (c) 22
Net cash (€m) 8.4

Business

Merrion is an Irish company that uses technology acquired from Elan to reformulate injectable drugs into oral formulations. Its lead projects are Orazol, insulin and GLP-1 (in collaboration with Novo Nordisk).

Valuation

	2008	2009e	2010e
P/E relative	N/A	N/A	N/A
P/CF	N/A	2.1	N/A
EV/Sales	N/A	N/A	N/A
ROE	N/A	N/A	N/A

Geography based on revenues (2008)

	Europe	US	Other
0%	100%	0%	0%

Analyst

Dr John Savin 020 3077 5713
jsavin@edisoninvestmentresearch.co.uk

Investment summary: Nil by needle

Merrion was created in 2004 through the acquisition of the assets of one of Elan's drug delivery units for €2m plus 5% equity and a 10% royalty. The company listed on the Irish Enterprise Exchange (IEX) in December 2007 at €4.05 a share to raise €8m gross giving a capitalisation of €67.2m. The company uses its GIPET technology to reformulate injectable pharmaceuticals, mostly already marketed, for oral delivery. An oral formulation can open up a completely new market and reshape an existing one – as could be the case for Orazol in early-stage breast cancer and in two \$58m funded collaborations with Novo, to develop oral insulin and GLP-1 for diabetes.

Valuation: DCF value of €5.50 per share pre Orazol partnering

The value rests Orazol in cancer and in oral insulin and GLP for diabetes. Orazol has significant upside and a 60% probability of successful technical development in our view. However, it needs to be partnered and we have made a further 50% risk adjustment to reflect this, taking the overall risk adjustment to 30%. Partnering should remove this uncertainty and could drive the indicative value substantially, but, without partnering, the project has little value. In addition, phase I/II data on oral insulin and GLP-1 maybe in 2010 should add substantive value although the Novo royalty is low. Using a risk-adjusted DCF methodology based on 2020 sales projections, a 12.5% discount rate and a prospective P/E multiple of 8, reflecting investor caution on emerging pharmaceutical shares, we have calculated an indicative value of €100m or €5.50 per share fully diluted.

Sensitivities

- The company's strategy is to partner projects after Phase I or Phase II. This is a particular sensitivity for Merrion as the decision to partner a generic molecule is very commercial.
- Some projects, for example Almerol (osteoporosis) and Acyline (cancer), may be commercially weaker than Orazol although MER-102 (antithrombotic) offers a defined niche opportunity.
- There is a high regulatory sensitivity as it needs to be established that the 505(b)2 fast-track pathway for generic reformulated compounds applies to Orazol.
- GIPET delivery seems technically validated. However, specific US patents on therapeutic-GIPET combinations are not yet granted; EU patents are granted with broad GIPET claims.
- Non-injected insulin has been a graveyard for innovation for over a decade. The GLP-1 market is highly competitive, with both biological and small-molecule products
- The company has expanded operations, with a new facility increasing capacity tenfold and extra staff to serve the funded Novo collaboration. The costs are covered by the Novo collaboration.

Financials

The Novo collaboration will generate revenues of €3.5m in FY09; other income could be €0.3m. From the accounts, up-front payments totalling €4.8m have been received from Novo; their recognition will be spread over the next five years with €0.9m recognised in FY09. Revenues reported will be around €4.7m in total. Interim cash increased to €8.4m in June, compared with €8.1m at the 2008 year end. Purchase of a €3.75m facility (part funded by a €2.1m mortgage and €0.75 equipment lease) will affect H2 cash flow. We expect significant milestones from Novo in FY 2010, and a partnering deal on Orazol in 2010/11 should generate a substantive up-front payment. Net operational costs remain low at around €7.5m per year.

Company description: Research heritage reworked

Merrion is an Irish company formed to acquire certain drug delivery technologies from Elan. It is based at facilities in Trinity College Dublin, but has just purchased a purpose-built facility outside Dublin, which will increase its capacity tenfold, enable the acceleration of several development programmes and also allow small scale manufacturing. It currently has 35 employees.

Merrion's core IP is the GIPET technology. Since its IPO, Merrion has enhanced the product portfolio acquired from Elan. Specifically, the Almerol programme has led to the development of Orazol, where the marketing advantages of GIPET are much clearer. In addition, a project with Novo Nordisk has progressed into a major \$116m collaboration with about €3.5m yearly development funding plus a royalty. As Merrion moves towards pivotal clinical studies on Orazol, the regulatory strategy of using the FDA's 505(b)2 regulations on generic equivalents will be tested.

Exhibit 1: Merrion's R&D portfolio

Product	Drug uses	Notes	Merrion clinical status
Orazol (zoledronic acid) /MER-101	Prevention of skeletal related events (fractures) and bone metastases in solid tumours and multiple myeloma and for osteoporosis.	Zometa (Novartis) is dosed as a 4mg iv infusion every month for SREs and as a once yearly 5mg iv infusion for osteoporosis. Novartis's patents expire in 2013 and, if successful, Orazol could be on the market by this time.	Phase II biomarker data indicate that weekly oral Orazol (20mg) is as effective as monthly iv Zometa (4mg). Intention is that a large partner would conduct registration trials, Novartis would be ideal.
Almerol/ (alendronate)/ MER-103	Bisphosphonate indicated for prevention/treatment of osteoporosis. Paget's disease.	Fosamax (Merck & Co) generic since 2008; other bisphosphonates patents expire 2011-12. Oral doses are 10mg/5mg per day or 70mg / 35mg weekly (treatment / prevention). Liquid dose is also available.	A Phase I study showed that 6mg Almerol might be equivalent to 70mg Fosamax. Advantages include night-time administration (although not with food).
MER-104 (acyline)	GnRH agonist for prostate/breast cancer.	Would require full clinical development. Addresses a large market but with many established products.	NIH has run trials of an injectable in 125 volunteers. Merrion has run a nine patient Phase I. and a 4 patient dose escalation study.
MER-102/ fondaparinux	Factor Xa antagonist for prevention/treatment of thrombosis and embolism following surgery.	Arixtra (GlaxoSmithKline) is available as daily 2.5mg sc injection. It is usually combined with an anticoagulant and typically administered for five to nine days.	Preclinical evaluation showing 13-17% bioavailability. GIPET shown to work with other heparin products in Phase I studies.
Oral insulin analogue	Diabetes. Possibly taken before or with meals as a supplement.	Potential major innovation with more 'natural' mode of insulin action but must deliver as a predictable dose and time.	Preclinical evaluation of candidates. Will require an extensive clinical development programme.
Oral GLP-1 analogue	Type 2 diabetes.	Byetta (exenatide, Lilly) is daily sc; a weekly formulation is under FDA review. Victoza (liraglutide, Novo) has EMEA approval.	Preclinical evaluation of candidates. Will require an extensive clinical development programme.
Ferring compound	N/A	Evaluation that may convert into a licensing deal. Product not disclosed.	Preclinical
Other	Various	Evaluations of oral versions of difficult products.	Research

Source: Merrion reports, Edison Investment Research commentary

GIPET – technically strong, but IP not fully secured

Merrion's GIPET (gastrointestinal permeation enhancement technology) uses well-known compounds to enhance drug absorption, all designated by the FDA to be Generally Regarded As Safe (GRAS, a food safety category), which simplifies regulatory submission. These are formulated using an enteric coated tablet to release the drug in the duodenum (upper small intestine). Merrion also has two other technology platforms that are not currently used.¹ GIPET offers a broad platform

¹ One (GIREs: gastrointestinal retention system) is a way of prolonging delivery of a drug to the stomach. The other patented system uses non-natural forms of amino acids (D rather than L), granted US patent 6,780,846.

to deliver many different peptides and hard-to formulate small molecules. It should allow Merion to develop many new products and collaborative deals to extend its portfolio and revenue base.

The US patent position on GIPET is not fully resolved with no granted patents as yet but the company states that it expects a number of patents specifying specific drug-GIPET combinations, including Orazol, to be allowed²; other patents may also might offer protection. The European GIPET patent³ was granted with all broad claims in 2008 and will be in force until February 2020.

Bisphosphonates

Bisphosphonates are a major drug class used for treatment and prevention of osteoporosis, the weakening of the bone particularly seen in postmenopausal women⁴ (Exhibit 2). However, bisphosphonates irritate⁵ the upper gastrointestinal tract so patients have to wash the tablet down with at least a glass of water⁶ and remain upright for 30 minutes. The drug also binds to food, reducing absorption by 90%, so it must be taken after fasting. In practice, this means first thing in the morning. As a result of these factors, there are significant patient compliance issues.⁷

Bisphosphonates are also used to treat of skeletal complications in advanced cancer. Cancers in the breast, prostate and lung often develop bone metastases causing pain and a high risk of fracture. Bone resorption also leads to high calcium levels (hypercalcaemia) which have deleterious cardiac and renal effects. In multiple myeloma, the cancer cells cause lytic lesions leading to vertebral fractures. Zometa (zoledronate) takes 99% of this market, which is worth c \$1.4bn. Orazol would give a new product post patent expiry in 2013.

Amgen steps in with denosumab; Merck tries something different

A major new product in this market is the monoclonal antibody Prolia (denosumab; Amgen, co-marketed by GSK), which could reach the market by H1 2010. Prolia is administered subcutaneously twice a year for osteoporosis.⁸ It is presumed that, as it is an antibody therapy, it will be much more expensive than generic bisphosphonates, perhaps \$15,000 per patient per year, and some analysts have forecast sales of \$2bn. Data comparing Zometa and Prolia in 2,049 advanced breast cancer patients were released in July and showed superiority for Prolia. Further data comparing Prolia to Zometa in 1,776 patients in other cancers were released in August and showed comparable efficacy. In metastatic cancer, Prolia is given as a 120mg infusion every four

² With respect to the US application (09/510,560, 22 Feb 2000), the US examiner would not allow the broad claims and narrower claims have been filed in a series of continuation patents. For example Orazol is potentially covered by a US patent application filed on 7 April 2006, number 2007/0196464 A1, as a continuation in part of the 2000 application. The 2000 patent cites insulin and aldrionate as examples (claim 9).

³ EP 1154761, although some national applications were allowed to lapse.

⁴ Bisphosphonates bind to bone and stop bone-resorbing cells (osteoclasts) from destroying bone. Bisphosphonates are not metabolised and the c 50% of absorbed drug that does not bind to bone is rapidly excreted in the urine. Dosing is accordingly affected by renal function, which can be a consideration in cancer, when renal function is often impaired. The major disadvantage with oral dosing of bisphosphonates is that it is very inefficient, with low bioavailability of only 0.6%. However, this profile is favourable for weekly, monthly and even yearly dosing. Other drugs used include Evista (raloxifene) and cacitonin.

⁵ A further complication can be osteonecrosis (this affects the jaw and is triggered by major dental work); there are also concerns over a possible atrial fibrillation risk, but this has unclear epidemiological data.

⁶ Administration with coffee or tea will reduce absorption by a further 60% so tablets can only be taken with water. Merck sells a raspberry-flavoured liquid formulation.

⁷ About half of all patients stop taking the drug within six months of starting therapy, and that for daily regimens only 15–30% of patients remain on treatment at the end of the first year.

⁸ Prolia 60mg iv twice yearly showed a 68% reduction in vertebral and a 40% reduction in hip fractures compared with placebo. In patients switched from Fosamax, bone density increased by 1.9% compared with 1.03% for those remaining on Fosamax. In addition, patients preferred twice yearly Prolia injections to oral weekly Fosamax. Head-to-head BMI data have not yet been released. Prolia may confer an increased risk of serious skin infections, but this was not particularly noticeable in the data.

weeks, which will considerably increase its cost. So far, FDA advisers have recommended the drug for treatment of bone loss in osteoporosis and prostate cancer in high-risk or unresponsive patients. It was not recommended for use in breast cancer due to safety concerns.

Merck has a new drug, odanacatib, in Phase III studies for osteoporosis, which could reach the market in 2013-14. The drug prevents destruction of bone collagen and should not inhibit bone formation; bisphosphonates can hinder this process.

Exhibit 2: Bisphosphonate products

Product	Brand (originator/co-marketer)	Indication	Comments
Alendronate	Fosamax (Merck & Co); now off patent	Osteoporosis, treatment/prevention; Paget's disease	Dosed orally at 10mg per day or 70mg per week for treatment. Prevention is dosed at 5mg per day of 35mg weekly. An oral liquid 70mg once per month formulation is available. Merck also sells a combination with vitamin D. Sales peaked at \$3.1bn in 2007.
Etidronate	Didronel (P&G/Sanofi-Aventis)	Heterotopic ossification; Paget's disease	Blocks bone destruction but also affects bone formation so has a more restricted use. Heterotrophic ossification is a disease of bone over-growth. Doses are 200mg and 400mg.
Ibandronate	Boniva, Bonviva (Roche/GSK)	Osteoporosis, treatment and prevention in women	Roche sold SwF1,108m in 2008 and GSK £237m (+37%). Patent expiry over 2011-12. Not indicated for men as trials were only conducted in women. The daily dose is 2.5mg. It was the first once per month product (in 2005) with a 150mg film coated tablet. There is an injectable once per three month 3mg formulation.
Ibandronate	Bondronat (Roche/GSK)	Metastatic breast cancer	EU approval for prevention of SREs in breast cancer. 2mg and 4mg iv monthly (1-4 hour infusion) and 50mg daily tablet formulations.
Pamidronate	Aredia (Pfizer/Novartis); off patent since 2001	Hypercalcaemia, metastatic bone cancer and myeloma	Sales in 2008 were \$21m. Its one use is that it seems to have a lower cumulative risk of osteonecrosis of the jaw relative to Zometa. Offsetting this is that the 90mg monthly dose requires a two-hour infusion. Teva has an injectable generic to overcome this issue.
Risedronate	Actonel, (P&G co-marketed with Sanofi-Aventis)	Osteoporosis, treatment and prevention; Paget's disease	Actonel is patented until May 2012, with other patents expiring in 2019. Teva mounted a US patent challenge to enable it to sell a generic but the court case failed. Dosing is 5mg daily, 35mg weekly, two 75mg tablets on consecutive days once per month, or a once-monthly 150mg tablet. P&G 2008 sales were \$714m; Sanofi reported €330m.
Tiludronate	Skelid (Sanofi-Aventis)	Paget's disease	This is available as two 200mg daily tablets given in three-month courses with at least six months between courses. Sales are trivial.
Zoledronic acid	Zometa (Novartis)	Hypercalcaemia, metastatic bone cancer and myeloma	US sales in 2008 were \$666m and ROW were \$716m, making \$1.4bn in total. The product is given as a 4mg, 15-minute infusion every four weeks. It is used to treat bone metastasis in breast, lung, prostate and renal cancers and myeloma.
Zoledronic acid	Reclast (Novartis)	Osteoporosis, male and female	This is a once-yearly treatment using a 5mg dose. The indication was approved in 2007 by the FDA. 2008 sales were \$254m.

Source: Edison Investment Research

Zometa and breast and other cancers

There has been much recent interest in the use of Zometa to improve breast cancer therapy. In a 2007 subgroup analysis⁹ of breast cancer patients treated with Zometa, a 40% reduction in the NTX bone biomarker was associated with an 11% lower risk of death and a 12% lower risk of a first skeletal-related event (SRE). In a 2009 published Austrian study on 1,800 patients, the use of Zometa plus endocrine therapy reduced the risk of disease progression by 36%, with 94% of patients having a disease-free survival of over 47 months compared with 90.8% on endocrine therapy alone (p=0.01). In a 2008 retrospective subgroup analysis from the AZURE¹⁰ trial, women who received Zometa plus chemotherapy before surgery had a 33% reduction in tumour size compared with chemotherapy alone (p=0.002), and fewer needed mastectomy. This provides strong evidence that Zometa could be used in early-stage, post-treatment breast cancer patients

⁹ Lipton, A. *et al.*, *The Oncologist*. 2007;12:1,035-1,043.

¹⁰ AZURE: adjuvant zoledronic acid to reduce recurrence. The data were presented at the 31st Annual CTRC-AACR San Antonio Breast Cancer Symposium in Dec 2008.

where a tablet would be the preferred dosing route; Orazol could be developed for this indication. A further indication could be for osteoporosis but this market is competitive with long-acting approved oral formulations. If developed, it could add 10-15% to sales volumes.

Zometa is also used in prostate cancer as 70% of late-stage cases have bone metastasis. There are many small-scale studies showing enhanced bone mineral density but only one placebo-controlled trial has been run. The current evidence is that Zometa is less effective in this disease.

Development of Almerol

Merrion reported on an indicative Phase I clinical study in 15 volunteers in January 2007. Almerol doses were given fasted in the morning, with food, and four hours after an evening meal. For the fasted and evening doses 10-12 times more alendronate was absorbed from 6mg Almerol compared with 35mg Fosamax.¹¹ This indicates that 6mg of the GIPET formulation could be equivalent to 70mg of Fosamax. If given with food, Almerol delivered more alendronate than Fosamax but 80% less than the fasted Almerol dose, so use with food is not indicated. No upper GI side-effects were seen in patients who took the evening dose and lay down, but this observation is purely indicative. Hence Almerol appears to have additional dosing flexibility. No further trials have been run. Further development depends on finding a partner; we use a technical risk of 30% but only assume a 25% partnering probability as no further development has occurred.

Development of Orazol

Orazol uses GIPET to deliver an oral dose of Zometa (zoledronic acid). The Zometa patent expires in March 2013.¹² The Orazol Phase II study data in 29 patients reported in May 2009 that, on the basis of bone markers¹³ and calcium, 20mg of Orazol weekly (22 patients treated) showed the same clinical effects as two 4mg iv doses of Zometa (seven patients) measured over 56 days. The finding is indicative as the trial was too small to gain statistical significance. That will need a better powered study and partner funding. There were indications that bone pain abated faster in Orazol patients than with Zometa (generally two iv doses are needed). Orazol was well tolerated.

Merrion has submitted documents to the FDA on a proposed trial design and a meeting is scheduled for October, which should clarify the agency's willingness to use the relatively less onerous 505(b)2 rules on equivalence, and notification should be received by November. Whereas biomarker studies may enable registration, marketing might need further studies looking at bone mineral density and SRE frequency.¹⁴ Discussions with the EMEA indicate that approval will be possible on the basis of bone markers in a six-month study involving 200 patients receiving Orazol and 100 patients receiving Zometa. There is a requirement for at least 100 patient years of data on Orazol. The trial will involve breast and prostate cancer patients.

Given the need for a partner, we assume that a deal will be signed in the six months following a definitive FDA agreement on the trial design; a deal beforehand is possible but less likely as the

¹¹ This was based on the excretion of alendronate in urine. As about half of any bisphosphonate absorbed is excreted unchanged in urine, this enables direct comparison of the effective dose.

¹² Novartis obtained a US paediatric extension to the patent, would otherwise expire in 2012. EU expiry is still in 2012. There may be patent challenges from 2010. Orazol cannot be marketed till the patent expires.

¹³ The bone markers used were NTX and CTX; these are collagen fragments released when bone is remodelled by osteoclasts. It is generally accepted from clinical studies that if these markers fall by 40-60% (as seen with Orazol), the risk of fracture is reduced. However, the link between bone mineral density and fracture rate is less clear. This is because bone density does not vary very much, by a few percentage points, and fracture risk depends on the strength of bone, which does not necessarily correlate with its density owing to the remodelling process. Hence, regulatory agencies have not used bone biomarkers to date as clinical trial endpoints.

¹⁴ To show that Actonel 5mg daily was equivalent to Actonel 150mg once a month, a 1,292-patient one-year trial was run. Merck ran a 889-patient trial to show Fosamax 70mg weekly was equivalent to 10mg daily.

partner will be unclear about the trial commitment. Assuming a deal is signed by spring 2010, clinical trials could start by mid 2010 with data by late 2011/early 2012. This could enable approval by the end of 2012 and launch in 2013 to coincide with the US Zometa patent expiry.

We would assume a substantive upfront payment on signing a deal, possibly €20m plus development milestones, but we have not built these into forecasts. We have assumed a 15% royalty but this may be conservative given the product profile. We also assume that further clinical studies in long-term post-operative therapy in breast cancer will be run as this is a new market suited to Orazol. The Austrian data (above) is extremely encouraging and off-label use is possible. The easiest and fastest indication would be the use of Orazol with chemotherapy before surgery. Overall, we assume a 60% technical probability of successful development. However, partnering is also critical and we have used a further 50% risk adjustment to reflect this uncertainty.

Novo collaboration: Oral insulin and GLP-1

Novo Nordisk is collaborating with Merion to develop oral insulin and oral GLP-1 for the diabetes market. Insulin could be applicable to both types 1 and 2 diabetes, whereas GLP-1 targets mid to late-stage type 2 diabetics. This collaboration is probably the most important for Merion as it provides research income of c €3.5m per year and a clear route to market for two potential blockbuster products. A particular strength of this collaboration is that Novo has a wide variety of insulin analogues to which other oral insulin projects do not have access. In addition, Novo has selected GIPET as suitable for delivery of these analogues.

Oral insulin

Based on Novo's sales figures and market share estimates, the 2008 global insulin market was worth around \$10bn. Novo claims to have a 55% share at c €3.9bn. Companies have tried to develop products that avoid injection but this has failed commercially even when solutions have been developed.¹⁵ Current oral insulin (and to a lesser extent GLP-1) development is mostly small-company based¹⁶ but these companies do not have novel insulin analogues as created by Novo.

No data have been released on any oral insulin candidates so assessing the potential is difficult. We view oral insulin as analogous to a short-acting mealtime insulin such as Humalog (insulin lispro; Lilly). Humalog annualised sales in 2009 will be around \$2bn. This is injected about 15 minutes before a meal. One could expect considerable switching of this market to an oral version that could be taken with food. However, it is very important to demonstrate that the dosing is reliable and consistent, and the initial market is likely to be type 1 patients as they are easiest to assess. It is known that oral insulin can be delivered, and insulin works, so we assume a 20% probability of reaching the market, high for a preclinical product, and a \$1bn+ potential; the royalty will be mid-

¹⁵ Inhaled insulin (Exubera, Pfizer) failed commercially and was withdrawn in 2008. This caused Novo to cease development of AERx iDMS; Lilly also ceased its development effort. However, Coremed (a US company) has initial clinical data on Alveair, an aerosol formulation. Mannkind (US listed) has an ultra-rapid mealtime inhaled insulin, Afresa; an NDA was accepted by the FDA in May 2009 so this could be marketed from 2010. Genexer (Canada) has an oral spray, Oral-lyn, approved in Ecuador and Lebanon and recruitment into a US Phase III study is ongoing in type 1 diabetes (data perhaps by 2011).

¹⁶ In the UK, Diabetology is working on oral insulin (Capsulin) with Phase IIa data in type 1 patients and preclinical GLP-1 data; key company management was associated with Cortecs in the 1990s which also tried to develop oral insulin. Oramed Pharmaceuticals (a US-listed Israeli company) has reported positive Phase IIa data on its oral insulin (ORMD-0801) in type 1 diabetics and is conducting a Phase IIb in type 2 patients in South Africa. Biocon, a major Indian company, is undertaking an Indian Phase III trial of its oral diabetes product (IN105). Given that Biocon is well connected with an acquired German subsidiary and links to Bristol-Myers Squibb, a successful Indian product could move readily into US clinical development. Coremed has preclinical data on its capsule-based oral insulin (Intesulin).

single digit (we assume 5%). The deal with Novo has \$58m of milestones. We assume that about a third is development related, with the rest paid on approval and on sales targets being reached.

The development route has not been disclosed but, from Danish press comments, the most promising formulations may enter clinical studies later in 2009 with data by mid-2010; this could presumably trigger a \$1-2m milestone. Novo will probably test several versions and doses before selecting Phase II candidates so one should not be too excited by initial results. A diabetes clinical development programme will take at least six years to run, indicating sales from 2015.

Oral GLP-1

This market was pioneered by Amylin and Lilly with Byetta (exenatide). Byetta is a twice per day injectable biological product, with sales of \$678m, that mimics natural GLP-1.¹⁷ Victoza (liraglutide) is a GLP-1 biological drug from Novo which was EMEA approved in July 2009 but is still under FDA review.¹⁸ Victoza will be a strong competitor for Byetta. A 2010 US launch is possible.

The GLP-1 related small-molecule products, Januvia, Onglyza and Galvus, are also directed to early to mid-stage type 2 patients. Other oral small-molecule products are in development. The market could reach \$3-5bn by 2012. This is competitive, big-pharma sales territory.

The oral GLP-1 product in preclinical development by Merion and Novo is probably based on liraglutide and its analogues modified to make them protease resistant and therefore more suited to oral delivery. It is difficult to be clear about the commercial implications and the probability of success as no data on the possible products are available and the market itself is still developing. One would envisage a market potential at least that of Byetta: c \$600m. However, Byetta is injectable, which limits sales, so an oral GLP-1 could have Januvia-like revenues of over \$1.5bn. Any oral GLP-1 needs to be clinically differentiated from the oral small-molecule alternatives to achieve blockbuster revenues. As a preclinical product, the standard of success is 5%, but we would see this as too low and assume c 10% at this time. We assume that the royalty will be 5%. The deal appears to be as for oral insulin with a similar timeframe targeting a 2015-16 launch.

MER-102: Deep vein thrombosis

This was a project started by Elan and developed further by Merion. The generic, fondaparinux, is marketed by GSK as Arixtra¹⁹ for deep vein thrombosis and pulmonary embolism. Arixtra is a small product, with £170m of sales, used for five to nine days after surgery to prevent cardiovascular complications. In patients at risk of DVT, up to 21 days' therapy is allowed. It competes in the low molecular weight injected heparin market dominated by Lovenox (enoxaparin; sales of €2.6bn).

Bayer (with J&J) has gained FDA recommended approval for short-term post surgical use of its oral product, Xarelto (rivaroxaban). Development involved four Phase III studies in 12,000 patients.

If MER-102 is to be developed, it will need a partner to manufacture fondaparinux and fund clinical trials. Despite the small market and new competition, this product occupies a protected niche that

¹⁷ Byetta improves insulin sensitivity and glucose regulation. Sales, mostly US, were \$678m in 2008 with growth of 7%. Sales slowed abruptly from August 2008 after an FDA alert that that the drug could trigger pancreatitis. Sales may be \$632m or less in 2009 based on Q109 data, although the clinical link with pancreatitis is not verified. An NDA has been filed for a once-per week version of Byetta. This uses a microencapsulation technology (Medisorb) from Alkermes.

¹⁸ The FDA committee was ambiguous with regard to a rare cancer risk based on rodent data.

¹⁹ Arixtra lost exclusivity in December 2006. However, no other company sells fondaparinux as it has a complex synthesis. An Australian company, Alchemia, claims a new synthesis route patented until 2027 and expects to enter the US market by 2010. Arixtra sales in 2008 grew by 53% to £170m; the sales rise seems to have been due to switching from heparin owing to contamination of some supplies.

may enable development with a specialist partner like Alchemia. We would not expect large sales but with the right deal, some form of JV or profit share, it could make a good profit contribution. We assume a 20% technical probability and a 50% partnering probability.

MER 104: Acyline for prostate cancer

Gonadotropin-releasing hormone (GnRH) triggers production of the sex hormones by affecting hormone receptors in the pituitary gland. There are a large number of marketed agonist products which stimulate the receptor.²⁰ This causes painful flare for a few days after which the system becomes downregulated, causing hypogonadism. Acyline has a different effect as it impedes the activation of the receptor. It has been used as an experimental drug in 10 clinical trials (nine NIH run) and given to over 125 people. Doses are adjusted for body weight.²¹ Oral dosing was tested by Merrion in summer 2007 in nine young male volunteers at 10mg, 20mg and 40mg doses. A further four patient dose escalation study was then run. Suppression of testosterone was seen but only the 40mg dose reduced this to under the normal range for only 12 hours. Injected acyline gives testosterone suppression for up to seven days at the highest dose (75µg/kg). We feel that further development is needed to get a viable candidate.

Sensitivities: Diversified opportunities and risks

- The company's strategy is to partner projects after Phase I or Phase II. This is a particular sensitivity for Merrion as the decision to partner a generic molecule is very commercial.
- Some projects, for example Almerol (osteoporosis) and Acyline (cancer), may be commercially weaker than Orazol although MER-102 (antithrombotic) offers a defined niche opportunity.
- There is a high regulatory sensitivity as it needs to be established that the 505(b)2 fast-track pathway for generic reformulated compounds applies to Orazol.
- GIPET delivery seems technically validated. However, specific US patents on therapeutic-GIPET combinations are not yet granted; EU patents are granted with broad GIPET claims.
- Non-injected insulin has been a graveyard for innovation for over a decade. The GLP-1 market is highly competitive, with both biological and small-molecule products.
- The company has expanded operations, with a new facility increasing capacity tenfold and extra staff to serve the funded Novo collaboration. The costs are covered by the Novo collaboration.

²⁰ Examples are Zoladex (goserelin) and Lupron (leuprolide). These products have to be injected or are formulated as long-acting depot products. Zoladex still sells £1.1bn although patents expired in 1999. Sex hormone synthesis can also be suppressed by other products, for example, Casodex, sales £1.2bn.

²¹ Acyline was designed as a possible male contraceptive. The clinical data were reported in 2002. Herbst *et al.* J. Clin. Endocrinology & Metabolism. 2002; 87: 3215-3220. Merrion has exclusively licensed the molecule in the US. The molecule is patented until 2014 but oral delivery is patent applications that could extend until 2017.

Valuation

To value the business, we have projected sales for key products with estimates of potential royalties (Exhibit 3). Merrion's portfolio could have a €3.4bn sales potential and generate over €300m of royalties (excluding milestones). The main value drivers are Orazol for metastatic cancer and oral insulin and oral GLP-1 as, despite the low royalty, the potential markets are large.

Exhibit 3: Valuation parameters

Note: Revenue estimates are not risk adjusted. Probability is the technical development risk adjustment multiplied by the probability of partnering, hence for Orazol 60% x 50% = 30%.

Product	Indication	Peak sales (€m)	Royalty (%)	2020 revenues (€m)	Probability (%)
Orazol	Early breast cancer	586	15	88	10
	Metastatic bone cancer	666	15	100	60
	Osteoporosis	100	10	10	10
Almerol	Osteoporosis	221	10	22	7.5
Oral insulin	Diabetes	1,200	5	60	20
Oral GLP-1	Diabetes	600	5	30	10
MER-102	Anti-thrombotic	50	20	8	10
Total		3,423		318	

Source: Edison Investment Research

DCF value of €5.50 with €8.80 potential on Orazol partnering

Using a risk-adjusted DCF methodology based on 2020 sales projections, a 12.5% discount rate and a prospective P/E multiple of 8, we have calculated an indicative value of €5.5 per share fully diluted, a capitalisation of €100m. There is scope for rapid value progression on Orazol to perhaps €8.80 per share when the 50% partnering risk is removed and the development timetable confirmed. Clinical data and on both oral insulin and GLP-1 analogues should be value enhancing.

Financial performance

Revenues

Revenues for the first half were €1.7m, and we forecast FY09 revenues of €4.7m (2008: €1.4m). Of this, some €3.4m are from Novo, about €0.3m from other contracts and €0.9m deferred revenues from the presumed up-front payments made by Novo. The new facility should allow a higher rate of development in the second half. It is possible that FY10 could see milestone payments from Novo in respect of Phase I/II oral insulin development and any licensing deal on Orazol could generate a major up-front payment. These payments are not in our forecast.

At the interim stage, the administration cost was €1.2m, in line with FY08. R&D was €2.6m, indicating an annualised expense of €5.2m (2008: €3.9m). In addition, about €1m of costs are directly associated with the Novo contract. Losses in 2009 should reduce to around €2.9m (2008: €5m) as revenues rise. Merrion pays 10% of its milestones and royalties to Elan as a royalty. The interim accounts show deferred revenue totalling €4.5m, an increase from €2.4m in December 2008. We assume that this relates to up-front payments from Novo, which caused cash at the interim stage to rise to €8.4m, up from €8.1m.

In July 2009, Merrion purchased a new, fully-equipped, specialist facility for €3.75m plus some additional costs. This 29,000ft² facility originally cost over €20m so is a real bargain. The equipment is funded by a €750k lease. The purchase is part-funded by a mortgage of €2.1m. This indicates year-end cash of about €6.5m. Tangible assets will rise to over €4m. Future cash will depend on milestones and up-front payments in FY10.

Exhibit 4: Financials

Year end 31 December	€000s	2007	2008	2009e	2010e
		IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue		469	1,340	4,700	5,482
Cost of Sales		(107)	(443)	(950)	(1,125)
Gross Profit		363	897	3,750	4,357
EBITDA		(5,624)	(5,056)	(3,408)	(3,894)
Operating Profit (before GW and except.)		(5,859)	(5,425)	(3,758)	(4,244)
Goodwill Amortisation		0	0	0	0
Exceptionals		0	0	0	0
Other		0	0	0	0
Operating Profit		(5,859)	(5,425)	(3,758)	(4,244)
Net Interest		(6,217)	363	180	6
Profit Before Tax (norm)		(12,076)	(5,062)	(3,578)	(4,239)
Profit Before Tax (FRS 3)		(12,076)	(5,062)	(3,578)	(4,239)
Tax		0	0	0	0
Profit After Tax (norm)		(12,076)	(5,062)	(3,578)	(4,239)
Profit After Tax (FRS 3)		(12,076)	(5,062)	(3,578)	(4,239)
Average Number of Shares Outstanding (m)		7.5	16.6	17.0	17.0
EPS - normalised (c)		(1.6)	(0.3)	(0.2)	(0.2)
EPS - FRS 3 (c)		(1.6)	(0.3)	(0.2)	(0.2)
Dividend per share (c)		0.0	0.0	0.0	0.0
Gross Margin (%)		77.3	67.0	79.8	79.5
EBITDA Margin (%)		N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)		N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets		967	788	3,438	3,388
Intangible Assets		180	0	0	0
Tangible Assets		787	788	3,438	3,388
Investment in associates		0	0	0	0
Current Assets		11,299	8,893	7,276	3,302
Stocks		0	0	0	0
Debtors		429	753	750	750
Cash		10,870	8,140	6,526	2,552
Current Liabilities		(2,131)	(4,009)	(5,525)	(5,740)
Creditors		(2,131)	(4,009)	(5,525)	(5,740)
Short term borrowings		0	0	0	0
Long Term Liabilities		0	0	(2,850)	(2,850)
Long term borrowings		0	0	(2,100)	(2,100)
Other long term liabilities		0	0	(750)	(750)
Net Assets		10,135	5,671	2,338	(1,900)
CASH FLOW					
Operating Cash Flow		(3,902)	(2,907)	306	(3,679)
Net Interest		174	299	180	6
Tax		0	0	0	0
Capex		(193)	(135)	(3,000)	(300)
Acquisitions/disposals		0	0	0	0
Financing		5,836	11	900	0
Dividends		0	0	0	0
Net Cash Flow		1,915	(2,732)	(1,614)	(3,974)
Opening net debt/(cash)		(8,967)	(10,870)	(8,140)	(5,176)
HP finance leases initiated		0	0	(750)	0
Other		(13)	3	(600)	0
Closing net debt/(cash)		(10,870)	(8,140)	(5,176)	(1,202)

Source: Edison Investment Research

Growth	Profitability	Balance sheet strength	Sensitivities evaluation	
N/A	N/A		Litigation/regulatory	●
			Pensions	○
			Currency	◐
			Stock overhang	○
			Interest rates	○
			Oil/commodity prices	○

Growth metrics	%	Profitability metrics	%	Balance sheet metrics		Company details	
EPS CAGR 06-10e	N/A	ROCE 09e	N/A	Gearing 09e	N/A	Address:	
EPS CAGR 08-10e	N/A	Avg ROCE 06-10e	N/A	Interest cover 09e	N/A	Biotechnology Building, Trinity College, Dublin 2, Ireland	
EBITDA CAGR 06-10e	N/A	ROE 09e	N/A	CA/CL 09e	1.3	Tel	+353 1 672.9272
EBITDA CAGR 08-10e	N/A	Gross margin 09e	79.8	Stock turn 09e	N/A	Fax	+353 1 672.9270
Sales CAGR 06-10e	N/A	Operating margin 09e	N/A	Debtor days 09e	58.2	www.merrionpharma.com	
Sales CAGR 08-10e	102	Gr mgn / Op mgn 09e	N/A	Creditor days 09e	429		

Principal shareholders	%	Management team
European Bioscience Fund I Ltd	19.5	Chairman: Patrick O'Sullivan
Growcorp Group Ltd.	15.4	Patrick O'Sullivan has been chairman since February 2009. He is a former CEO of Leo Pharma in Ireland and a board member of the parent Leo Pharma Group in Denmark (until 2006). Mr O'Sullivan holds an MBA and is a registered pharmacist. He is also a Director of Warner Chilcott.
Declan Ryan	14.5	
AIB plc	7.0	
John Lynch (CEO)	2.7	CEO: John Lynch
Michael McKenna	4.7	John Lynch is a founder of the company and has been CEO since 2008, COO since 2005 and MD from 2004. Before that, he spent 15 years with Abbott in the US and UK in senior positions. Earlier in his career Mr Lynch held financial positions with Bayer Diagnostics and Ernst & Young.
Bank of Kernal Capital	3.4	
Forthcoming announcements/catalysts	Date *	CFO: Jonathan O'Connell
Final results	March 2010	Jonathan O'Connell was appointed CFO in November 2005. He has over 13 years' experience in international finance and operations. Prior to Merrion, Mr O'Connell was the CFO at Spectel which was sold in 2004. From 1992 to 2000 he was CFO of Trinity Biotech. He joined Trinity from Arthur Andersen.
Interims	September 2010	
<i>Note: * = estimated</i>		

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Lincoln House, 296-302 High Holborn, London, WC1V 7JH ■ tel: +44 (0)20 3077 5700 ■ fax: +44 (0)20 3077 5750 ■ www.edisoninvestmentresearch.co.uk
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