EDISON

Laboratorios Farmacéuticos ROVI

Outlook on DORIA

DORIA low risk, high reward

Pharma & biotech

Laboratorios Farmacéuticos ROVI's (ROVI) investment case rests on the growth opportunities in its speciality pharmaceuticals portfolio, in particular the ongoing European roll-out of its biosimilar enoxaparin. However, over the next 12-18 months we expect increased investor interest in the proprietary ISM-patented R&D pipeline. Risperidone ISM or DORIA, a long-acting injectable (LAI) for schizophrenia, is due to read out data in Q219 from the ongoing Phase III PRISMA-3 trial. DORIA's potential US and EU approval (2020) and launch (2021) will validate ROVI's long-acting formulation capabilities. With peak sales opportunities of US$411m (US and EU), this high gross margin product will be highly value enhancing to ROVI's long-term profit growth. We value ROVI at €1.16bn or €23.3/share.

Year end	Operating revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/16	265.2	30.3	0.58	0.18	29.3	1.1
12/17	275.6	20.3	0.40	0.12	42.5	0.7
12/18e	293.6	16.4	0.31	0.09	54.8	0.5
12/19e	314.9	27.1	0.52	0.16	32.7	0.9

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

Enoxaparin key near-term growth driver

ROVI's internally developed biosimilar enoxaparin (Enoxaparin Becat, EB) is a key driver of near-term, top-line growth. ROVI has guided to sales of $20-30m for 2018, which seems reasonable, and acceleration of sales in 2018 and 2019 will depend on growth in Germany and the UK, and launching in further European countries.

ISM enables novel, long-acting formulations

ROVI's R&D efforts continue, with focus on its proprietary ISM technology, which centres on developing novel, long-acting (once a month or once every three months) formulations of approved drugs. Assets include Risperidone ISM (DORIA) and Letrozole ISM (Phase I breast cancer). The aim is to provide alternative methods of drug administration to improve patient adherence and thereby clinical outcomes.

DORIA: High-margin US$411m peak sales opportunity

DORIA is a fast onset of action LAI version of risperidone (off-patent). As well as rapid onset of action, key advantages are that there is no need for a loading dose or oral supplementation. The schizophrenia market is vast and growing steadily. We believe DORIA's profile will provide it with a 5% share of the LAI market and drive peak sales of US$411m (US and Europe) in 2027. DORIA is a high gross margin asset (85-95%) and will be the critical long-term driver of operating margins.

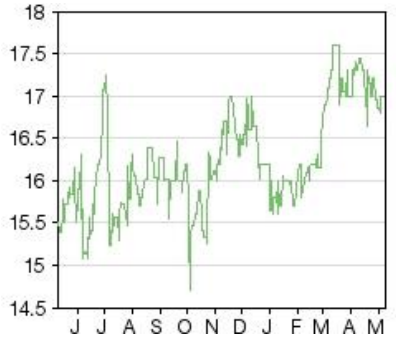
Valuation: €1.16bn or €23.3/share

Our increased valuation is €1.16bn (€23.3/share) from €0.96bn previously. We now separately value the Phase III asset, Risperidone ISM (DORIA), which we include on a risk-adjusted basis. Compared to ROVI's current portfolio of drugs and footprint, the US opportunity for DORIA is large and a key valuation driver (accounting for 16% of our valuation; EU DORIA accounts for 9%).

9 May 2018

Price	**€17.00**
Market cap	**€850m**
Net debt (€m) at 31 March 2018	1.5
Shares in issue	50m
Free float	11.86%
Code	ROVI
Primary exchange	Madrid
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(1.7)	6.3	9.7
Rel (local)	(6.4)	1.9	19.7
52-week high/low		€17.6	€14.7

Business description

Laboratorios Farmacéuticos ROVI is a fully integrated Spanish speciality pharmaceutical company involved in the development, in-licensing, manufacture and marketing of small molecule and speciality biologic drugs with a particular expertise in low molecular weight heparin (LMWH).

Next events

Biosimilar enoxaparin launch in select European countries	Ongoing
PRISMA-3 DORIA data	Q219

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Edison profile page

Laboratorios Farmacéuticos ROVI is a research client of Edison Investment Research Limited

Investment summary

Company description: Next step ISM technology validation

ROVI, a profitable, Spanish speciality pharmaceutical company, is engaged in the research and development, as well as the manufacturing and marketing of a broad range of small molecule and speciality biologic products primarily in its domestic market (Spain accounted for 71% of net revenues in 2017). Internally developed biosimilar enoxaparin is the first to launch in the European market (Germany and the UK) and is a key driver of near-term revenue and profit. Sustainable long-term growth is dependent on successful R&D investments. ROVI's efforts here lie in investing in its ISM technology assets: Risperidone ISM (DORIA), a long-acting, injectable, atypical antipsychotic therapy for the treatment of schizophrenia, and Letrozole ISM, a long-acting aromatase inhibitor for hormone-dependent breast cancer. This note focuses on DORIA's opportunity in schizophrenia. DORIA is a high gross margin asset (85-95%), and will be the critical long-term driver of operating margins for the business. For details of ROVI's marketed products, see our initiation note, Ace of Spain.

Valuation: €1.16bn or €23.3/share

We value ROVI at €1.16bn or €23.3 per share, on a sum-of-the-parts basis, based on a three-stage DCF including our forecasts to 2025 (10% discount rate, long-term tax rate of 15%, 2.0% terminal growth rate) for the core business (excluding DORIA), and risk-adjusted NPV for DORIA US and the EU opportunity. Our DCF model consists of ROVI's base business (product sales and toll manufacturing revenues), including our forecasts for biosimilar enoxaparin. We now separately value Phase III asset, Risperidone ISM (DORIA), which we include on a risk-adjusted basis. Compared to ROVI's current portfolio of drugs and footprint, the US opportunity for DORIA is large and a key value driver (accounting for 16% of our valuation; EU DORIA accounts for 9%).

Sensitivities: Evolution of the heparin business is key

ROVI is subject to various sensitivities common to speciality pharmaceutical companies, including commercialisation (pricing, reimbursement, uptake and competition), manufacturing and financing risks. The key sensitivities for ROVI relate to successful European commercialisation of both Hibor and biosimilar enoxaparin (two years after launch [2019] enoxaparin represents 13% of our total revenue forecasts), while crystallising value from its R&D pipeline will prove critical in the longer term. Ongoing in-licensing deals are required to renew the portfolio offering in Spain and replace some of the mature products, which are facing patent expiry over the next few years. We do not value the technology platform, early-stage ISM (in situ micro particle implants) R&D pipeline and any future collaborations, all of which could represent upside. ROVI is a majority family-owned business; the principal shareholder (Norbel Inversiones) holds 69.64% of the business, thus the limited free float has an impact on liquidity.

Financials: Cash-generative and stable dividend policy

In 2017 ROVI reported total revenues of €275.6m (+4% y-o-y) and EBITDA of €30.5m (-22%), leading to a lower EBITDA margin of 11.1% vs 14.8% in 2016. 2017 saw a significant rise in R&D expenses (62%) to €28.3m to support investment in portfolio products, Risperidone ISM and Letrozole ISM. In the medium term we expect operational leverage from the fully vertically integrated LMWH manufacturing and distribution business to aid margin expansion. We forecast an absolute 1.30% improvement in the operating margin from 10.7% in 2016 to 12.0% in 2020. Beyond this period, the enoxaparin contribution will continue to contribute to margin expansion. However, the game changer will be DORIA; by 2024 we believe this high-margin asset could support margins of 29%.

R&D: Next focus is ISM technology

ROVI's proprietary, patented ISM technology is based on the formation of in situ microparticle implants (ISM) for sustained drug release (long-acting intramuscular, administered by injection). The advantages for the patient are that it reduces plasma drug concentration variability, reduces the number of doses necessary for treatment, removes the need to remember to take a daily oral medication, and thus improves patient adherence and clinical outcomes. ROVI's focus is on targeting long-term illnesses (schizophrenia and breast cancer), but we expect its ISM technology to be extended to other chronic indications. The ISM technology combines the advantages of technologies such as preformed microparticles with implants. Risperidone ISM (DORIA), the first clinical asset developed using its proprietary drug development technology (US and EU approval likely in 2021) would not only serve to validate this technology but, importantly, introduce a high-margin, high sales potential asset to ROVI's P&L.

Technology primer

ROVI's sustained-release injectable technology (ISM) is based on two separated syringes; one contains the active pharmaceutical ingredient and a polymer (solid state), and the other contains the solvent (liquid state). The ISM technology is patent protected until 2033. ROVI has been successful in the aseptic filling of the dry powder active pharmaceutical ingredient (API) into a syringe, which has eluded other formulation developers. There is no need for refrigeration of the two separate components of the injection. Patients are administered the injection once a month by a healthcare professional. At time of injection, the two components are mixed together so the active ingredient plus polymer mixes with the liquid and the suspension is then injected intramuscularly into the deltoid or gluteal muscle. The suspension precipitates into a biodegradable solid or semisolid implant at the injection site. The implant contains the API and, as it erodes, it releases the active substance over time in a sustained and controlled manner (Exhibits 1 and 2 demonstrate DORIA's pharmacokinetic profile). ROVI's proprietary technology is intended to overcome some of the disadvantages of prolonged-release oral or injectable formulations. Management believes that the advantages include an injection that is simpler to administer; high encapsulation efficacy; greater stability of active substance; and greater control of the initial release of the drug. Taking the last two points in context, we note that DORIA achieves therapeutic blood levels within hours of injection, whereas none of the currently available LAIs is (either concomitant oral drug therapy overlap is required for the first few weeks, or a booster injection after one week before regular maintenance dosing is possible, in the case of Johnson & Johnson's [J&J] Invega Sustenna).

DORIA: Understanding the schizophrenia opportunity

ROVI's long-acting injectable (LAI) formulation of risperidone (Risperidone ISM or DORIA) is an improved version of the long-acting antipsychotic drug, risperidone, currently available on the market (J&J's Risperdal Consta). While multiple long-acting formulations of different antipsychotic drugs are approved, none has the perfect profile. DORIA will provide another product in the LAI schizophrenia treatment armament that will benefit physicians and patients as it addresses some of the issues with other LAIs on the market and in late-stage development. While multiple LAI antipsychotic drug formulations should be available by the time we assume DORIA launches (US and EU in 2021), and DORIA's key advantages aside, our analysis shows that the overall LAI market in the US is underutilised. In the US 8% of patients are treated with LAI vs 40% in Europe in 2014. A multitude of scientific literature and a change in World Federation of Societies of Biological Psychiatry (WFSBP) guidelines (2013) point to increased use of LAIs.

PRISMA clinical trials programme for DORIA in schizophrenia

The Phase II PRISMA-2 clinical trial evaluated the safety and tolerability of DORIA in 67 patients with schizophrenia. This open-label study looked at a 75mg dose, injected intramuscularly (gluteal or deltoid) every 28 days for four months. Importantly, oral supplementation with risperidone was not required. Recently published data reported that the mean Cmax of the active moiety was achieved 24-48 hours (Tmax) after each administration and ranged over four consecutive doses from 39.6-53.2ng/mL and 54.1-61ng/mL when given in the gluteal or deltoid, respectively (see Exhibits 1 and 2). Importantly, all patients achieved therapeutic levels (>10ng/mL for the active moiety) between two and eight hours after drug administration and sustained release of drug was available throughout the 28-day dosing period. Side effects were in line with risperidone medications (hyperprolactinaemia 53.7%, injection site pain 32.8%). There were no significant changes across the study either on the PANSS (see later) or extrapyramidal symptoms scale.

Exhibit 1: DORIA PK profile (gluteus IM injection)

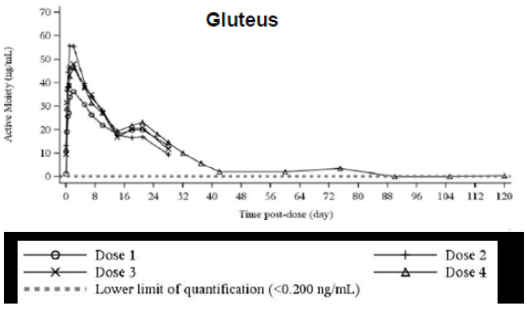
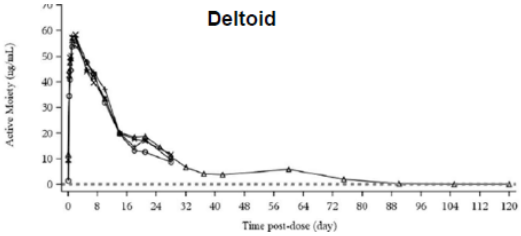


Exhibit 2: DORIA PK profile (deltoid IM injection)

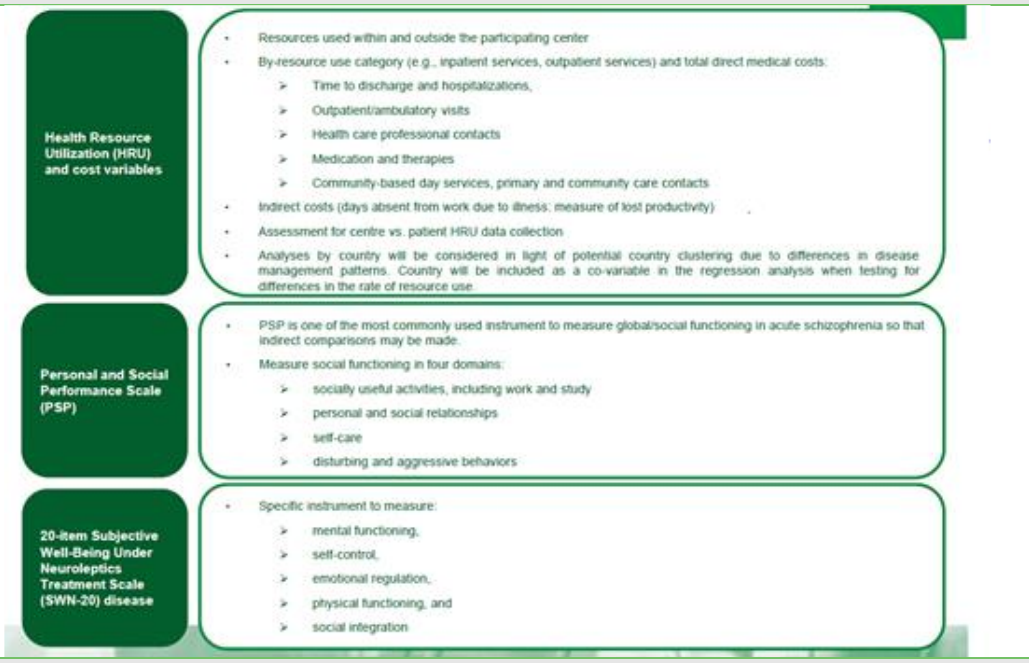


Source: ROVI presentations, Anta et al: A phase II study to evaluate the pharmacokinetics, safety, and tolerability of Risperidone ISM multiple intramuscular injections once every four weeks in patients with schizophrenia. International Clinical Psychopharmacology, 2018 Mar; 33(2):79-7.

PRISMA-3 readout expected in Q219

The ongoing Phase III PRISMA-3 (ClinicalTrials.gov Identifier NCT03160521) clinical trial is evaluating the efficacy, safety and tolerability of DORIA (75mg and 100mg administered intramuscularly into the gluteal or deltoid muscle once a month for three successive months) in patients with acute schizophrenia in a multi-centre, randomised, double blind, placebo-controlled trial. Patients who have never taken risperidone before are required to undertake a brief trial of oral risperidone to ensure there is no clinically significant adverse hypersensitivity reaction before receiving the first DORIA dose. The primary outcome measure is the PANSS score mean change from baseline to endpoint over a 12-week period (plus one year follow-up). The Positive and Negative Syndrome Scale (PANSS) is a standardised clinical interview assessing and scoring 30 standardised symptoms (seven positive symptoms, seven negative symptoms and 16 general psychopathology symptoms). PRISMA-3 is assessing whether an improvement in PANSS from day 4 is achievable and statistically significant. If so and if included in its label, DORIA would have a unique selling point versus its competitor LAIs. Secondary outcome measures are the Clinical Global Impression-severity (CGI-S) score mean change from baseline to endpoint, CGI-I score mean at endpoint, overall response rate and PANSS response rate at endpoint. The trial is also looking at health economic-related outcomes (Exhibit 3), which could be relevant in pricing and reimbursement negotiations. PRISMA-3 is expected to read out in Q219, leading to NDA and marketing authorisation applications (MAAs) filing in late 2019. We forecast DORIA launch in 2021.

Exhibit 3: DORIA – PRISMA-3 study HEOR variables



Source: ROVI presentations

DORIA: Clinical and practical advantages

Exhibit 7 provides a visual guide to DORIA's advantages versus competing LAIs on the market and about to launch. While we highlight these advantages we note that the complexity of schizophrenia means one size does not fit all and DORIA provides an additional formulation for physicians to consider on an individual patient basis. Later in this note we highlight the scientific evidence from medical literature on why LAI antipsychotics on the whole are increasingly considered to be better than oral medications in disease control. While we would not expect LAI to replace oral medications completely, the reality is that LAIs are underutilised, particularly in the US. DORIA's advantages are as follows:

- rapid onset;
- no need for oral supplementation;
- no need for loading dose or maintenance dose one week after initial injection;
- once-a-month intramuscular injection coincides with once-a-month maintenance outpatient visits; and
- potential for PANSS reduction from day 4 on the prescribing label. The primary efficacy measure in schizophrenia is the PANSS total score. PRISMA-3 is assessing whether an improvement in PANSS from day 4 is achievable and statistically significant. If so and if included in its label, DORIA would have a unique selling point versus its competitor LAIs.

DORIA: Regulatory strategy

In the US ROVI will pursue regulatory NDA filing under section 505(b)(2) of the FD&C Act (as agreed at the special protocol assessment [SPA] meeting with the FDA). Under this section provision (2) of the 505 act, the FDA is permitted to rely on data not developed by the applicant for approval of an NDA. ROVI will use the published literature on oral risperidone as part of the application for the treatment of schizophrenia, in addition to the PRISMA-1, PRISMA-2 and PRISMA-3 efficacy outcomes and safety data. Under the amendment to the act, the FDA aimed to have a slighter faster approval time frame to NME (by months), but in practice this has not panned out.

In Europe ROVI will file a hybrid application with the European Medicines Agency (EMA) for the treatment of acute exacerbation of schizophrenia. The EMA defines a hybrid medicine as "a medicine that is similar to an authorised medicine containing the same active substance, but where there are certain differences between the two medicines such as in their strength, indication or pharmaceutical form". We forecast a normal approval time frame for DORIA rather than an expedited one.

We forecast DORIA peak sales of US$411m in schizophrenia

According to the US National Institutes of Health, the prevalence of schizophrenia in the US adult population is 1.1%. We apply the same prevalence rate to the European population to derive total US/EU schizophrenia patient numbers of 5.6 million. According to the National Institute of Mental Health's Clinical Antipsychotic Trials of Intervention Effectiveness (the CATIE programme), 75% of patients are incomplete responders (including drug discontinuation due to side effects). In the US 8% of patients are treated with LAI vs 40% in Europe. Given the low LAI penetration rates in the US and an increase in the number of differing LAIs on the market or to be launched within the next few years, we believe the improved formulations should see a rise in overall LAI penetration rates. This derives our eligible LAI patient population in 2021. Given that DORIA's clinical development programme (PRISMA-3) is focused on acutely exacerbated schizophrenic patients, we apply a conservative 5% share of the total LAI market in both Europe and the US. In the US the average LAI is priced at ~$10,700 pa – we note that Invega Sustenna monthly maintenance (based on 0.75ml of 117mg) is priced at $1,200 per month (retail price). In Europe the average LAI is priced at $3,500 pa. For DORIA we have assumed US pricing of $10,500 pa and EU pricing of $4,000 pa. Depending on the HEOR outcomes data from PRISMA-3 (see above), DORIA could command higher pricing versus our expectations.

DORIA: The commercial opportunity for ROVI

ROVI's commercialisation strategy for DORIA will vary between the US and EU. In the US ROVI is filing for 'treatment of schizophrenia' as the labelled indication vs 'treatment of acute exacerbation of schizophrenia' in Europe. The small but important nuance here is that the US label implies DORIA can be used at any time during the course of the disease. In practice, US physicians are more likely to consider an LAI in the acute setting (either onset or relapse) as this is the most pertinent time to consider changing a medication or switching to a long-acting formulation, given that, in many cases, lack of patient adherence to medication may have precipitated the relapse. ROVI has developed DORIA specifically as a once-a-month administration (vs weekly, fortnightly or every three months) to coincide with monthly outpatient visits. LAIs facilitate regular contact between patients and psychiatrists, which is essential for monitoring patient welfare and clinical progress.

We anticipate that in Europe ROVI will launch via its subsidiaries in key European markets: Germany, UK, Spain, Italy, France and Portugal. ROVI will need to hire specialist medical reps to support launch and marketing to physicians. In terms of sales and marketing expenses, it will need to extend its sales rep footprint to target the psychiatrists working in the acute medical setting – these physician numbers are relatively small and we believe ROVI can service the major European countries through a salesforce the size of 100 reps. In Europe LAI pricing is $3,650 pa on average and use of LAIs is estimated at 40% penetration. As such, we believe the US opportunity is larger (due to higher pricing – $10,700 pa and relative underutilisation of LAIs versus oral meds). In the US ROVI will need to build a salesforce of a similar size (80 reps) to cover the ~4,000 psychiatrists working in the acute clinical setting. However, ROVI could elect to partner the product in return for royalties and milestones on sales. Competition in the US is entrenched, with J&J, BMS, Lilly and AstraZeneca dominating the market. Nonetheless, given DORIA's profile and assuming ROVI elects to market, we believe a 5% share of the relevant market is achievable. Furthermore, we

expect DORIA to piggyback on the LAI segment versus the oral market from the increasing detailing by competitors.

DORIA is a high-margin asset

In the US market we believe DORIA operating margins can reach 40% by 2024. DORIA fits well into ROVI's fully vertically integrated pharmaceuticals business strategy and we believe the company's manufacturing efficiency could enable high gross margins (95% in the higher-priced US market and 85% in Europe). In the US we assume a salesforce of 80 reps and additional overhead expenses totalling €49m by 2024 to place SG&A expenses at 56% of sales. This seems reasonable for the early launch years. However, beyond 2024 we would anticipate further operating leverage. In Europe we forecast DORIA operating margins will reach 14% in 2024 and 23% in 2025. We model 100 reps for Europe, but lower overhead costs given ROVI's existing presence in the major European countries through its subsidiaries. The main drag on margins in comparison to the US is the lower pricing opportunity in Europe and thus higher gross margins (we model 85%).

Schizophrenia: A complex and chronic disorder of the brain

Schizophrenia is a chronic and severe mental disorder that affects how a person thinks, feels and behaves. Prevention of relapse is a key challenge in schizophrenia as poor adherence to antipsychotic medications leads to high rates of hospitalisation rates and related burden of care, particularly at the onset or during acute episodes/relapses. Genetic predisposition (multiple genes have been implicated) combined with environmental exposures (eg recreational drugs) and/or stresses during pregnancy and childhood are thought to contribute or trigger risk of disorder. The condition affects 1.1% of the world's population over the age of 18 (source: National Institute of Mental Health); actual rates vary slightly from country to country (about 0.5-1% of the population). Patients are typically diagnosed with the disorder in early adulthood.

The disorder is characterised by a breakdown in the relation between thought, emotion and behaviour, leading to faulty perception and the inability to function normally. Signs and symptoms of schizophrenia can vary by severity, duration and frequency, although the incidence of severe psychotic symptoms often decreases during a patient's lifetime. Non-adherence to taking medications as prescribed, use of alcohol or recreational drugs, and stressful situations tend to increase symptoms. Generally, symptoms are classified into several categories:

- Positive symptoms include hallucinations, delusions, thought disorders and movement disorders.
- Negative symptoms include flat effect (reduced expression of emotion), social withdrawal and lack of interest in everyday activities.
- Cognitive symptoms include trouble focusing, poor 'executive functioning' and problems with 'working memory'.

While the condition cannot be cured, the success rate of treatment with antipsychotic medications and psychosocial therapies can be high but is dependent on a variety of factors (eg side effects, patient compliance and adherence, patient insight and insurance coverage). Drug therapy usually requires long-term maintenance treatment using one or more antipsychotic drugs (the two main classes of drugs are the 'typical' and the 'atypical' antipsychotic drug classes). Antipsychotic medications can be taken orally on a daily basis or less frequently (fortnightly/monthly) by intramuscular or subcutaneous injection of LAI formulations of antipsychotic drugs.

Atypical antipsychotics are main stay of drug treatment

There is no cure for schizophrenia and drug treatments focus on eliminating symptoms; the current mainstay of which are the atypical and typical antipsychotic drugs. Both oral and long-acting

injectable antipsychotics have shown efficacy, tolerability and safety as treatments for patients with schizophrenia.

First-generation or so-called typical antipsychotics were developed in the 1950s. Examples include chlorpromazine (1950s), fluphenazine (introduced in the 1960s) and haloperidol. These drugs are dopamine (D2) antagonists so side effects include sedation, hypotension and in some cases non-reversible tardive dyskinesia (drug-related involuntary movements).

Clozapine was the first second-generation drug developed; these drugs work as serotonin/dopamine antagonists, D2 partial agonists or serotonin partial agonists at 5-HT. Clozapine was not available in the US (risk of agranulocytosis) but is available in some countries in Europe. Subsequently, other second-generation or atypical antipsychotics were developed in the 1990s. Examples include risperidone (Janssen's Risperdal), aripiprazole (BMS's Abilify), olanzapine (Lilly's Zyprexa), and quetiapine (AstraZeneca's Seroquel). While this newer generation of atypical antipsychotics improved on the toxicity profile of the typical antipsychotics, drug-related side effects remain troublesome and include sedation, metabolic changes (weight gain, diabetes, hyperlipidemia) and endocrine changes (sexual side effects). Nonetheless, second-generation oral antipsychotics have become the first-line treatment in schizophrenia. In terms of unit volume, risperidone is the most used active drug principle.

Antipsychotic drugs with LAI formulations were developed to reduce the problem of non-adherence, which is estimated to be as high as 40%. The first LAI antipsychotic to be developed was fluphenazine enanthate (ER Squibb & Sons) in 1966, which displayed numerous potential advantages (including better correlation between dose and blood plasma concentrations, better monitoring of compliance, ease of administration and less risk of overdose). Disadvantages included slow titration to dose and a longer duration to therapeutic dosing. During the past 20 years improved versions of second-generation LAIs have been available on the market: Risperdal Consta in 2004 and its follow-up, Invega Sustenna, in 2009.

Long-term drug treatment of schizophrenia has major limitations

Long-term drug treatment of schizophrenia has major limitations; the US National Center for Biotechnology Information (NCBI) estimates that 25-33% of patients are treatment resistant and relapse rates remain high (relapse rates over two years in medication-treated chronic schizophrenia patients are approaching 41% (source: Crow et al 1986); the cumulative relapse rate for first-episode patients with good adherence over a three-year period was 36%, whereas the rate for poorly adherent patients was 57% (Chen et all Schizophr Res. 2005). Non-adherence to antipsychotic medication is common among patients with schizophrenia, and is the greatest challenge for recovery and prevention of relapse with greater risk of hospitalisation. This is particularly so during the early days of diagnosis when patients are coming to terms with their disorder and may not appreciate the necessity of adhering to the medication regimen. Discontinuation of antipsychotic medication in patients achieving remission leads to a relapse in more than 52% of patients in 6.5 months (source: Gilbert et all, 1995). Leucht et all points to a higher risk of relapse if antipsychotic drug medication is discontinued in patients despite them being stable on treatment for five years; this is reflected in treatment guidelines such as those of the World Federation of Societies of Biological Psychiatry, which recommend continuation of antipsychotic drugs for the treatment of first-episode psychosis for at least two years after first remission, and with a minimum of five years relapse-free stability (maybe even throughout life) before considering slow drug withdrawal (over six to 24 months). There is an unmet need in schizophrenia for novel mechanism and new formulations of antipsychotic drugs that can improve patient adherence, reduce persistent psychotic symptoms in antipsychotic-treated patients with fewer side effects and improve on negative and cognitive symptoms.

Evidence supports use of LAI antipsychotics

LAI antipsychotics are often used only when oral medications have failed rather than first-line therapy. Evidence increasingly supports their use as a first choice (WFSBP 2013 updated guidelines). Multiple effectiveness studies show the superiority of LAI antipsychotics, particularly in the case of risperidone.

- Olivares et all (Neuropsychiatry 2011, Comparison of long-acting antipsychotic injection and oral antipsychotics in schizophrenia) conducted a systematic review of medical literature and selected 71 papers for comparison. One of the main conclusions was that "most of the effectiveness studies show a superiority of long-acting injectables, particularly in the case of risperidone, when compared with oral antipsychotics in relation to adherence, clinical improvement, reduction of relapses and hospitalizations, or cost-effectiveness".
- Kenneth et al reported the link between risperidone non-adherence and the return of positive symptoms during the early course of schizophrenia (n=49).
- Significantly lower rates of rehospitalization and treatment failure (defined as psychiatric rehospitalization, suicide attempt, discontinuation or switch to other medication, or death).Tiihonen et all (JAMA Psychiatry July 2017) compared the real world effectiveness of antipsychotic treatments for patients with schizophrenia through a prevalence cohort from the Swedish population of 29,823 patients. During a mean follow-up period of 5.7 years, 43.7% of patients were rehospitalized and 71.7% experienced treatment failures. The authors reported that the risk of rehospitalization is c 20-30% lower during LAI treatments compared with equivalent oral formulations and suggested that the improved efficacy of LAIs may be due in part to improved patient adherence on LAI. However, this prospective study did not evaluate other outcome measures.
- Olivares et al reports on the cost effectiveness of switching antipsychotic medication to long-acting injectable risperidone in patients with schizophrenia using the e-STAR patient database in Spain. The authors state: "In terms of effectiveness, at 12 months after switching to long-acting injectable risperidone, there was a higher percentage of patients who did not require hospitalization (89.1%), did not relapse (85.4%) or neither required hospitalization nor relapsed (82.4%) as compared retrospectively with the same period for the previous treatment (67%, 47.8% and 59.8%, respectively)". Furthermore, while LAI risperidone was more costly per month at €405.8 vs oral at €128.2, cost effective ness per month per patient was lower in three patient scenarios: without hospitalization (€539.82 vs €982.13), without relapse (€519.67 vs €1,242.03), and without hospitalization and without relapse (€597.22 vs €1,059.39).
- Underutilising LAIs appears to originate more from psychiatrist and physician inertia rather than patients' negative attitude to these formulations. However, there is an increasing acceptance that physicians should be considering the use of LAIs more often in the treatment of schizophrenia and at an earlier point of diagnosis (Heres, S: Long-Acting Injectable Antipsychotics: An Underutilized Treatment Option, Journal of Clinical Psychiatry 2014).
- Brisso et al reviewed the role of long-acting injectable in schizophrenia, and summarised the key advantages and disadvantages of LAIs in clinical practice (Exhibit 4). This review was published in 2014 – we provide comments on DORIA's profile as an LAI where relevant in the notes section.

Exhibit 4: Advantages and disadvantages of LAI antipsychotics vs oral antipsychotics

Advantages	Notes
No need for daily administration	Compared to oral medication
Guaranteed administration and transparency of adherence	Injections are administered by psychiatric nurses
Allows healthcare professionals to be alerted and to intervene appropriately if patients fail to take their medication	
Less probability for rebound symptoms and rapidly occurring/abrupt relapses	Fewer issues with medication compliance
Overcome partial adherence or overt non-adherence	
If a relapse occurs, it is due to other reasons beyond non-compliance	
Reduced risk of unintentional or deliberate overdose	
Lower relapse rates	
Minimal gastrointestinal absorption problems, circumventing first-pass metabolism	
More consistent bioavailability	
More predictable correlation between dosage and plasma levels	
Reduced peak-trough plasma levels and improved patient outcomes	
Improved patient and physician satisfaction	
Regular contact between the patient and mental healthcare team	
Disadvantages	
Slow dose titration	
Longer time to achieve steady state	Depends on the brand. DORIA steady state achieved within eight hours of administration
Less flexibility of dose adjustment	
Delayed disappearance of distressing and/or severe side effects	
Pain at the injection site can occur, and leakage into the subcutaneous tissue and/or the skin may cause irritation and lesions (especially for oily long-acting injectable)	DORIA is injected intramuscularly and not subcutaneously
Burden of frequent travel to outpatient clinics or home visits by community nurses for their administration	DORIA's once-a-month administration designed to coincide with monthly outpatient visits. LAIs facilitate regular contact between patients and psychiatrists, which is essential for monitoring patient welfare and clinical progress
Risperidone long-acting injectable needs refrigeration, which may be cumbersome in some latitudes	DORIA does not require refrigeration
Perception of stigma	

Source: Edison Investment research, published literature by Brisso et al The role of long-acting injectable antipsychotics in schizophrenia: a critical appraisal Therapeutic Advances in Psychopharmacology 2014 Oct; 4(5): 198–219.

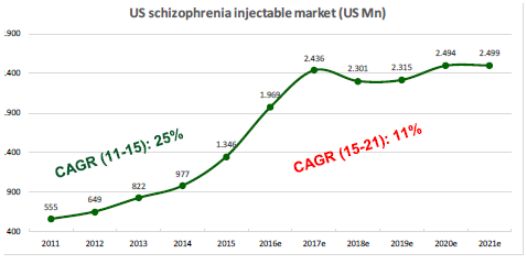
Antipsychotic drugs a vast market for oral and LAI antipsychotics

According to IMS Midas, the US was the largest market for antipsychotics, with 2015 sales of $14.2bn, and sales in the top five largest European markets were $2.6bn. In the US oral formulations represented 87% of the value ($12.4bn) and LAIs accounted for the remaining 13% ($1.8bn) of the value. In the top five European markets, oral represented 69% and injectable 31% in terms of value in 2015. However, as antipsychotic drugs are used to treat a myriad of conditions (including schizophrenia but also depression, bipolar disorder, schizoaffective disorders and are also used off-label to treat acute psychotic episodes in dementia), a better understanding of market opportunity is required to assess the historic schizophrenia injectable market size.

US market opportunities: LAI for schizophrenia

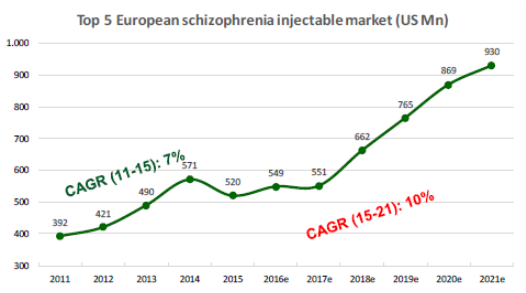
According to IMS Midas, the US is the largest schizophrenia injectable market with MAT Q317 sales of €2.8bn and 2.0m units. Exhibit 5 shows the 25% CAGR (2011-15) in the injectables segment in value. Average pricing for LAIs in the US is ~$10,700 per annum. The market leader by volume (in units) in 2015 was risperidone (32% market share) followed by paliperidone (25% market share). In terms of value in 2015, paliperidone had the highest market share (60%), followed by risperidone (25%). The difference between unit and value relate to pricing; risperidone generics have been available in the US since 2008.

Exhibit 5: US schizophrenia injectable market (US$m)



Source: ROVI presentations, IMS Midas

Exhibit 6: Top 5 schizophrenia injectable market (US$m)



Source: ROVI presentations, IMS Midas

IMS Midas reports top five European injectable market sales of €793m and 3.2m units. Exhibit 6 shows the 7% CAGR (2011-15) in the injectables segment by value – average LAI pricing per annum is €3,650. IMS Midas forecasts monthly/fortnightly formulations to have 55% market share in 2021 (every two months or every three months formulations). The market leader by volume (in units) is risperidone (59% market share) followed by paliperidone (33% market share). In terms of value in 2015 paliperidone had the highest market share (55%) followed by risperidone (39%).

Competitive landscape

Exhibit 7 highlights the main competitors in the LAI antipsychotic market and DORIA's competitive positioning on key clinical and practical metrics. An important general comment is that the choice of LAI will firstly depend on the antipsychotic drug itself; some patients will fare better with risperidone rather than aripiprazole or paliperidone or vice versa.

The key competing LAI antipsychotic products are:

- **Risperdal Consta** (Janssen): developed by J&J and Alkermes (utilizing its Medisorb technology) and the first long-acting, second-generation antipsychotic to be approved by the FDA (October 2003). This two-weekly formulation (which requires refrigeration) requires three weeks of concomitant oral risperidone medication. J&J (Janssen) reported peak sales of $1.6bn in 2011. Sales erosion from peak was in part due to J&J launching its follow-up LAI Invega Sustenna.
- **Invega Sustenna/Invega Trinza** (Janssen): Sustenna is a long-acting (once-a-month) injectable suspension of paliperidone (the primary active metabolite of risperidone). A booster dose of Invega Sustenna is required one week after initial dose, then once a month. Trinza is a three-monthly formulation that can only be administered after patients have been receiving once-a-month Sustenna for a minimum of four months. J&J reported worldwide Invega Sustenna/Trinzia sales of $2.2bn in 2017.
- **ARISTADA** (Alkermes): a long-acting formulation of aripiprazole lauroxil was approved by the US FDA in 2015. The product requires three weeks of concomitant oral aripiprazole medication at the start and reported FY17 sales of $93.5m. Alkermes has guided to FY18 sales of $140-160m. Alkermes has submitted an NDA for Aripiprazole Lauroxil NanoCrystal Dispersion for initiation onto Aristada (PDUFA date 30 June 2018), which would remove the need for overlap of three weeks of oral meds. The formulation has additional advantages of faster dissolution, leading to more rapid achievement of aripiprazole plasma therapeutic levels.
- **RBP-7000 (Indivior):** a monthly injectable risperidone in the ATRIGEL delivery system given as a subcutaneous injection. The NDA has been submitted to FDA (PDUFA date 28 July 2018). The drawbacks of ATRIGEL are the need for refrigeration and more painful injections.

Exhibit 7: Long-acting injectables for schizophrenia – a comparison

	RISPERDAL CONSTA® (Risperidone)	INVEGA SUSTENNA® / XEPLION® (Paliperidone)	INVEGA TRINZA® / TREVICTA® (Paliperidone)	ABILIFY MAINTENA® (Aripiprazole)	ARISTADA® (Aripiprazole Lauroxil)	RBP-7000 (Risperidone Atrigel®) 4	DORIA® 4 (Risperidone)
Acute Treatment	×	✓	×	×	✓	✓	✓
Once Monthly Administration	×	✓	✓✓ 3	✓	✓	✓	✓
No Oral Supplementation	×	✓	✓	×	×	✓	✓
Therapeutic Levels[1] within First 8 h	×	×	×	×	×	✓	✓
Intramuscular Injection	✓	✓	✓	✓	✓	✓✓ 5	✓
Deltoids & Gluteal administration	✓	✓	✓	✓	✓	×	✓
PANSS[2] reduction from day 4	×	×	×	×	×	×	✓ 6

Sources: Gefvert O, et al. Int J Neuropsychopharmacol 2005;8(1):27-36. Odou P, et al. Clin Drug Invest 2000;19(4):283-92. Nyberg S, et al. Am J Psychiatry 1999;156(6):869-75).
(1) The therapeutic concentration range of risperidone is quite wide and can vary from 10 ng/mL to 80 ng/mL or even higher
(2) PANSS: positive and negative syndrome scale. Scale used to evaluate the symptoms of patients with schizophrenia
(3) Quarterly administered
(4) Not marketed yet
(5) Subcutaneous
(6) To be confirmed in the currently ongoing phase III trial PRISMA-3 (ClinicalTrials.gov Id. #NCT03160521)

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Source: ROVI presentations

ISM technology expanded to breast cancer

Letrozole ISM for hormone receptor positive breast cancer

Advances in the treatment of breast cancer over the last 20 years have, in certain cases (hormone-dependent or HER-2 status), led to improved survival and many patients becoming cancer free. Novartis's Femara (letrozole), an aromatase inhibitor, is used to treat post-menopausal women with oestrogen receptor positive primary breast cancer. Letrozole is prescribed as an adjuvant to surgery. The drug is usually continued for five years, as aromatase inhibitors decrease the risk of developing a new breast cancer in the same or opposite breast (studies are underway to evaluate longer-term use, eg 10 years). However, once a patient is breast cancer free, adherence to an oral daily 'cancer medication' can be an issue as some patients elect to or forget to take the product. The opportunity for a once every three months, slow-release, intramuscular depot formulation of the drug is multi-fold and include improved patient quality of life (lower dose frequency and reminder of illness), reduced healthcare costs and possible improved clinical outcomes. ROVI has initiated Phase I (LISA-1) clinical trials to evaluate the pharmacokinetic and pharmacodynamic profile of Letrozole ISM at differing doses in healthy post-menopausal women. We do not currently reflect Letrozole explicitly in our ROVI valuation.

Sensitivities

ROVI is subject to various sensitivities common to speciality pharmaceutical companies, including commercialisation (pricing, reimbursement, uptake and competition), manufacturing and financing risks. The key sensitivities for ROVI relate to successful European commercialisation of both Hibor and its biosimilar enoxaparin, and crystallising value from the ISM pipeline. Enoxaparin represents

13% of our total revenue forecasts in 2019 (its second year of commercial availability). The largest near-term driver of our sales and net profit expectations is enoxaparin. Compared to ROVI's current portfolio of drugs and footprint, the US opportunity for DORIA is large and a key valuation driver (accounting for 16% of our valuation; EU DORIA accounts for 9%).

Valuation

Our revised valuation of €1.16bn or €23.3/share reflects a change to our sum-of-the-parts methodology (Exhibit 8). Our previous three-stage, DCF-based valuation of ROVI at €0.96bn or €19.1/share used our sales and P&L model, and included peak sales of €76.2m for DORIA in these cash flows. The major source of uplift reflects the change in our assumptions for US and European DORIA sales and operating cost assumptions. We now value DORIA US and EU through standalone NPV calculation (Exhibit 10) and derive value for the rest of the business by using a DCF of our sales and P&L model excluding DORIA (Exhibit 9). We have not changed our sales assumptions for the rest of the business. Compared to ROVI's current portfolio of drugs and footprint, the US opportunity for DORIA is large and a key valuation driver (accounting for 16% of our valuation; EU DORIA accounts for 9%).

Exhibit 8: ROVI sum-of-the-parts valuation

	Value (€m)	Value per share (€)
DCF of base business	869.5	17.4
rNPV of DORIA	294.5	5.9
Valuation	1,164.0	23.3

Source: Edison Investment Research

Exhibit 9: Three-stage DCF valuation of base business (excludes DORIA cash flows)

	€m
Sum of for DCF for forecast period to 2025	316
Sum of DCF for growth 2026 to 2030 (transition period)	167
Terminal value	388
Enterprise value	**871**
Net debt at 31 March 2018	(1.5)
Value of equity of base business	869.5
Value per share of base business	17.4
Discount rate	10%
Terminal growth rate	2%
Number of shares outstanding (m)	50

Source: Edison Investment Research

Exhibit 10: DORIA NPV

	Indication	Launch	Peak sales ($m)	Value (€m)	Probability	rNPV (€m)	rNPV per share
NPV DORIA US	Schizophrenia	2022	236	256.6	75%	187.5	3.8
NPV DORIA Europe	Schizophrenia	2022	176	150.4	75%	107.0	2.1

Source: Edison Investment Research

Our sum-of-the-parts valuation consists of:

- NPV calculation for DORIA US and EU opportunity. We forecast US peak sales of $236m (€195m) and EU peak sales of $176m (€145m) in 2027; this is predicated on achieving a 5% peak penetration rate of the LAI antipsychotic market in both territories. We discuss our DORIA-related cost assumptions earlier in **DORIA is a high-margin asset** above. We assume a probability of launch of 75% and apply a 12.5% discount rate commensurate with our treatment of clinical-stage assets.
- DCF for ROVI's base business of marketed products and toll manufacturing revenue (we strip out DORIA sales and associated costs). We utilise our sales and P&L forecasts in these cash flows (out to 2025) and from 2026 to 2030 apply a transition growth rate (reflecting the fact that

ROVI is growing at a high rate during our forecast period). Finally, we apply a 2.0% terminal growth rate (terminal value represents 30% of our total ROVI valuation). 10% is our standard discount rate assumption for companies with approved products and minimal development risk.

- We use a 15% tax rate from 2030. The current tax rate is c 8%, but over time this is expected to normalise to the mid-teens.

Financials

ROVI reported 4% growth in operating revenue to €275.6m in 2017 (vs 8% to €265.2m in 2016), aided by strong growth in the toll manufacturing business. Total revenues grew 12% to €76.0m in Q118 driven by strong growth in the speciality pharmaceutical business (+23% to €63.8m). Biosimilar enoxaparin reported fledgling Q118 sales of €4.1m despite only being available in Germany since September 2017 and in the UK since March 2018. For more details on Q118 results and FY17 results see our notes Stunning growth in speciality pharmaceuticals and Steady as she grows.

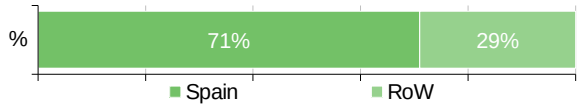
We have made no changes to our financial forecasts. We expect operating margins to further decrease in 2018 (from 10.7% in 2016 and 6.9% in 2017) to 4.6% in 2018, mainly due to higher R&D expenses but also to the small increase in SG&A to support new product launches. We anticipate margin growth from 2019 to 7.6%, mainly due to operational leverage as we still anticipate c €32m in R&D costs in 2019. We forecast an absolute 1.3% improvement in operating margin from 10.7% in 2016 to 12.0% in 2020. Longer-term margins should continue to ramp up beyond this period as the operational leverage from enoxaparin sales starts to flow through to the P&L, and the impact of high-margin asset, DORIA, becomes evident. In the US market we forecast that DORIA operating margins could reach 40% by 2024 and in Europe we believe DORIA operating margins could reach 23% in 2025.

At 31 March 2018 ROVI had €40.4m in bank borrowings and debt, and cash and cash equivalents of €39.0m.

Exhibit 11: Financial summary

Accounts: IFRS, Year-end: December, €m	2014	2015	2016	2017	2018e	2019e
PROFIT & LOSS						
Hibor revenue	72.7	75.1	79.7	83.9	86.3	82.6
Enoxaparin revenue	0.0	0.0	0.0	1.5	26.7	44.5
Other (Pharma & Manufacturing)	165.4	170.9	185.5	190.3	180.7	187.8
Operating revenues	238.0	246.0	265.2	275.6	293.6	314.9
Cost of sales	(94.6)	(97.1)	(112.0)	(110.2)	(120.4)	(127.5)
Gross profit	143.5	148.9	153.1	165.5	173.2	187.4
Gross margin %	60.3%	60.5%	57.8%	60.0%	59.0%	59.5%
SG&A (expenses)	(97.8)	(101.7)	(101.9)	(108.5)	(116.6)	(119.7)
R&D costs	(12.0)	(16.5)	(17.5)	(28.3)	(32.0)	(32.0)
Other income/(expense)	2.9	1.0	5.6	1.8	1.8	1.8
EBITDA (reported)	36.6	31.8	39.3	30.5	26.4	37.5
Depreciation and amortisation	(8.9)	(10.0)	(11.0)	(11.5)	(12.8)	(13.5)
Normalised Operating Income	29.2	23.8	30.7	21.8	17.1	27.4
Reported Operating Income	27.7	21.8	28.3	19.0	13.6	24.0
Operating Margin %	11.6%	8.9%	10.7%	6.9%	4.6%	7.6%
Finance income/(expense)	(2.1)	(0.9)	(0.5)	(0.9)	(0.7)	(0.3)
Exceptionals and adjustments	0.0	0.0	0.0	0.0	0.0	0.0
Normalised PBT	27.1	22.9	30.3	20.3	16.4	27.1
Reported PBT	25.6	20.9	27.9	17.5	12.9	23.6
Income tax expense (includes exceptionals)	(1.5)	(1.1)	(1.8)	(0.3)	(0.7)	(1.2)
Normalised net income	25.6	21.8	28.5	20.0	15.7	25.9
Reported net income	24.1	19.8	26.1	17.2	12.3	22.4
Basic average number of shares, m	49.8	49.5	49.0	50.0	50.0	50.0
Basic EPS (€)	0.48	0.40	0.53	0.34	0.25	0.45
Normalised EPS (€)	0.51	0.44	0.58	0.40	0.31	0.52
Dividend per share (€)	0.17	0.14	0.18	0.12	0.09	0.16
BALANCE SHEET						
Property, plant and equipment	73.6	81.8	82.8	89.1	95.6	102.6
Goodwill	0.0	0.0	0.0	0.0	0.0	0.0
Intangible assets	17.2	18.9	24.9	27.1	27.1	23.7
Other non-current assets	8.5	9.1	13.1	14.1	14.1	14.1
Total non-current assets	99.3	109.8	120.8	130.2	136.8	140.3
Cash and equivalents	26.7	29.3	41.4	40.7	35.9	39.8
Inventories	67.6	63.9	67.4	75.5	69.3	69.9
Trade and other receivables	63.7	57.0	53.8	49.7	56.3	56.1
Other current assets	4.1	3.9	4.5	2.2	2.2	2.2
Total current assets	162.0	154.1	167.1	168.2	163.7	168.0
Non-current loans and borrowings	32.0	32.6	20.8	27.0	22.4	20.7
Other non-current liabilities	8.7	7.2	7.2	6.4	5.9	5.3
Total non-current liabilities	40.7	39.8	28.0	33.5	28.2	26.0
Trade and other payables	55.0	45.7	59.9	52.9	63.9	62.3
Current loans and borrowings	4.3	10.1	13.0	16.2	4.7	1.6
Other current liabilities	2.8	3.3	3.6	4.1	4.1	4.1
Total current liabilities	62.1	59.2	76.4	73.2	72.6	68.0
Equity attributable to company	158.5	164.8	183.4	191.7	199.7	214.2
CASH FLOW STATEMENT						
Profit before tax	25.6	20.9	27.9	17.5	12.9	23.6
Depreciation and amortisation	8.9	10.0	11.0	11.5	12.8	13.5
Share based payments	0.0	0.0	0.0	0.0	0.0	0.0
Other adjustments	2.5	(1.1)	(2.7)	(1.2)	0.7	0.3
Movements in working capital	(7.4)	2.3	12.7	(9.8)	10.0	(2.5)
Interest paid / received	(2.7)	(0.6)	0.0	0.0	(1.1)	(0.7)
Income taxes paid	(3.9)	(2.0)	(3.4)	0.1	(0.7)	(1.2)
Cash from operations (CFO)	23.0	29.4	45.5	18.0	34.7	33.0
Capex	(25.1)	(19.9)	(18.1)	(19.9)	(19.4)	(17.1)
Acquisitions & disposals net	0.0	0.0	0.0	0.0	0.0	0.0
Other investing activities	16.6	0.6	1.7	0.7	0.4	0.4
Cash used in investing activities (CFIA)	(8.5)	(19.3)	(16.3)	(19.2)	(19.0)	(16.7)
Net proceeds from issue of shares	(2.0)	(5.1)	(0.5)	0.5	0.0	0.0
Movements in debt	2.7	5.9	(9.7)	9.0	(16.2)	(4.7)
Other financing activities	(8.0)	(8.3)	(6.9)	(9.0)	(4.3)	(7.9)
Cash from financing activities (CFF)	(7.3)	(7.6)	(17.1)	0.5	(20.5)	(12.5)
Cash and equivalents at beginning of period	19.4	26.7	29.3	41.4	40.7	35.9
Increase/(decrease) in cash and equivalents	7.3	2.6	12.1	(0.7)	(4.8)	3.8
Cash and equivalents at end of period	26.7	29.3	41.4	40.7	35.9	39.8
Net (debt) cash	(9.6)	(13.5)	7.6	(2.5)	8.9	17.4

Source: Company Accounts, Edison Investment Research

Contact details	Revenue by geography
Laboratorios Farmacéuticos ROVI Julian Camarillo 3528037 Madrid Spain +34 91 375 62 30 www.rovi.es	

Management team	Management team
Chairman: Juan López-Belmonte López	**Chief Executive officer: Juan López-Belmonte Encina**
Juan López-Belmonte López has been the chairman of ROVI for the last 22 years. He graduated in economic and business sciences from the Universidad Complutense de Madrid in 1969. He is also president of the Madrid Chamber of Commerce, a member of the Plenary Session of the Spanish Chamber of Commerce and a member of the governing body of the IFEMA (Madrid Trade Fair Institute). He is a shareholder of Norbel Inversiones (ROVI's controlling shareholder).	Juan López-Belmonte Encina has been CEO since October 2007. He has been working for the company since 1994 and was appointed general manager in 2001. He graduated in economic and business sciences from CEU San Pablo, Madrid, specialising in auditing, in 1993. Prior to this he worked for international pharmaceutical companies (Nielsen Group, Tyco Group and Boots Pharmaceuticals). He is a vice-president of the board of governors and executive board of Farmaindustria and chairman of the R&D&I Commission of the CEOE (Spanish Confederation of Business Organizations). He is a shareholder of Norbel Inversiones (ROVI's controlling shareholder).
Chief Financial Officer: Javier López-Belmonte Encina	
Javier López-Belmonte Encina has been CFO since 2001 and is second deputy chairman of ROVI's board of directors. He graduated in economic and business sciences from CUNEF, Madrid, specialising in financing, in 1998. He began his professional career in the banking sector in 1998, working for Argentaria in the UK as an analyst and in the pharmaceutical sector with Medeva Pharma. He joined ROVI in 2000. He is a member of the board of governors and vice-president of the executive committee of the CEIM (Madrid Business Confederation). He is chairman of the Health and Social Affairs Commission of the CEIM and a member of the board of directors of Avalmadrid, representing the Madrid Business Confederation-CEOE. He is also a member of the Social Council of the Universidad Autónoma de Madrid and a shareholder of Norbel Inversiones (ROVI's controlling shareholder).	

Principal shareholders	(%)
Norbel Inversiones S.L.	69.64%
JO Hambro Capital	5.47%
Alantra asset management	5.02%
Indumenta Pueri	5.00%
T. Rowe Price	3.01%

Companies named in this report

Johnson & Johnson (J&J), Bristol-Myers Squibb (BMS), Alkermes (ALKS), Indivior (INDV)

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