COMPANY UPDATE

SUN PHARMACEUTICALS

Specialty business - Steep learning curve ahead

India Equity Research| Pharmaceuticals

Sun Pharma (SUNP) is the only company among peers to have made significant investments (~USD1.5bn) in specialty US business. The company's 'string of pearls' strategy of sourcing external innovation by acquiring assets rather than companies, involves low risk but also offers low returns. Our deep-dive analysis of SUNP's specialty portfolio suggests – 1) significant challenges in the build-up stage, 2) cash guzzle over next three-four years, and 3) potential over-estimation by the street. Specialty pipeline likely to add USD300mn revenue in next 5 years as decline in *Absorica* and *Levulan-Kerastick* offset key assets – *Ilumya (tildrakizumab)* and *Seciera*. Though, Sun's strategy of moving into specialty is a prudent step, shifting from generics will have a steep learning curve. We maintain 'HOLD' with a revised target price of INR480 (INR550 earlier).

A comprehensive deep-dive into SUNP's specialty investments

This report comprises a detailed analysis of SUNP's specialty investments. Our analysis dives into each therapeutic area, comprising a bottoms-up study of each molecule. We channeled our efforts on understanding the market, competitive landscape, revenue potential and the probable breakeven timelines.

Significant challenge and cash guzzle over next 3-4 years

Ilumya (*tildrakizumab*) is the most important specialty asset, where SUNP has spent USD300-350mn on development and purchase. It will be a challenge to make a mark in a market where five biologics with better efficacy have already been launched in the last two years. Further investment will be needed to create a front-end to sell the drug and to perform clinical trials for label extension. SUNP will also need to make investments in the lifecycle management of *Absorica* and *Levulan-Kerastick*, failing which ~USD350mn revenue is at risk.

Upside to be neutralized by decline in existing basket

We forecast that SUNP's specialty pipeline has the potential grow to ~USD650mn (currently USD365mn) in the next five years, with the bulk to come from *tildrakizumab* and *Seciera*. However, *Absorica* and *Levulan-Kerastick*, which currently contribute ~USD350mn, will see tough competition. Sandoz has settled for the launch of *gAbsorica* in Nov 2020. Also *Levulan* competitor Ameluz, which is better in efficacy, was launched in the US recently.

Potential overestimated by street; cut estimates & maintain 'HOLD'

As SUNP have made large upfront investments in US specialty, we believe valuations are set to remain buoyant. However, challenges like: 1) failure to resolve the Halol warning letter for the past three years, 2) slowdown in US generics, and 3) investments in specialty, are likely to keep the earnings under pressure. We cut our estimates by 20%/16% for FY19E/FY20E, and believe that consensus will follow. Maintain **'HOLD/SU'** with a revised target price of INR480.

EDELWEISS 4D RATINGS	
Absolute Rating	**HOLD**
Rating Relative to Sector	Underperform
Risk Rating Relative to Sector	Medium
Sector Relative to Market	Equalweight

MARKET DATA *(R: SUN.BO, B: SUNP IN)*	
CMP	: INR 502
Target Price	: INR 480
52-week range (INR)	: 720 / 433
Share in issue (mn)	: 2,399.3
M cap (INR bn/USD mn)	: 1,209 / 18,607
Avg. Daily Vol.BSE/NSE('000)	: 5,687.0

SHARE HOLDING PATTERN (%)

	Current	Q2FY18	Q1FY18
Promoters *	54.4	54.4	54.3
MF's, FI's & BK's	14.9	13.9	12.0
FII's	17.2	18.2	7.9
Others	13.5	13.6	25.8
** Promoters pledged shares (% of share in issue)*	:		*0.4*

PRICE PERFORMANCE (%)

	Stock	Nifty	EW Pharma Index
1 month	(9.5)	(0.9)	(5.0)
3 months	1.1	1.5	(2.0)
12 months	(26.6)	14.6	(11.1)

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A bird's eye view

Specialty business – The way forward

As the generic space becomes crowded and growth gets challenging, moving up the specialty value curve is the option left with SUNP. The specialty business, unlike generic, is a different ball game altogether entailing high entry barriers in terms of development, regulations and convincing payers and doctors. Prerequisites for specialty business are: (i) doctor and payer reach in that therapy; (ii) portfolio breadth; and (iii) balance sheet might. Sun Pharma is the lone player, among domestic players, which qualifies on all three criteria and has the potential to transform into a specialty player.

Specialty business – Journey till now

SUNP started its specialty journey 5 years ago, with acquisition of Dusa in FY13. So far, the company has invested ~USD 1.5bn in its specialty pipeline, via the organic and inorganic route. ~Close to 60% of the investment was in dermatology, followed by ophthalmology.

Fig. 1: Chronology of Sun Pharma's Specialty Journey

Year	Transaction	Therapy	Investment	Comments/ Rationale
FY17	Acquired 14.58% stake in scPharmaceuticals	Others	USD13mn	The Company is developing a portfolio of transformative pharmaceutical products for subcutaneous delivery
	Acquired Odomzo	Oncology	USD175mn + milestone	Opportunity to expand established branded dermatology busn and support expansion into Branded Oncology with a launched brand.
	licensing deal with Moebius Medical	Others - pain		The novel liposomal non-opiod pain product for osteoarthritis will help build a branded product pipeline and enrich global portfolio for pain products..
	Acquired Ocular Technologies	Opthal	USD40mn + milestone	Enhances Specialty Ophthalmic Pipeline with Seciera, undergoing a confirmatory Ph-3 trial for treatment of dry eye disease.
	Inlicensed Elepsia from SPARC	CNS	USD10mn + milestone	Facilitating entry into the proprietary CNS segment (Sun Neurosciences business unit) in the US
FY16	Acquired 14 brands from Novartis	Others	USD293mn	Facilitates entry into the Japanese prescription market and provides an opportunity to build a larger product portfolio in the future
	Acquired InSite Vision	Opthal	USD48mn + debt	Strengthens specialty ophthalmology pipeline in US, with 4 late stage assets + 2 marketed products. Company has recently launched one of the products (Bromsite) from the acquired portfolio.
	Inlicensed Xelpros from SPARC	Opthal	USD16mn	Facilitating entry into the branded Ophthalmology segment in US, and strengthen US Specialty segment
FY15	Inlicensed MK-3222 (Tildrakizumab)	Derma	USD80m + milestone	Building pipeline of innovative dermatology products (preparing to file BLA in US and outlicensed the product for EU markets)
FY14	JV with Intrexon	Opthal		Develop controllable gene-based therapies for the treatment of ocular diseases
FY13	Acquired DUSA	Derma	USD200mn	Gets access to patented drug-device combination (Levulan) useful for treating Actinic Keratosis
FY07	Demerger of SPARC	Others		Demerger of the innovative R&D arm into a separate company

Source: Edelweiss research

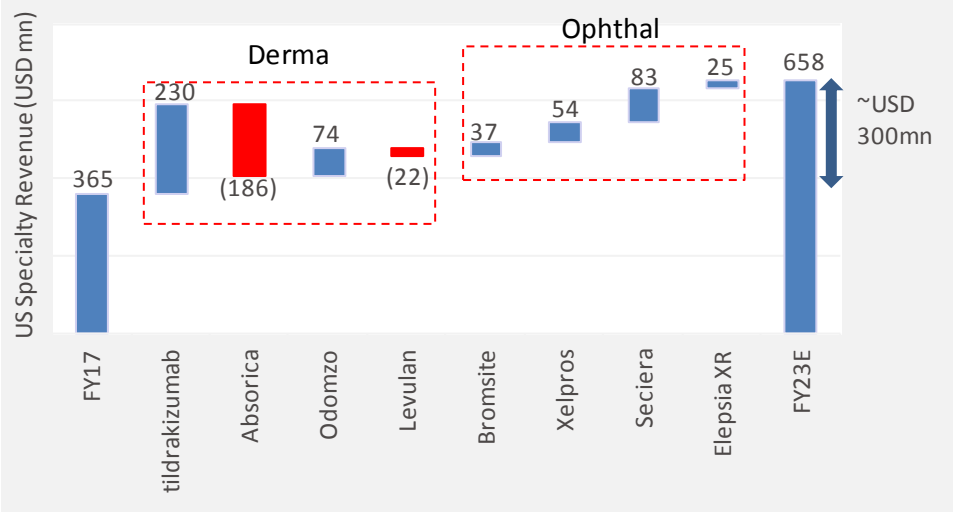
Dermatology – High stakes

Dermatology is a ~USD10.5bn market in US, growing at ~5-6% CAGR. It is a highly fragmented market with large unmet needs and limited innovation due to heavy consolidation in the past. We believe this therapy is the right choice for a company to enter specialty pharmaceuticals and carve a niche where the 'Big Pharma' is not looking aggressively. SUNP dermatology portfolio addresses ~70% of the market i.e. psoriasis, acne, actinic keratosis (AK) and skin cancer, which can add ~USD300mn incremental revenue over the next five years, lead by *Odomzo* and *tildrakizumab*. However, *Absorica* and *Levulan-Kerastick*, which together contributed ~USD350mn in FY17, will decline, as competition builds up over the next three years. As a result, net revenue from dermatology is expected to increase only by ~USD100mn to ~USD450mn by 2023. Company has invested ~USD900mn so far.

Ophthalmology – Low investment but high return

Ophthalmology is a ~USD12bn market in the US, growing at 4-5% CAGR. With the help of incubation partner SPARC and with the acquisition of InSite Vision, SUNP has built a comprehensive ophthalmic portfolio of late stage assets. There are assets across most areas within ophthalmic eye diseases – cataract, glaucoma, age related macular degeneration, dry-eye, conjunctivitis, blepharitis, etc. *Seciera*, *Xelpros*, and *BromSite* are the key products that can generate ~USD180mn in revenue by FY23E. At present, there is hardly any revenue coming from this therapeutic area. Total investment in this area is less than USD100mn.

Chart 1: US Specialty revenue to increase by ~USD300mn over next 5 years



Source: Edelweiss research

Valuations to remain buoyant, but earnings remain under pressure

As SUNP is the only company among peers to have made large upfront investments in US specialty, we believe valuations are set to remain buoyant. However, challenges like: 1) failure to resolve the Halol warning letter for the past three years, 2) slowdown in US generics, and 3) investments in specialty, are likely to keep the earnings under pressure. We cut our earnings by 20%/16% for FY19E/FY20E and believe that consensus will follow. Our revised target price of INR480 is based on 22x FY20E earnings.

Dermatology

Dermatology is a ~USD10.5bn market in US, growing at ~5-6% CAGR. It is a highly fragmented market with large unmet needs and limited innovation due to heavy consolidation in the past. We believe this therapy is the right choice for a company to enter specialty pharmaceuticals and carve a niche where the 'Big Pharma' is not looking aggressively. SUNP dermatology portfolio addresses ~70% of the market i.e. psoriasis, acne, actinic keratosis (AK) and skin cancer, which can add ~USD300mn incremental revenue over the next five years, lead by Odomzo and tildrakizumab. However, Absorica and Levulan-Kerastick, which together contributed ~USD350mn in FY17, will decline, as competition builds up over the next three years. As a result, net revenue from dermatology is expected to increase only by ~USD100mn to ~USD450mn by 2023. Company has invested ~USD900mn so far.

A fragmented chronic market that lacks innovation

Dermatology is a ~USD10.5bn market in US, growing at ~5-6% CAGR. Key big players in the dermatology drugs market are AbbVie, AstraZeneca, GlaxoSmithKline, Johnson & Johnson, LEO Pharma, and Pfizer. According to a report that used 2013 healthcare claims data drawn from insurance enrollment databases, the number of individuals with skin diseases in the US exceeded that with cardiovascular disease or diabetes. In other words, ~85mn Americans i.e. one in four reported receiving treatment for at least one skin disease in 2013. Nearly 50% of Americans over the age of 65 have some skin disease with an average of 2.2 skin disease each. Growth of the segment is being propelled by factors like an ageing population (~70% of patients are >40 years old) and rising diagnosis of skin cancers (incidence growing at ~2% CAGR).

Dearth of innovation has lead to significant unmet needs

However, unmet needs in the segment are significant with limited innovation due to consolidations in the past. Physicians rely on antibiotic and corticosteroids for several diseases and generics tend to dominate prescriptions. The market has been dominated by life cycle management and reformulation of active ingredients, owing to which physicians are dissatisfied with a number of factors like poor efficacy and challenging safety profiles with chronic use. Thus, there is a vast and unmet need for improved and safer treatments. This therapy is the right choice for a company to enter into specialty pharmaceuticals to carve a niche where big pharma companies are not looking aggressively.

Table 1: Dermatology is a highly fragmented but chronic market which lacks innovation

Drug class	Market Size (USD mn)	% of total	Sun's existing products/ pipeline	Competition
Psoriasis	6,500	63%	Tildrakizumab (MK-3222)	Stelara, Cosentyx, Taltz, Siliq, Enbrel, Humira, Remicade
Acne	1,000	10%	Absorica	Solodyn, Ziana, Doryx, Duac, BenzaClin
Actinic Keratosis	1,000	10%	Levulan	Ameluz
Rosacea	500	5%	-	Oracea
Skin cancer	150	1%	Odomzo	Erivedge
Other oral agents	1,200	12%		Aldara, Lamisil
Total	**10,350**			

Source: Edelweiss research; Note: Excludes aesthetics market

Large, yet fragmented market opportunity

Dermatology is a highly fragmented therapeutic market and category. The key sub therapeutic areas under dermatology are psoriasis, acne, rosacea and Actinic keratosis and skin cancer.

Psoriasis: It is estimated that about 8mn U.S. patients suffer from psoriasis, or 2-3% of the population. About 85-90% of these patients have plaque-type psoriasis. And up to 25% of psoriasis patients could be classified as moderate-to-severe. This contributes 63% of the overall market in dermatology and is growing at double digits. Market growth is driven by anti-TNFs agents. Recently launched *Cosentyx* (Novartis) and *Taltz* (Eli Lilly), both of which target the IL-17 have the most promising efficacy profiles. While Sun Pharma has filed an NDA for IL-23-blocking *tildrakizumab*, Johnson & Johnson (J&J) has already launched *Tremfya* in this space. This space is getting competitive and crowded with new and better drugs coming. Generic competition in *Enbrel* and *Humira* over the next one-two years will add to the pressure. J&J's *Stelara*, an IL-12/23 blocker, is an established drug, which clocked USD2.8bn of US revenue in CY17.

Acne: For close to 30 years, topicals and isotretinoins were the predominantly used treatment regimes. Two most widely prescribed antibiotics are doxycycline and minocycline. Doxycycline is effective in treating inflammatory acne, but can cause sun sensitivity in some patients. Minocycline has a long history of use in treating acne. It is often effective in treating acne that has not responded to other oral antibiotics and also seems to produce fewer incidents of antibiotic resistance.

Rosacea: Rosacea is a chronic skin disease that affects more than 16mn Americans; of these, only about 1.4mn are treated. The cause of Rosacea is unknown and there is no cure for this disease. However, research has helped doctors develop a course of treatment that effectively controls Rosacea by minimizing its symptoms. Galderma/Collagenex's *Oracea*, a low-dose version of doxycycline are effective against Rosacea.

Dermatology has had fair amount of consolidation

Merger and acquisition announcements in the healthcare space are being made at a frenetic pace, as payers and providers join forces to become more powerful in an increasingly complex healthcare environment. What's happening with the big corporations across healthcare has trickled down to the dermatology industry as well. The US pharmaceutical dermatology market is worth ~USD10.5bn, addressed to by ~10,000 dermatologists. Dermatologists as well as patients have high-touch servicing needs, whether it is education on clinical differentiation and benefits, or dispensing. Fragmentation of the market into multiple small sized markets has led to a consolidation effect in the industry that has seen a number of transactions.

Table 2: Dermatology has had fair amount of consolidation

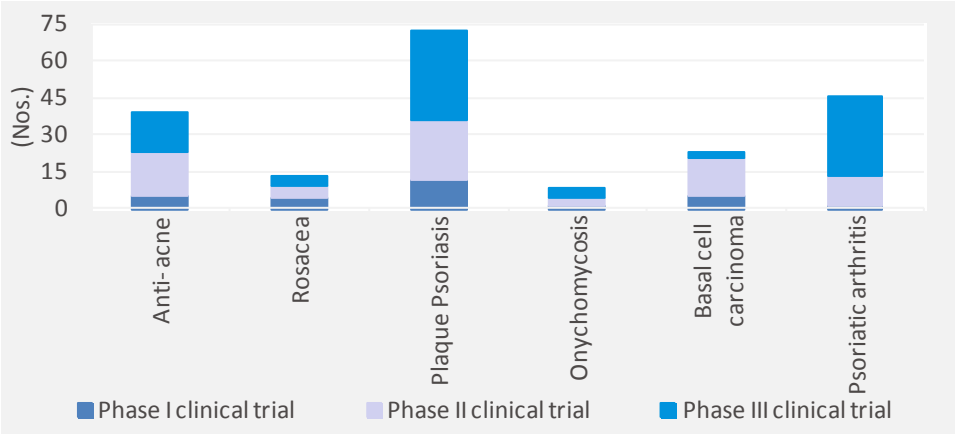
Acquirer Name	Target Name
Allergan	Skinmedica
Novartis	Fougera
GSK	Stiefel, Barrier Therapeutics, Connetics
Valeant	Medicis, Coria Labs, Dermik, Graceway, Obagi, PreCision Dermatology, Triax
Nestle	Galderma, Collgenex, Q-med
Bayer	Intendis
Takeda	Nycomed, Doak Dermatologics
Almirall	Polichem
Merz	Ulthera
Pierre Fabre	Collaboration with Hill Dermaceuticals for AK drug
Integra Lifesciences	Derma Sciences, BioD
Sun Pharma	DUSA Pharmaceuticals

Source: Bloomberg, Edelweiss research

Plaque psoriasis and acne are focus of industry's R&D efforts

Clinical trial efforts mirror the size of the opportunities in dermatology. As plaque psoriasis and acne make up bulk of the commercial share of the market, most clinical trials are focused on assets addressing them.

Chart 2: Clinical trials across dermatology



Source: FDA, clinicaltrials.gov, Edelweiss research

Specialty fits the bill for SUNP

Through Taro, SUNP has realised the benefits of limited generic competition in an area with little incremental innovation. This market fits the bill of limited competition between innovators as well going forward, a low and shrinking number of prescribers who are not satisfied with the existing bouquet of products. Thus, there is an opportunity for new players who can provide innovation to bridge such unmet needs in the therapy area.

However, significant gaps exist in SUNP's portfolio

While SUNP has assets in sub-therapies like plaque psoriasis, acne, and actinic keratoses and basal cell carcinoma, it has not currently built/acquired any assets in rosacea, dermatitis, onychomycosis, pigmentary disorders, etc. Eventually, building critical mass in the therapy will require SUNP to also evaluate aesthetic dermatology. Not only does the company need more breadth with respect to covering portfolio gaps, it also needs more depth in the Dermatology therapy as it currently lacks multiple products covering prescriber's needs in the categories it covers.

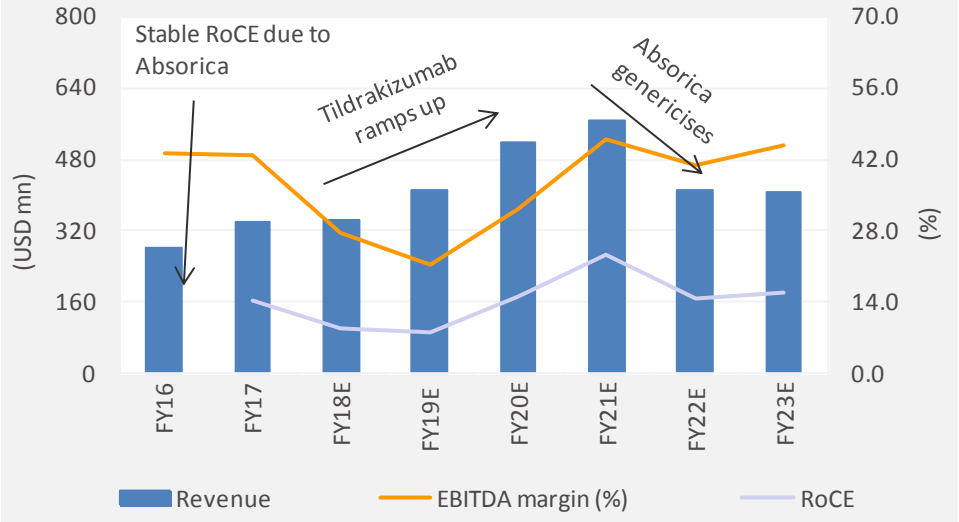
For instance, while SUNP covers actinic keratoses with *Levulan*, it does not cover squamous skin cell carcinoma, which is an advanced version of actinic keratoses whereas competitors do. This essentially implies that there is still a significant amount of investment needed for SUNP to emerge into a dominant player in this therapy area.

Table 3: Dermatology EBITDA margin to rebound in FY21E

Dermatology SBU	FY16	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
Revenue	280	357	366	435	541	595	441	452
Gross Profit	211	270	274	323	409	475	374	387
Gross Margin (%)	76	76	75	74	76	80	85	86
Milestone	-	-	20	20	20	-	20	-
Royalty payout	27	33	37	46	64	71	47	47
Promotional Costs	30	38	37	42	50	55	43	44
Employee Expenses	26	33	36	51	55	59	64	69
R&D	8	8	34	60	35	11	12	13
EBITDA	121	158	110	104	184	280	189	214
EBITDA margin (%)	43	44	30	24	34	47	43	47

Source: Edelweiss research

Chart 3: RoCE for the Dermatology SBU cushioned by Absorica



Source: Edelweiss research

Therapy: Levulan Kerastick (aminolevulinic acid HCl topical solution) + BLU-U (Blue Light Photodynamic Therapy)

Status: Approved Levulan (1999), BLU-U (2000). Launched September 2000. Sun acquired DUSA in late 2012.

Indication: Treatment of minimally to moderately thick actinic keratosis of the face or scalp

Mechanism of action: Photosensitisation

Competitive landscape: Recently launched competitor Ameluz has much impressive clinical efficacy data and a much better label. It will erode into Levulan's sales going forward.

Peak sales potential: USD130 mn, no para-IV challenges yet

Levulan and BLU-U combination (DUSA)

Background

SUNP bought Dusa Pharmaceuticals in late 2012 for USD230mn, thus entering the photodynamic therapy (PDT) platform with a dermatology field-force. DUSA's key product is *Levulan-Kerastick* (*aminolevulinic acid HCl* topical solution) + BLU-U (Blue Light Photodynamic Therapy) drug device combination, prescribed for treatment of minimally to moderately thick actinic keratosis (AK) of the face or scalp. Additionally, since September 2003 Dusa has clearance from the FDA, to market BLU-U without *Levulan* for the treatment of moderate inflammatory acne vulgaris and general dermatological conditions.

As a small, loss-making company, Dusa had its own capital limitations. The SUNP acquisition was in part meant to resolve these capital issues. However, the subsequent launch of Biofrontera's *Ameluz*, which had a superior clinical benefit and a shorter incubation period than *Levulan*, was a major impediment to SUNP's plans. *Ameluz* received its specific J-code in January 2018, significantly streamlining the reimbursement process and making the drug more attractive for dermatologists. Ongoing clinical trials for *Levulan* study the effect of - (1) reducing *Levulan's* incubation time, and (2) *Levulan* under daylight PDT, success in these studies is unlikely to offset threat from better efficacy of the closest competitor.

Indication to be treated - actinic keratosis (AK)

AKs are precancerous skin lesions caused by chronic sun exposure. The market for actinic keratosis treatments is estimated to be over USD1bn. Approximately 10% of total cases can develop over two years into a form of skin cancer called squamous cell carcinoma (SCC), the second most common skin cancer. More than 58mn Americans (6.5% of population) have AKs. The condition is characterised by presence of rough-textured, dry, scaly patches on the skin caused by excessive exposure to ultraviolet light such as sunlight. These patches are primarily seen in Caucasians with pale skin, living in sunny climates, past the age of forty. Additionally, organ transplant recipients are at an increased risk of developing skin cancer due to immunosuppressive therapies.

Multiple treatment options:

Current treatments for AK include cryosurgery (freezing), surgical excision, curettage (scraping), laser surgery, chemical peels, and various topical creams. The traditional lesion directed methods of treating AKs are cryotherapy (deep freezing of skin using liquid nitrogen) and surgery (for especially thick or suspicious lesions); or topical therapies which include various fluorouracil formulations, *imiquimod* 5% cream (*Aldara*/*Zyclara*), *Picato*, and *diclofenac* 3% gel (*Solaraze*).

Other topical agents such as *colchicine* and *tretinoin* have been used but there are no clinical trials to substantiate their use. Fluorouracil is available in 5% (*Efudex*), 1% (F*luoroplex*), and 0.5% (*Carac*) formulations. Cryotherapy is non-selective, and thus can cause a pain, blistering and loss of skin pigmentation. Patients generally experience long-term scarring and there is a potential of localised pain and irritation.

Table 4: Treatment options

Intervention	Pros	Cons	Comment
Surgery/excision	Well-established and effective for discrete lesions	Poor cosmetic outcomes (particularly for larger lesions)	Traditionally the mainstay treatment
Radiotherapy	Effective if cancer covers extensive area/is difficult to reach	Long-term risks from radiation	Can be used for BCC or SCC
Curettage/scraping	Effective for discrete hyperkeratotic lesions	Limited use for multiple lesions Long healing times	Particularly useful for hypertrophic AK of the extremities
Cryotherapy	Fast and can be conducted in an outpatient setting	Variable cosmetic outcomes and higher recurrence rate	Historically the treatment of choice for AK in the US
Laser therapy	Effective long-term outcomes	High recurrence rates Common risks – Infection, scarring/discolouration	Limited standards of use
PDT	Superior cosmetic outcomes and amenable to "field" therapy	Pain ("burning sensation")	Other advantages include reduced therapy duration & patient compliance
Topical therapies	Non-invasive and can be administered by the patient	5-FU associated with toxicity and the potential for skin irritation	Typically used for superficial lesions; compliance an issue

Source: Edelweiss research

PDT is a non-traditional field directed treatment modality that can produce varying degrees of pain during light exposure, but the therapy is generally well tolerated. The topical application plus blue light illumination is a two step (drug plus blue light) treatment. While this procedure requires just a single topical application, patients have to experience radiation 14-18 hours later. Additionally, patients feel burning and stinging. The resulting redness or inflammation is generally resolved within days without any change in pigmentation.

Compliance is better with PDT as there is no daily medication to keep track of. There is no prescription to be filled as the treatment is conducted in a clinical setting. Since it is a non invasive method, cosmetic results are excellent. Earlier, PDT growth was mostly at the expense of topicals, but with the guideline pressure towards field therapy, it is also increasingly taking market share from cryotherapy.

Photodynamic therapy (PDT)

PDT is a two-step process:

- The first step is application of a drug known as "photosensitizer," or a pre-cursor of this type of drug, which tends to collect in specific cells; and
- The second step is activation of the photosensitizer by controlled exposure to a selective light source in the presence of oxygen.

Levulan-Kerastick: It is a single-use, disposable applicator, which allows for uniform application of *Levulan* topical solution in standardised doses. This is a two component system consisting of a plastic tube containing two sealed glass ampules and an applicator tip. The 20% topical solution is prepared just prior to the time of use by breaking the ampules and mixing the contents by shaking the applicator. While Dusa gets *Levulan* manufactured at Sochinaz SA, it manufactures Kerastick at its Wilmington facility.

BLU-U: This is a unique, specially designed blue light that kills the P. acnes bacteria in skin. The device is placed in the doctor's clinic and patients undergo ~17 minute sessions once or twice a week. While the Wilmington facility does have FDA approval for manufacturing the BLU-U device, Dusa utilizes National Biological Corporation as a third party manufacturer.

Intellectual property

Levulan's NCE exclusivity expired on December 3, 2004, and no para-IV challenges have emerged thus far. It has patent validity until June 2019.

Mechanism of action

Energy from the light activates the photosensitizer. *Aminolevulinic acid (ALA)* is not a photosensitizer, but rather a metabolic precursor of protoporphyrin IX (PpIX), which is a photosensitizer. In PDT, the activated photosensitizer transfers energy to oxygen molecules found in cells, converting the oxygen into a highly energised cytotoxic form known as "singlet oxygen," which destroys or alters the sensitised cells by a phenomenon called programmed cell death. *Methyl-aminolevunate (MAL)* is another prodrug utilised in PDT.

Blue light does not penetrate deeply into tissues, so it is generally better suited for treating superficial lesions. Red light penetrates more deeply into tissues, and is therefore generally better suited for treating cancers and deeper tissues. The lipophilic nature of the nano-emulsion is believed to facilitate superior delivery of the active ingredient through the outermost skin layer (stratum corneum) into the lesion, potentially explaining competitor *Ameluz's* higher efficacy.

Competition

There have been two other approved PDT products for AK in US - *Metvixia* (16% MAL emulsion with red light PDT, Galderma, approved in Jul 2004 and withdrawn in 2014 due to Galderma's failure to meet post approval obligations) and *Ameluz* (10% ALA nano-emulsion with BF-RhodoLED PDT, Biofrontera, approved in May 2016). *Ameluz* is a new entrant which is approved for use in lesion or field directed PDT of AK. It has superior efficacy to *Levulan* which is depicted in the chart below.

Table 5: Comparison of Ameluz versus Levulan

	Ameluz (Biofrontera)	Levulan (SUNP)
Efficacy (3 months)	91%	66%
Efficacy scalp	82%	50%
Lamp	red light	blue light
Application	gel	liquid
Incubation time	3hr	14-18hr
Illumination time	10 mins	16 mins
Skin rejuvenation	described in label	not covered by label
Treatment area	field	lesion

Source: Biofrontera, Edelweiss research

Note: gel formulation results in enhanced penetration and easier application

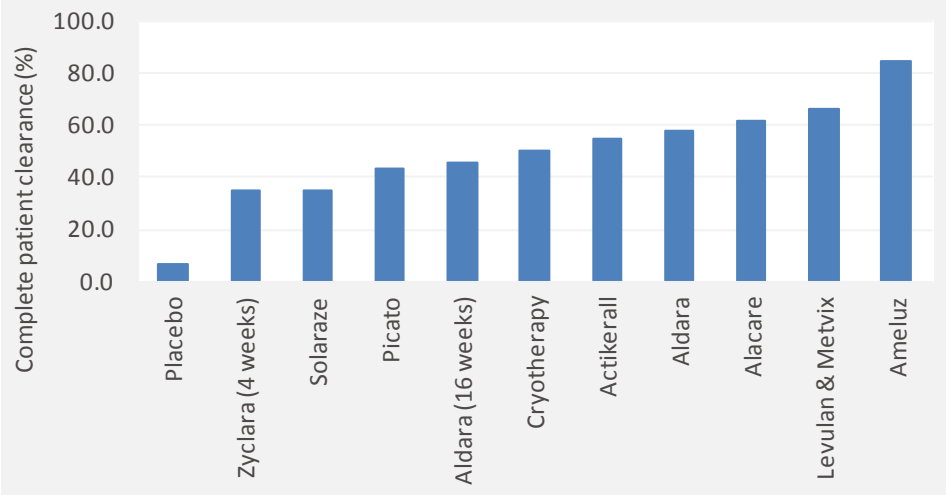
Ameluz – New competitor with better efficacy

Amulez, which has better efficacy than *Levulan*, is also looking for label extension. The company is conducting clinical trials to add daylight PDT and BCC indication which will increase the addressable market of this product by 3-4x to USD 700-800 mn in the US. With Ameluz having received its specific J-code, prescriptions will start reflecting in sales numbers more effectively. We believe *Levulan* will not be able to compete against *Ameluz*.

Dusa recently filed a legal suit against Biofrontera, claiming that Biofrontera's BF-RhodoLED infringes two of its patents. Patents '991 and '289, entitled "Illuminator for Photodynamic

Therapy", cover all such devices that may be described as "a plurality of light sources configurable in a spaced relationship to a patient to treat or diagnose a dermatological condition". As per Dusa, Biofrontera's Ameluz + BF-RhodoLED solution meets all conditions set forth in DUSA's patents. However, DUSA's litigation filing comes in ~18 months after Ameluz's launch. We believe Dusa does not have a very strong case as it relies on the wide, all encompassing language in the patent.

Chart 4: Ameluz – most effective therapeutic option for AK treatment



Source: Biofrontera, FDA, Edelweiss research

Revenue potential

While *Levulan-Kerastick* sales contributes ~90-95% to DUSA's revenue and accrues ~90% gross margin, BLU-U sales contribute ~5-10% to revenue and accrues <10% gross margin. Average selling price for the *Levulan-Kerastick* units is ~USD160, while that for BLU-U units is ~USD8k. In the past, Dusa had applied for label extension to prophylactic usage in subjects (organ recipients) that are at risk of SCC, but the USFDA denied this application. The company is also exploring prophylactic label extension for Levulan in a broad area / short drug incubation method (BASDI) through a phase III trial.

There are an estimated 5.2m AK visits in the US per year, of which around 60% are made by the Medicare population (>65 years). AK has been recognised as an occupational disease since 2013. Since then, occupational insurance associations have been obliged to cover for the duration of these patients' lives the treatment costs of patients who have worked predominantly outdoors for a long period and who fulfill certain criteria. Accordingly, PDT is taken into account and can be used and invoiced for the treatment of occupational AK.

As of FY17, DUSA's revenue was USD132mn, growing at ~28% YoY post slight decline in FY16. We believe growth for the *Levulan*/BLU-U combination, will stall, owing to competitor *Ameluz'* strong clinical data. We believe long term potential will hinge on lifecycle strategies.

Table 6: Levulan sales set to decline due to strong competition

	FY14	FY15	FY16	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
AK - Total potential patients (mn)	4.9	5.0	5.2	5.4	5.5	5.7	5.9	6.0	6.2	6.4
Annual PDT market share	9.9%	14.3%	12.4%	15.0%	15.2%	15.4%	15.6%	15.8%	16.0%	16.2%
AK - Total PDT treated patients (mn)	0.49	0.72	0.64	0.80	0.84	0.87	0.91	0.95	0.99	1.03
Average PDT Treatment cost (USD)	145	152	160	165	170	175	180	185	191	197
PDT Market Size (USD mn)	71	110	103	132	142	153	164	176	189	203
YoY Growth (%)		56	(6)	28	8	7	7	7	7	7
Levulan market share	100.0%	100.0%	100.0%	100.0%	80.0%	70.0%	60.0%	58.0%	56.0%	54.0%
Levulan Sales (USD mn)	71	110	103	132	114	107	98	102	106	110
YoY Growth (%)		56.0	(6.4)	28.2	(14.0)	(5.9)	(7.9)	3.9	3.7	3.6

Source: Edelweiss research

Therapy: Odomzo (sonidegib)

Status: Approved (Jul 2015). SUNP acquired from Novartis in December 2016 for an upfront payment of USD175mn.

Indication: Locally advanced basal cell carcinoma

Mechanism of action: Hedgehog signaling pathway inhibitor

Competitive landscape: Direct competitor to Erivedge (Roche) which is currently a ~USD150mn product.

Peak sales potential: ~USD80 mn

Odomzo

Background

SUNP acquired *Odomzo* (*sonidegib*) from Novartis for an upfront payment of USD175mn and additional milestone payments. *Odomzo* was approved by the US FDA in July 2015 for treatment of adult patients with locally advanced basal cell carcinoma who are either not eligible for, or have failed surgical or radiation modalities of treatment. While ~70% of the drug's volume is prescribed by dermatologists, the balance is prescribed by oncologists, making *Odomzo* the first branded oncology product for SUNP. This is the second hedgehog signaling pathway inhibitor approved by the US FDA after Genentech's *Erivedge*.

However, unlike *Erivedge*, which is also approved for metastatic basal cell carcinoma (mBCC), *Odomzo* is only approved for locally advanced basal cell carcinoma (laBCC). Both *Odomzo* and *Erivedge* carry a boxed warning for embryo-fetal toxicity, alerting healthcare professionals that the drug may cause death or severe birth defects in a developing fetus when administered to a pregnant woman or a female of reproductive potential. *Odomzo* is also known to cause musculoskeletal reactions like muscle spasms and myalgia.

Indication to be treated - Locally advanced basal cell carcinoma

Basal cell carcinoma (BCC) is one of the most common skin cancers in the United States. While two-thirds of the cases occur on sun exposed areas of the body, a third occur in other areas. BCCs can often come in association with other lesions of the skin, such as AK, seborrheic keratosis, and squamous cell carcinoma. LaBCC refers to basal cancers that have not spread to other parts of the body, but cannot be curatively treated with local treatments, specifically surgery and radiation. BCC almost never spreads (metastasizes) beyond the original tumour site. Only in exceedingly rare cases can it spread to other parts of the body and become life threatening.

Treatment paradigm

After BCC has been confirmed with a skin biopsy, the physician may prescribe treatments from a host of surgical procedures - radiation, cryosurgery, photodynamic therapy, laser therapy or topical gels or creams - depending on the type, size, location, and depth of penetration of the tumour, the patient's age and general health. Topical therapies like *imiquimod* and *fluorouracil* are used to treat superficial BCC with cure rates of ~80-90%. Surgical procedures like curettage, electrodessication, and excision are reserved for small lesions around critical areas and have a cure rate above 95%. The 'Mohs surgery' has come to be accepted as the gold standard for treating BCCs with 99% cure rate.

Alternative treatment is usually reserved for when surgery may not be the best choice or when BCCs that cannot be cut out in patients with bleeding disorders or intolerance to anesthesia. However, cure rates for these treatments are much lower (~70%) and relapses are common. *Odomzo* addresses this unmet need, being approved specifically for patients whose tumours have recurred following surgery or radiation, or who are not candidates for surgery or radiation therapy. However, in cases where the cancer has metastasised to the surrounding tissue, *Erivedge* is the better candidate.

Mechanism of action

Odomzo inhibits the hedgehog signaling pathway (Hh), a molecular pathway that transmits cell differentiation information during embryonic and postnatal periods. Under normal conditions, Hh is under inhibition and gets activated upon binding of the Hh ligand to a

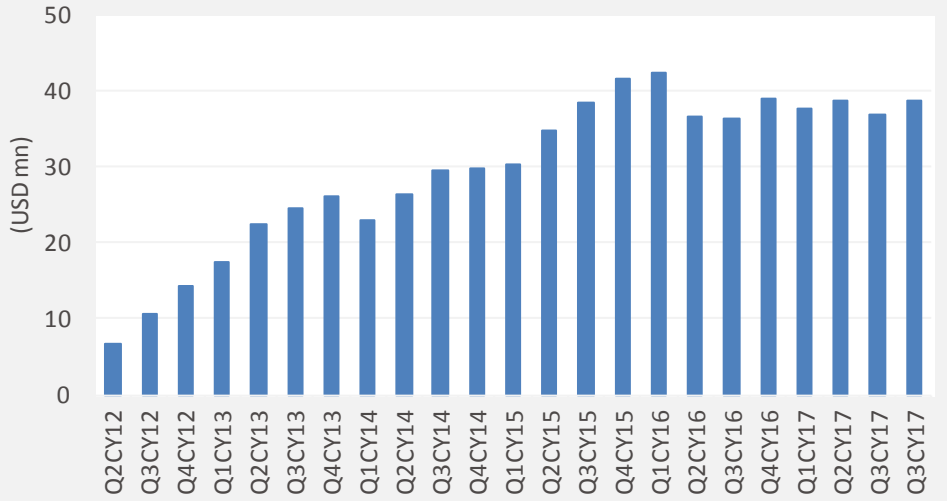
trans-membrane receptor. The abnormal signaling of Hh can cause tumour growth. By suppressing this pathway, *Odomzo* may stop or reduce the growth of cancerous lesions.

Competition

Erivedge (*vismodegib*) was the first hedgehog signaling pathway inhibitor to be approved by the US FDA. It is indicated for both metastatic and locally advanced BCC, which has either relapsed after surgery, or cannot be treated with surgery or radiation. While the timing of slowdown in *Erivedge's* and *Odomzo's* launch matched, we believe *Odomzo* did not cause the slowdown. Innovator Novartis simply failed to gain market share due to its oncology focus, which lead to a lack of penetration within the dermatologist community.

Though *Odomzo* and *Erivedge* yield similar clinical benefit, the latter has a better label as it is approved for both locally advanced as well as metastatic BCC. Disease control rates are slightly better for *Odomzo*. In terms of safety, while both the drugs have a boxed warning for embryo-natal toxicity, *Odomzo* has a slightly better safety profile.

Chart 5: Erivedge's sales ramp up



Source: Company, Edelweiss research

Table 7: Clinical data for Odomzo vs. Erivedge

	Odomzo (sonidegib)				Erivedge (vismodegib)	
Manufacturer	SUN Pharmaceuticals				Novartis	
Mechanism	Hedgehog pathway inhibitor				Hedgehog pathway inhibitor	
Study name	BOLT study (30-month analysis)				ERIVANCE study (39-month analysis)	
Arms	200mg laBCC	200mg mBCC	800mg laBCC	800mg mBCC	150mg laBCC	150mg mBCC
No of participants	66	13	128	23	63	33
Objective response rate (ORR)	56%	8%	45%	17%	60%	49%
Complete response rate (CRR)	5%	0%	2%	0%	32%	0%
Disease control rate (DCR)	91%	92%	82%	91%	84%	48%
Duration of response (DOR)	26.1 mth	24.0 mth	23.7 mth	NR	26.2 mth	14.8 mth
Progression free survival (PFS)	22.1 mth	13.1 mth	22.0 mth	11.1 mth	12.9 mth	9.3 mth
2-yr overall survival (OS)	93%	69%	91%	69%	86%	62%
Adverse events (AE)	92%		97%		99%	
Serious AEs	14%		30%		35%	

Source: FDA, clinicaltrials.gov, Edelweiss research

Intellectual property

Odomzo's NCE exclusivity expires on July 24, 2020. There is one Type II active DMF filed for *sonidegib* on March 1, 2017, by MSN Laboratories. In addition, there are two orange book composition patents that expire in 2029.

Table 8: Orange book patents for Odomzo

Patent no.	Patent expiration	Patent	Claim
8063043	15-Sep-29	Salts of N-[6-cis-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide	Composition
8178563	06-Feb-29	Compounds and compositions as hedgehog pathway modulators	Composition

Source: FDA, Edelweiss research

Revenue potential

Odomzo costs ~USD10.5k/month versus *Erivedge*, which costs ~USD12k/month. Based on the trailing 24-month TRx numbers, we believe Novartis has not been able to aggressively market this product in the US, leading to slow ramp-up. As ~75% of prescriptions in this drug class come from dermatologists, Novartis' oncology focus did not address the entire market. Though *Erivedge* has the first-mover advantage, *Odomzo* is still a good second choice for prescribers after *Erivedge*, and could take up ~20% market share in the hedgehog inhibitor drug class. Experience with *Erivedge* has shown that despite the broad label given to the class of drugs, prescription volumes have been slightly lower than expectation likely on account of the numerous adverse effects.

Table 9: Peak sales of ~USD80mn

Odomzo Revenues	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
US Market Size (Rx/ annum)	2,217	2,283	2,352	2,422	2,495	2,570	2,647
YoY Growth (%)		*3.0*	*3.0*	*3.0*	*3.0*	*3.0*	*3.0*
Mkt. Share, (Rx %)	3.0%	5.0%	10.0%	15.0%	20.0%	22.0%	24.0%
Market share gain/ loss (bps)		200 bps	500 bps	500 bps	500 bps	200 bps	200 bps
Odomzo (Rx/ annum)	67	114	235	363	499	565	635
Pricing (USD/ Rx/ annum)	1,00,000	1,04,000	1,08,160	1,12,486	1,16,986	1,21,665	1,26,532
Odomzo revenue (USD mn)	7	12	25	41	58	69	80
YoY Growth (%)		*78.5*	*114.2*	*60.7*	*42.8*	*17.8*	*16.9*

Source: Edelweiss research

Therapy: Absorica (isotretinoin capsule)

Status: Approved (May 2012)

Indication: Severe recalcitrant nodular acne only, distributed through the iPLEDGE program (REMS)

Mechanism of action: Oral retinoid

Competitive landscape: Several branded generic isotretinoin products in market currently within which Absorica has gained market share. New class of compounds unlikely to hurt sales during patent protection.

Peak sales potential: USD290 mn, will genericize Dec '20 onwards

Absorica

Background

Absorica (isotretinoin) was first marketed by Roche under the brand name *Accutane* for the treatment of severe recalcitrant nodular acne (SRNA). Roche discontinued *Accutane* due to adverse side effects like depression. Cipher's reformulation of *isotretinoin* was approved by the US FDA in May 2012 and was ***out-licensed*** to Ranbaxy, which launched it in Q4CY12. Ranbaxy paid just USD1mn upfront, with additional commercialisation milestone payments of ~USD23mn and revenue royalty in the mid-teens.

SUNP announced the Ranbaxy acquisition in April 2014 and effectively became the marketer for the drug in March 2015 post completion of the deal. The product is manufactured by Galephar in their Puerto Rico facility. Since *Absorica* can cause severe birth defects, it is not prescribed to pregnant women. Because of this risk, *Absorica* is available only through a restricted REMS (Risk Evaluation and Mitigation Strategies) programme called iPLEDGE.

Proprietary technology summary

Due to its high lipophilicity, oral absorption of isotretinoin is enhanced when given with a high-fat meal. However, *Absorica*, which is formulated using patented Lidose technology, can be given without regards to meals. Because meal compliance among teenagers is generally poor, they form a large portion of *Absorica's* patient base.

Treatment paradigm

Acne, a common skin disorder, occurs because of a poorly understood combination of hormones and heredity. SRNA, also known as cystic acne, is the hardest form of acne to treat. For treatment of acne, just three product classes were available for over 30 years.

Table 10: Acne - USD 3.7bn global market with limited therapeutic options

Product class	Sales (USD bn)	Target	Limitations
Topical retinoids	0.9	Follicular hyperkeratinization	Skin irritation, moderate efficacy
Topical, oral antimicrobials	1.9	P. acnes, inflammation	Bacterial resistance, waning efficacy
Oral isotretinoin	0.7	Excess sebum production	Significant systemic toxicity

Source: Edelweiss research

Severe recalcitrant nodular acne does not respond to standard acne treatment, including oral antibiotics. *Isotretinoin* is the most effective therapy for SRNA. *Isotretinoin* is prescribed only in severe cases owing to the risks involved. *Absorica* is the top ranked player in the ~USD750mn isotretinoin market, and has continuously gained market share. *Zenatane* (Dr. Reddy's), *Claravis* (Teva), *Myorisan* (Douglas) and *Amnesteem* (Mylan) are the other AB rated *isotretinoins* for *Accutane* that are marketed as brands.

Table 11: Acne treatment paradigm

	Mild		Moderate		Severe
	Non-inflammatory Comedonal	Inflammatory Papular/ pustular	Non-inflammatory Papular/ pustular	Inflammatory Nodular	Inflammatory Nodular/conglobate
First choice	Topical retinoid	Topical retinoid + Topical antimicrobial	Oral antibiotic + topical retinoid +/- BPO	Oral antibiotic + topical retinoid +/- BPO	Oral isotretinoin
Alternatives (males and females)	Azelaic acid or salicylic acid	Alt. Topical antimicrobial agent + alt. Topical retinoid or azelaic acid	Alt. oral antibiotic + alt. topical retinoid +/- BPO	Oral isotretinoin or alt. oral antibiotic alt. topical retinoid +/- Benzoyl peroxide /azelaic acid	High-dose oral antibiotic + topical retinoid + BPO
Alternatives (females only)	See first choice	See first choice	Oral anti-androgen + topical retinoid/ azelaic acid +/- Benzoyl Peroxide	Oral anti-androgen + topical retinoid +/- oral antibiotic +/- alt. Antimicrobial	High-dose oral antiandrogen + topical retinoid +/- alt. topical Antimicrobial
Maintenance therapy	Topical retinoid		Topical retinoid +/- Benzoyl Peroxide		

Source: Edelweiss research

Mechanism of action

Absorica is an oral retinoid, which when administered in pharmacologic dosages of 0.5 to 1 mg/kg/day, inhibits sebaceous gland function and keratinisation. Clinical improvement in nodular acne patients occurs in association with a reduction in sebum secretion. The decrease in sebum secretion is temporary and is related to the dose and duration of treatment with isotretinoin, reflecting a reduction in sebaceous gland size and an inhibition of sebaceous gland differentiation. The exact mechanism of action of *Absorica* is unknown.

Intellectual property

Watson (now Actavis) filed an ANDA with para-IV challenge for *Absorica* in December 2012. In October 2015, SUNP and Actavis settled the resulting litigation allowing generic launch in December 27, 2020, approximately nine months before patents expiry. There are no other litigations related to the product.

Table 12: Orange book patents for Absorica

Patent no.	Patent expiration	Patent	Claim
7435427	21-Sep-21	Pharmaceutical semi-solid composition of isotretinoin	Composition
8367102	21-Sep-21	Pharmaceutical semi-solid composition of isotretinoin	Composition
8952064	21-Sep-21	Pharmaceutical semi-solid composition of isotretinoin	Composition
9078925	21-Sep-21	Pharmaceutical semi-solid composition of isotretinoin	Composition
9089534	21-Sep-21	Pharmaceutical semi-solid composition of isotretinoin	Composition

Source: FDA, Edelweiss research

Revenue potential

We expect *Absorica* to retain market share, and the category to continue steady growth at ~10% CAGR over FY17-21 leading to ~USD290 peak sales for the drug by FY20. Beginning FY21, genericisation will erode *Absorica's* revenue.

Table 13: Peak sales of ~USD290mn, and genericisation FY21 onwards

	FY14	FY15	FY16	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
Market Size (USD mn)	539	598	619	763	840	924	1,016	1,067	1,067	1,067
YoY Growth (%)		11.1	3.4	23.3	10.0	10.0	10.0	5.0	-	-
Absorica Market share (%)	16	26	29	29	29	29	29	23	5	3
Absorica (USD mn)	**84**	**153**	**177**	**218**	**240**	**264**	**291**	**245**	**53**	**32**
YoY Growth (%)		82.1	15.7	23.3	10.0	10.0	10.0	(15.6)	(78.3)	(40.0)
Zenatane Market share (%)	4	16	23	27						
Claravis Market share (%)	46.6	23.7	21.7	23.3						
Myorisan Market share (%)	10	12	10	18						
Amnesteem Market share (%)	23.4	22.2	16.5	5.2						

Source: Edelweiss research

Therapy: Ilumya (tildrakizumab)

Status: success in phase III, BLA being prepared

Indication: Moderate-to-severe plaque psoriasis

Mechanism of action: IL-23p19 inhibitor

Peak sales potential: USD230mn

Competitive landscape: Biologics taking market share and expanding the market itself. Within Biologics, Interleukins taking market share from Anti-TNF-α.

Upcoming Newsflow: BLA filing (CY17) and PDUFA (CY18)

Ilumya (tildrakizumab)

Background

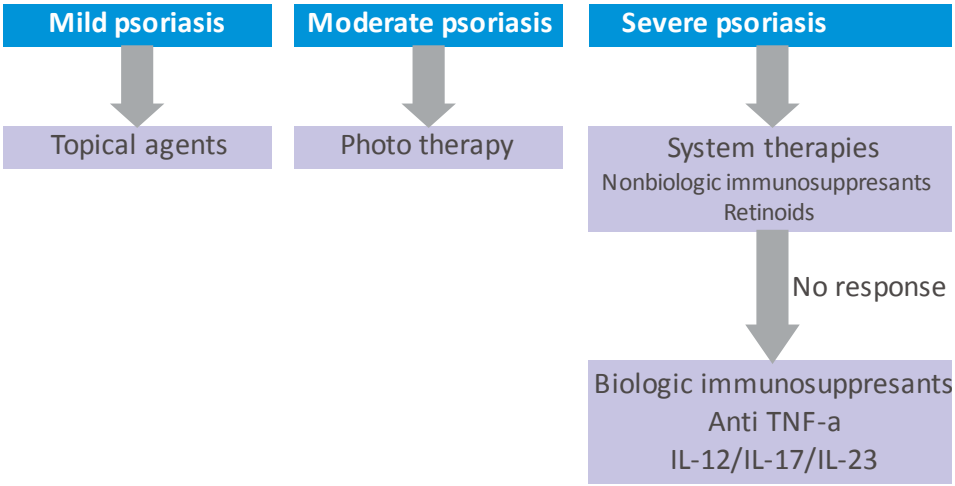
In September 2014, SUNP in-licensed a Ph-3 investigational IL-23p19 inhibitor novel biologic asset called *tildrakizumab* (earlier MK-3222) from Merck, for an upfront payment of USD80mn. It has reimbursed Merck for the two pivotal clinical trials that were underway for chronic plaque psoriasis and will pay milestones/royalties during the product's progress. In May 2016, Sun Pharma announced positive top-line data for phase III trials and in October 2016 presented the fine print of clinical data at the 25th European Academy of Dermatology and Venereology (EADV) Congress in Vienna, Austria. **In March 2018, SUNP announced the US FDA approval *tildrakizumab*, under the brand name *Ilumya*.** In Europe, SUNP announced an out-licensing agreement for *tildrakizumab* for an initial upfront payment of USD50mn. The company will be eligible to receive development and regulatory milestone payments and, additionally, sales milestone payments and royalties on net sales. Other potential indications for *tildrakizumab*, which may be evaluated in future, include psoriatic arthritis and Crohn's disease.

Plaque psoriasis

Psoriasis is a skin disease affecting ~3% of the global population. It the most prevalent autoimmune disease with a diagnosed prevalence of ~9mn people in US alone. Nearly 30% of the subjects have chronic plaque psoriasis in which patients suffer with thick red skin and scaly patches that can affect any part of the body and may be itchy and painful. Plaque psoriasis frequently affects elbows and knees. Though causes of psoriasis are not fully clear, they are broadly understood to be related to the immune system. It is not yet curable, but its chronic symptoms are treated with a variety of therapies according to disease severity.

Treatment paradigm

Fig. 2: Biologics forms the second-line therapy at the moment



Source: Edelweiss Research

Topical agents are usually utilised for mild disease. *Phototherapy* is utilised for moderate disease. For severe psoriasis where patients become resistant to topical agents and phototherapy, systemic treatment therapies are used. Systemic treatment includes non-biologic immunosuppresants like methotrexate, ciclosporin, and forms of Vitamin-A like retinoids, etc. *Otezla* (*apremilast*, a PDE4 inhibitor marketed by Celgene), an oral therapy,

was approved by FDA in 2014. It has steadily been winning US market share, hitting USD1bn in CY16 and still growing. Improved patient compliance and expanding access to insurance reimbursement are behind the product's stellar market share gain. Celgene has guided for ~USD1.5-1.7bn in CY17 on back of this.

Patients who do not find adequate response to their ailment from the above agents are subjected to second line biologic immunosuppresants. These biologics target certain specific components of the immune system (TNF-α, T-cells, CD-11a, IL-12, IL-23, IL-17, etc) that contribute to psoriasis. Long-term outcome data has demonstrated biologics to be safe for long-term use in moderate to severe plaque psoriasis and biologics are subsequently taking market share from other therapies. Within biologics, Interleukins have established a clear efficacy advantage over anti TNF-α and thus are gaining market share. The current IL-17/IL-23 pipeline for plaque psoriasis indicates that the ~USD7-8bn market will get crowded in time. An interesting scenario will play out over the next few years as the Interleukin market starts getting crowded with various products that have better safety/ efficacy/ dosing profiles as well as older biosimilars for anti TNF-α products start getting launched in the market.

Mechanism of action

Tildrakizumab is a monoclonal antibody (MAB) designed to block IL-23 (interleukin-23), a protein that is instrumental in the immune system. *Tildrakizumab* is the second molecule after J&J's *Tremfya* (*guselkumab*) to target IL-23, specifically the p19 component of the cytokine, and to have demonstrated positive results in a plaque psoriasis trial.

Competition

Eli Lilly and Novartis have targeted the IL-17 route, while J&J and SUNP are targeting the IL-23 route. J&J's *Stelara* (*ustekinumab*, ~USD1.7bn) targets both IL-12 and IL-23 and was the leader in the psoriasis space. Now Novartis' *Cosentyx* (*secukinumab*) has taken the lead.

IL-17 space:

1. Novartis leads here with *Cosentyx*, clocking USD625mn revenue in Q4FY17. The company established clinical superiority against *Stelara* in head-to-head studies. Currently, the molecule is indicated in dermatology and rheumatology, of which only ~40% prescriptions are from dermatology.
2. Eli Lilly launched *Taltz* (*ixekizumab*) last year, an IL-17A blocker with the best PASI75 and PASI90 score, clocked USD173mn in revenue in Q4FY18.
3. Valeant launched *Siliq* (*brodalumab*), an IL-17A blocker in H2FY17 as the lowest-priced injectable. It has the best PASI100 score with 42% compared to 35% for Lilly's Taltz which is the second best.

IL-23 space:

1. J&J recently launched *Tremfya* in H2FY17 and clocked USD 47mn in revenue in Q4FY17. It has demonstrated superiority against *Humira* in phase III trials. The company guided for USD1bn per annum revenue for this product.

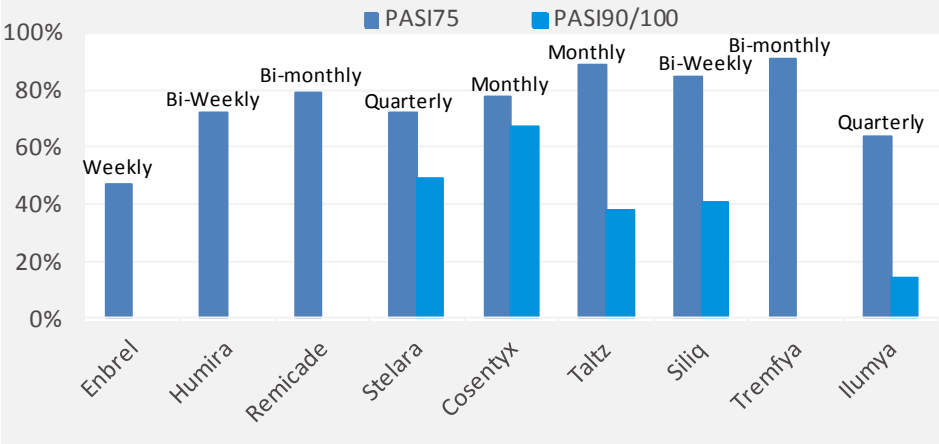
It is expected that PASI90, safety profile and dosing convenience will become critical data points in differentiating between Interleukins. SUNP believes the product's dosing advantage and its safety profile (comparable to placebo) offer an attractive proposition for the psoriasis market. Almirall's tie up in Europe further validates the product's commercial potential.

Table 14: Comparison of approved and clinical interleukins in the plaque psoriasis market

		Ilumya (tildrakizumab)			Tremfya (guselkumab)		Stelara (ustekinumab)		Cosentyx (secukinumab)		Taltz (ixekizumab)	Siliq (brodalumab)	
PRODUCT DETAILS	Manufacturer	SUN Pharmaceuticals			Janssen		Janssen		Novartis		Eli Lilly	Valeant	
	Mechanism	IL-23 blocker			IL-23 blocker		IL-12/23 blocker		IL-17A blocker		IL-17A blocker	IL-17A blocker	
	Dosage frequency	Week 0, 4 -> every 12 weeks			Dose 0, 4 weeks -> every 8 weeks		Week 0,4 -> every 12 weeks		Week 0,1,2,3,4 -> every 4 weeks		Week 0 (160mg) -> week 2,4,6,8,10,12 (80mg) -> every 4 weeks (80mg)	Dose 0,1,2 -> every 2 weeks	
EFFICACY		reSURFACE1			VOYAGE1		STUDY 1		STUDY 1		STUDY 1	STUDY 1	
	PASI 75	64%	62%	6%	91%	70%	67%	66%	71%	82%	89%	83%	
	PASI 90	35%	35%	3%	73%	41%	—	—	—	—	71%	—	
	PASI 100	14%	14%	1%	—	—	—	—	—	—	35%	42%	
	PGA 0/1	58%	59%	7%	84%	61%	59%	61%	51%	65%	82%	76%	
		reSURFACE2			VOYAGE2		STUDY 2		STUDY 2		STUDY 2	STUDY 2	
	PASI 75	61%	66%	48%	91%	70%	67%	76%	67%	76%	90%	86%	70%
	PASI 90	39%	37%	21%	83%	63%	—	—	—	—	71%	—	—
	PASI 100	12%	12%	5%	—	—	—	—	—	—	40%	44%	22%
	PGA 0/1	55%	59%	48%	74%	62%	68%	73%	51%	62%	83%	79%	61%
SAFETY PROFILE	Warnings	Nasopharyngitis, Upper respiratory tract infection			Infection, tuberculosis		Nasopharyngitis, headache, Upper respiratory tract infection		Nasopharyngitis, diarrhea, Upper respiratory tract infection		Injection site reactions, upper respiratory tract infections	BLACK BOX WARNING	
	Adverse events (AE)	44%	49%	54%	49%	46%	27%		48%		58%		
	Serious AEs	1%	2%	2%	1.9%	2.6%	0.3%		1.2%		2%		
	Contraindications	—			—		—		Hypersensitivity		Hypersensitivity	Crohn's disease	

Source: FDA, clinicaltrials.gov, Edelweiss research

Chart 6: Tildrakizumab lags competitors in terms of efficacy



Source: FDA, clinicaltrials.gov, Edelweiss research

Intellectual Property

Novel biologics are subject to 12 years of exclusivity. Patent protection that would be available for the product beyond 12 years is currently not known.

Commercial opportunity

Psoriasis affects 125mn people globally. More than one-third patients with plaque psoriasis suffer from moderate-to-severe form of the disease. The psoriasis market is USD7-8bn in size in the US alone, and biologic therapies cost ~USD25k/annum.

The total market for Psoriasis is ~USD6bn in US and growing at single digit. The interleukin category contributes ~35% of the overall market and is growing at much higher rate. Though *tildrakizumab* has been approved, we believe up take is likely to be slow till the molecule gets enrolled with the formularies. We feel SUNP is quite late in this crowded market and unless the company offers an attractive price, it will be difficult to make a mark. In best case scenario, we believe tildrakizumab can generate USD230mn peak annual revenue in its fifth year.

Table 15: Peak sales of USD230mn

tildrakizumab Revenues	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
US Market Size (Rx/ annum)	3,00,000	3,09,000	3,18,270	3,27,818	3,37,653	3,47,782	3,58,216
YoY Growth (%)		*3*	*3*	*3*	*3*	*3*	*3*
Mkt. Share, (Rx %)		0%	1%	2%	3%	3%	3%
Market share gain/ loss (bps)			60 bps	110 bps	110 bps	20 bps	0 bps
Tildrakizumab (Rx/ annum)			1,910	5,573	9,454	10,433	10,746
Pricing (USD/ Rx/ annum)			20,000	20,000	20,000	20,400	21,420
Tildrakizumab revenue (USD mn)			38	111	189	213	230
YoY Growth (%)				*192*	*70*	*13*	*8*

Source: Edelweiss research

Ophthalmology

Ophthalmology is a ~USD12bn market in the US, growing at 4-5% CAGR. With the help of incubation partner SPARC and with the acquisition of InSite Vision, SUNP has built a comprehensive ophthalmic portfolio comprising late stage assets. There are assets across most areas within ophthalmic eye diseases – cataract, glaucoma, age related macular degeneration, dry-eye, conjunctivitis, blepharitis, etc. Seciera, Xelpros, and BromSite are the key products, which can generate ~USD180mn in revenue by FY23E. At present, there is hardly any revenue coming from this therapeutic area. Total investment in this area is less than USD100mn.

Ophthalmology is a well consolidated, fast growing area

Ophthalmology is a ~USD12bn market in the US, growing at 4-5% CAGR. Owing to demographic factors and market concentration, this market is ripe for innovation and growth. The market is currently served by relatively few specialised companies as a number of players like Inspire Pharma, ISTA, Aton, Seron, among others were acquired by the likes of Alcon, Allergan and Valeant (Bausch + Lomb). Prescribers want to see the rise of players who can fill the void left by the dynamics of the previous decade, which witnessed a number of smaller companies being acquired by major players. The market continues to grow rapidly as people are living longer and eye ailments typically afflict people later in life.

Table 16: SUNP's pipeline covers US ophthalmology market substantially

Drug class	Market size (USD bn)	% of total	Sun's existing products/ pipeline/ projects	Competition
Glaucoma	1.6	22%	Xelpros	latanoprost, bimatoprost and travoprost. Other agents include beta blockers, carbonic anhydrase inhibitors, alfa agonists, miotics and combination products
Retinal Disorders				
AMD	1.9	25%	Intrexon JV	Lucentis, Eylea, Avastin (off label)
Diabetic Macular Edema	0.4	5%		
Retinal Vein Occlusion	0.4	5%		
Dry Eye	2.5	34%	Seciera, ISV-101	Restasis, Xiidra
Anti-inflammatory/ infectives/allergy	0.6	8%	Azasite, Besivance, Bromsite, Dexasite, Azasite Plus	Single agent antibiotics and steroids and combinations, NSAIDs like bromfenac.
Total	**7.3**			

Source: Edelweiss research

Portfolio breadth and depth much better than dermatology

With the help of incubation partner SPARC and a number of inorganic initiatives, SUNP has built an ophthalmic portfolio of late stage assets as well as ambitious therapies. Not only does SUNP have assets in the anterior segment like *BromSite* and *Xelpros*, but also has assets targeting the posterior segments, with the Intrexon JV, which is focused on gene therapy. There are assets across most areas within ophthalmic eye diseases – cataract, glaucoma, age related macular degeneration, dry-eye, conjunctivitis, blepharitis, etc. Thus, SUNP has a more balanced portfolio in ophthalmology versus that in dermatology.

Ophthalmologists seek more competition in the market

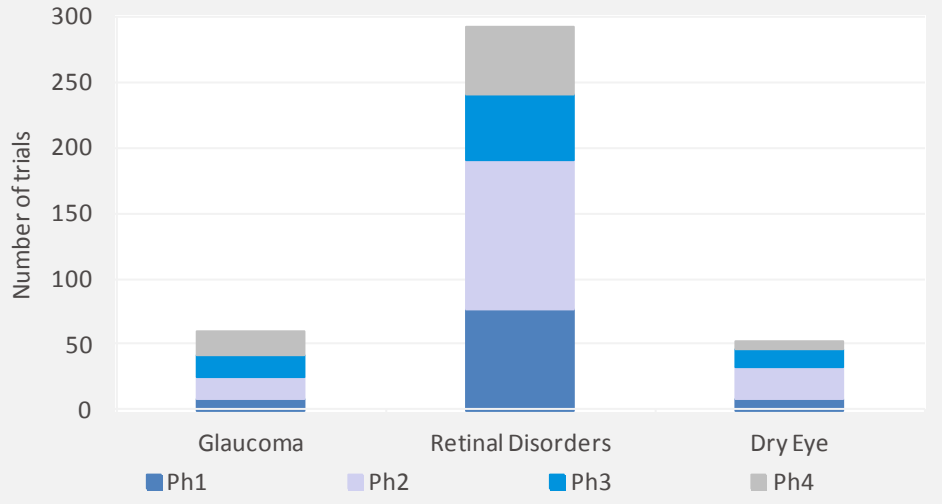
In a market dominated by large incumbents, innovation and technological advancements in ophthalmology mostly come from new entrants and smaller players. As a result, larger, established companies continuously look to acquire innovative technologies to spur growth. Practitioners, thus, continue to look for new entrants in the space beyond the three-four large players.

Table 17: Large companies have carried out significant M&A over the last few years

Acquirer Name	Target Name
Novartis	ONL Therapeutics Inc
Roche	ForSight VISION4 Inc
Novartis	Encore Vision Inc
Allergan	RetroSense Therapeutics LLC
Allergan	ForSight VISION5 Inc
Novartis	Transcend Medical Inc
Allergan	AqueSys Inc
Allergan	Oculeve Inc
Novartis	WaveTec Vision Systems Inc
Novartis	Ophthalmic division (Sensomotoric Instruments Inc)
Novartis	Rights for ocriplasmin (ThromboGenics)
Merck & Co.	Inspire Pharmaceuticals Inc
Novartis	Alcon Inc

Source: Bloomberg, Edelweiss research

Chart 7: Clinical trials across Ophthalmology



Source: FDA, clinicaltrials.gov, Edelweiss research

SUNP ophthalmic portfolio – Physicians' hyper-focused approach

SUNP's approach in its ophthalmics SBU is to be hyper focused on eye care professionals and cater to their needs by delivering 'concierge level' customer care.

Table 18: Ophthalmology business to break-even in FY21E

Ophthalmology	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
Revenue	8	17	26	54	114	168	181
Gross Profit	6	14	21	45	97	143	155
Gross Margin (%)	80	80	80	82	85	85	85
Milestone	-	7	20	7	20	20	40
Royalty payout	-	-	-	3	14	23	25
Promotional Costs	1	2	3	5	11	16	17
Employee Expenses	9	22	35	38	41	45	48
R&D	5	10	-	-	-	-	-
EBITDA	(8)	(26)	(37)	(9)	11	40	25
EBITDA margin (%)	(105)	(151)	(146)	(16)	9	24	14

Source: Edelweiss research

The commercial differentiation of DuraSite platform is that it requires only one to two doses per day to provide comparable efficacy of approved molecules.

Therapy: AzaSite (azithromycin ophthalmic solution 1%)

Status: Approved (April 2007)

Indication: Bacterial Conjunctivitis (USD 600mn market)

Mechanism: Macrolide Antibiotic

Royalty to SUNP:
9% on sales of <USD20mn
12.5% on sales of USD20-50mn
15% on sales of >USD50mn

InSite Vision Portfolio

InSite Vision acquisition

In September 2015, SUNP announced its offer to acquire InSite Vision, a company focused on developing new specialty ophthalmic products. Delivering drugs to the eye is one of the most significant challenges in ophthalmology, as the eye is extremely efficient at eliminating topically instilled drugs due to its inbuilt drainage system. Conventional eye drops have limited efficacy due to their short residence time. Up to 90% of the medication is lost in the first 15-30 seconds post administration. This means frequent dosing is required and thus, patient compliance is poor.

InSite Vision has developed the *DuraSite* and *DuraSite2* drug delivery platforms which are capable of extending the duration of drug retention, thus resulting in lower dosing frequency, and potentially enhanced efficacy. *DuraSite* is a non-toxic and biocompatible polymer that can maintain therapeutic doses of a drug on the eye's surface for up to six hours (***Link***).

Commercialised products

InSite Vision has two commercialised products based on the *DuraSite* platform, which are approved for the treatment of bacterial eye infections - *AzaSite* (azithromycin ophthalmic solution) 1%, and *Besivance* (besifloxacin ophthalmic suspension) 0.6%. While *AzaSite* is marketed through a partner (Akorn), *Besivance's* rights were sold to Bausch + Lomb in 2003 and royalty rights were sold in 2014 with covenants to return (***Link***). It also has two products in the market and two others in the pipeline. Clinical trials for *ISV-101* (***Link***) have been withdrawn as the project has been postponed.

Table 19: Acquisition of InSite Vision beefed up SUNP's specialty ophthalmic portfolio

Product	Formulation	Status	Proprietary Platform	Indication	Comment
AzaSite	azithromycin ophthalmic solution 1%	Launched August 2007	Durasite	bacterial conjunctivitis	Marketed through Akorn
BromSite (ISV-303)	bromfenac ophthalmic solution 0.075%	Launched November 2016	Durasite	postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery	Launched by Sun Pharma
DexaSite (ISV-305)	dexamethasone 0.1%	phase III (not yet started)	Durasite	non-bacterial blepharitis	No current approved drugs, Sun Ophthalmics will market
AzaSite Plus (ISV-502)	1.0% azithromycin + 0.1% dexamethasone	phase III	Durasite	eye infections	Will cannibalize DexaSite if approved
ISV-101	bromfenac ophthalmic solution	phase I/II (withdrawn)	Durasite	dry-eye disease and inflammation	Studies have been withdrawn as the project has been postponed

Source: FDA, clinicaltrials.gov, Edelweiss research

AzaSite

AzaSite is a macrolide antibiotic indicated for the treatment of bacterial conjunctivitis (USD 600mn market). It is the first ophthalmic application of *azithromycin*. *AzaSite* posted sales of ~USD20mn in 2017. In 2011, Sandoz filed an ANDA for AzaSite with paragraph-IV challenge. In ***October 2013***, district court upheld all patents protecting the product. Mylan has also filed an ANDA with paragraph-IV challenge which was settled in ***March 2015***.

Table 20: Orange book patents for AzaSite

Patent no.	Patent expiration	Patent	Claim
6239113	31-Mar-19	Topical treatment or prevention of ocular infections	Composition
6569443	31-Mar-19	Topical treatment or prevention of ocular infections	Composition
6861411	25-Nov-18	Method of treating eye infections with azithromycin	Method of use
7056893	31-Mar-19	Topical treatment for prevention of ocular infections	Composition

Source: FDA, Edelweiss research

AzaSite Plus

Therapy: AzaSite Plus (1.0% azithromycin + 0.1% dexamethasone)

Status: Phase III studies completed

Indication: blepharitis

AzaSite Plus (*ISV-502*) is a product candidate in the AzaSite family currently under development for the treatment of conditions such as blepharitis, which involves bacterial infection as well as inflammation. The drug is a fixed-dose combination of an antibiotic (1.0% *azithromycin*) and an anti-inflammatory steroid (0.1% *dexamethasone*). *AzaSite Plus* is formulated with the *DuraSite* drug delivery technology.

In 2008, it failed to reach primary endpoint in a phase III trial in patients with blepharoconjunctivitis. In this trial, *AzaSite Plus* (*azithromycin plus dexamethasone*) showed superiority over *AzaSite* (*azithromycin*) but not against *DexaSite* (*dexamethasone*). FDA requires that a combination product like *AzaSite Plus* establish superiority to each of its components in a phase III trial.

Intellectual property

A 917 patient ***clinical trial*** began in October 2011 and has ended in June 2013. The study evaluated the efficacy and safety of *AzaSite Plus* versus *dexamethasone* alone in treating patients with non-bacterial blepharitis. The study also comprised a third arm with vehicle in subjects with non-bacterial blepharitis. The primary outcome measure was clinical resolution in 15 days.

BromSite

Therapy: BromSite (bromfenac ophthalmic solution 0.075%)

Status: Approved (April 2016), Launched November 2016

Indication: Postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery

Mechanism: Nonsteroidal anti-inflammatory drug

Peak sales potential: USD45 mn

Background

BromSite (*ISV-303*, *bromfenac* ophthalmic solution 0.075%) is formulated in *DuraSite* and is SUNP's first specialty launch in ophthalmology.

Cataract pain

A cataract is a clouding of the lens in the eye which leads to a decrease in vision. Cataracts often develop slowly and can affect one or both eyes. Symptoms may include faded colours, blurry vision, haloes around light, trouble with bright lights and trouble seeing at night. Up to 40% of people undergoing cataract surgery experience mild to moderate postoperative pain and take oral pain medications.

Treatment paradigm

Early on, the symptoms may be improved with glasses. If this does not help, surgery to remove the cloudy lens and replace it with an artificial lens is the only effective treatment.

Mechanism of action

Bromfenac is a non-steroidal anti-inflammatory (NSAID) drug. The mechanism of its action is thought to be due to its ability to block prostaglandin synthesis by inhibiting cyclooxygenase 1 and 2.

Intellectual Property

Since this is a Novel Drug Delivery System (NDDS) product, it has no NCE exclusivity. However, since InSite Vision had conducted clinical trials to generate a PDUFA date, the product has a New Product Exclusivity of 3 years, which ends in April 2019. The lone composition patent listed in Orange Book expires in September 2029.

InSite Vision conducted two phase III trials for *BromSite* (268 patients each) - one focusing on pain data and the other on inflammation data. Both the trials were randomised double-masked studies to compare safety, tolerability and efficacy of *BromSite* versus placebo, delivered in *DuraSite* vehicle to patients who have previously had cataract surgery. The trials measured post-surgical ocular inflammation and pain. Statistically significant higher proportion of subjects were pain free on Day 1 post surgery (77%/82% versus 48%/62% for placebo) and were inflammation free on Day 15 post surgery (57%/38% versus 19%/22%).

Table 21: Clinical trial data for BromSite

	Visit	BromSite	Vehicle	Treatment difference (95% CI)
Study 1	Day 8	54/168 (32.1%)	7/85 (8.2%)	23.9% (14.7%, 33.1%)
	Day 15	96/168 (57.1%)	16/85 (18.8%)	38.3% (27.1%, 49.5%)
Study 2	Day 8	40/168 (23.8%)	8/85 (9.4%)	14.4% (5.5%, 23.3%)
	Day 15	64/168 (38.1%)	19/85 (22.4%)	15.7% (4.2%, 27.3%)
Proportion of Subjects who were Pain Free				
Study 1	Day 1	129/168 (76.8%)	41/85 (48.2%)	28.6% (16.2%, 40.9%)
Study 2	Day 1	138/168 (82.1%)	53/85 (62.4%)	19.8% (8.0%, 31.6%)

Source: FDA, Edelweiss research

Table 22: Orange book patents for BromSite

Patent no.	Patent expiration	Patent	Claim
8778999	03-Sep-29	Non-steroidal anti-inflammatory ophthalmic compositions	Composition

Source: FDA, Edelweiss research

Competition

The active ingredient *bromfenac* was first approved in March 2005 as *Xibrom* (ISTA Pharmaceuticals) for the treatment of inflammation following cataract surgery. This was approved for a twice daily application of the ophthalmic solution with 0.09% concentration. *Bromday* was approved in October 2010 on clinical evidence that one drop of its formulation with 0.09% concentration was safe and effective. *Prolensa* was approved in April 2013 on clinical evidence that one drop of its 0.07% concentration solution was safe and effective. Lower concentration is important as class labeled NSAIDs have concerns about corneal toxicity issues. *Prolensa* (~40% market share, marketed by Bausch + Lomb) and Nevanac (~15% market share, marketed by Alcon) are key products in the segment.

BromSite is the first NSAID approved to prevent ocular pain (prophylaxis) and treat inflammation in the eye following cataract surgery; other NSAIDs in this class are currently indicated for the treatment of inflammation and reduction of pain. Hence, it is likely to expand the market apart from taking a reasonable share of existing market.

Table 23: BromSite looks good to carve a decent market share

Indication	Brand	Molecule/ Strength/ Dosing	Label
Inflammation	Xibrom	Bromfenac 0.09% ophthal solution twice daily	Postoperative Inflammation in patients who have undergone cataract extraction
	Vexol	Rimexolone 1% ophthal suspension 4 times daily	Postoperative inflammation following ocular surgery and in the treatment of anterior uveitis
	Voltaren	Diclofenac 0.1% ophthal solution 4 times daily	Postoperative inflammation in patients who have undergone cataract extraction and for the temporary relief of pain and photophobia in patients undergoing corneal refractive surgery
	Acular	Ketorolac 0.5% ophthal solution 4 times daily	Treatment of inflammation following cataract surgery, temporary relief of ocular itching due to seasonal allergic conjuctivitis
Inflammation + Pain	Nevanac	Nepafenac 0.1% ophthal suspension 3 times daily	Pain and inflammation associated with cataract surgery
	Durezol	Difluprednate 0.05% ophthal emulsion 4 times	Inflammation and pain associated with cataract surgery
	Bromday	Bromfenac 0.09% ophthal solution once daily	Postoperative Inflammation and reduction of ocular pain in patients who have undergone cataract extraction
	Lotemax	Loteprednol Eetabonate 0.5% ophthal ointment 4 times daily	Postoperative Inflammation and pain following ocular surgery
	Ilevro	Nepafenac 0.3% ophthal suspension once daily	Pain and inflammation associated with cataract surgery
	Prolensa	Bromfenac 0.07% ophthal solution once daily	Postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery
Prophylaxis (Pain + Inflammation)	Bromsite	Bromfenac 0.075% ophthal solution once daily	Prevent pain and treat inflammation in the eye for patients undergoing cataract surgery

Commercial opportunity

The US NSAID Ophthalmic market is ~USD400mn in sales and about 4mn prescriptions. *BromSite's* differentiated label bodes well for commercial success.

Table 24: Peak sales of ~USD45mn

Bromsite Revenues	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
US Market Size (mn Rx/ annum)	4	4	4	4	5	5	5
YoY Growth (%)		*3.0*	*3.0*	*3.0*	*3.0*	*3.0*	*3.0*
Mkt. Share, (Rx %)	2.0%	4.0%	5.5%	7.0%	7.0%	7.0%	7.0%
Market share gain/ loss (bps)		200 bps	150 bps	150 bps	0 bps	0 bps	0 bps
Bromsite ('000s Rx/ annum)	80	165	233	306	315	325	334
Pricing (USD/ Rx/ annum)	100	105	110	116	122	128	134
Bromsite revenue (USD mn)	8	17	26	35	38	41	45
YoY Growth (%)		*116.3*	*48.7*	*37.6*	*8.2*	*8.1*	*8.2*

Source: Edelweiss research

Therapy: DexaSite (0.1% dexamethasone)

Status: Phase III

Indication: Non-bacterial Blepharitis and Ocular Inflammation

Mechanism: Glucocorticoid

DexaSite

Background

Following *BromSite's* approval, *DexaSite* (*ISV-305*) is the most advanced clinical asset in the pipeline acquired from InSite Vision. Phase III trial for *DexaSite* in patients with ocular inflammation (blepharitis) is expected to start.

Blepharitis

Blepharitis (from the Greek word blepheron, meaning eyelid) is an inflammation of eyelids, particularly eyelid margins where the eyelashes grow. It's a common disorder, which results from a malfunction of oil glands at the base of the eyelashes. This malfunction can lead to growth of bacteria, which can irritate and inflame eyelids. An eyelid with blepharitis may become itchy and appear red and swollen with scaly, greasy debris along the lid margin.

Treatment paradigm

Blepharitis can be a chronic condition that is difficult to treat. There are no approved drugs and current standard of care includes lid hygiene products, anti-inflammatories, antibiotics, and combinations of anti-inflammatory and antibiotic agents. Topical antibiotics (like *chloramphenicol* ointment) have been effective in providing symptomatic relief and clearing bacteria in anterior blepharitis. Topical steroids provide symptomatic relief but are ineffective in clearing bacteria from eyelids.

Mechanism of action

Glucocorticoids are a class of corticosteroids, which are a class of steroid hormones. They are corticosteroids that bind to the glucocorticoid receptor, which is present in almost every vertebrate animal cell. They are part of the feedback mechanism in the immune system, which reduces certain aspects of immune function, such as reduction of inflammation.

Intellectual property

A 550 patient ***clinical trial*** was expected to begin in February 2018 and end by August 2019. However, the trial has not yet started recruiting patients. The trial evaluates efficacy and safety of *DexaSite* versus vehicle, in subjects with non-bacterial blepharitis. The primary outcome measure is clinical resolution in 15 days.

Commercial opportunity

Blepharitis is a significant unmet medical need in ophthalmology. It is one of the most common conditions encountered in clinical practice with 37% and 47% of patients seen by ophthalmologists and optometrists, respectively, presenting with signs of the disease. There is currently no FDA-approved drug specifically for the treatment of blepharitis. It is estimated that there are potentially more than 2.5mn blepharitis-related prescriptions written per year in the US, in addition to the use of non-prescription and non-pharmaceutical treatments. The Center for Disease Control (CDC) estimates the number of blepharitis sufferers at ~8mn. Senju Pharmaceuticals is developing *SJP-0118* for bacterial conjunctivitis, but has not yet started any clinical trials in US.

Therapy: Seciera (cyclosporine 0.09% topical solution)

Status: Successful phase III reported (Jan 17)

Indication: Keratoconjunctivitis Sicca (dry eye syndrome)

Mechanism: Immunosuppressant

Peak sales potential: USD80mn

*Dec'17: NDA accepted by FDA (**Link**)*

Seciera (renamed OTX-101)

Background

Seciera is SUNP's patented nanomicellar cyclosporine 0.09% solution for topical ophthalmic administration. It was bought with Ocular Technologies from Auven Therapeutics for an upfront payment of USD40mn plus contingent development and sales milestones, and tiered royalties. Recently, SUNP reported positive results for it from phase III trial for treatment of dry-eye syndrome. *Cyclosporine* is also the active ingredient in Allergan's *Restasis*, one of the two prescription products currently approved for dry eye patients.

Dry eye disease

Dry eye disease occurs when the eye does not produce sufficient tears, or when the tears evaporate too quickly. While causes of dry eye may vary, it is frequently associated with inflammation of the surface of the eye surface, the lacrimal gland, or the conjunctiva. A potentially chronic condition that can occur at any age, dry-eye disease is most prevalent among the elderly. Dry eye syndrome is generally characterised by debilitating symptoms that, if left untreated, can result in blurred vision or even vision loss.

Treatment paradigm

Artificial tears are the usual first line treatment. Artificial tears are synthetic lubricants, characterised by hypotonic or isotonic buffered solutions containing electrolytes, surfactants and several types of viscosity agents. Inflammation occurring in response to tears film hypertonicity can be suppressed by mild topical steroids or with topical immunosuppressants such as *Restasis*. Shire's *Xiidra* (*lifitegrast*) is a new drug that was approved by the FDA for the treatment of the condition in 2016.

Competition

Allergan's *Restasis* is the top selling product in the therapy, and posted US sales of ~USD1.4bn in CY17. Recently approved *Xiidra* is now being prescribed to nearly half of new patients and clocked ~USD260mn sales in CY17. In addition, a number of clinical trials are currently underway to tap this fast growing market.

Table 25: Open Ph-III/IV trials for dry eye/keratoconjuctivitis sicca

Product	Sponsor	Trial Identifier	Study Completion date	Status
Abatacept	Bristol-Myers Squibb	NCT02915159	Nov-19	Active, not recruiting
RGN-259	ReGenTree	NCT02974907	Nov-17	Active, not recruiting
KCT-0809	Kissei Pharmaceutical	NCT02503189 NCT02503163	Mar-18	Completed
OmegaD oral softgels	OmegaD	NCT02980224	May-17	Completed
Omega 3 (OM3) tear	Allergan	NCT02871440	Oct-17	Active, not recruiting
OTX-101	Sun Pharma	NCT02688556 NCT02845674	Dec-16	Completed
KPI-121	Kala Pharmaceuticals	NCT02813265 NCT02819284	Sep-17	Completed
CKD-350 (Xenobella)	Chong Kun Dang Pharmaceutical	NCT02777723	Sep-16	Recruiting
Tavilermide (MIM-D3)	Mimetogen Pharmaceuticals USA	NCT01960010 NCT02634853	May-17	Completed
Ikervis	Santen	NCT03237936	Jul-18	Recruiting (phase IV)

Source: FDA, clinicaltrials.gov, Edelweiss research

Mechanism of action

The most important effect of cyclosporine is to lower the activity of T cells and their immune response.

Intellectual property

Seciera has successfully reported data from a phase III trial that showed efficacy within 12 weeks. *Seciera* demonstrated statistical improvement in the primary end-point, Schirmer's score (a measure of tear production), at the end of 12 weeks, which was better than *Restasis*, the other cyclosporine approved for the same indication. Since *Seciera's* approval will entail this clinical trial, it will be eligible to receive three years of new product exclusivity.

Table 26: Clinical trial data for Seciera

Trial	Phase/Status	Start Date	Enrollment	Completion Date	Description
NCT02254265	III/completed	Sep-14	455	May-15	Safety and efficacy of 2 different dose concentrations of OTX-101 administered twice a day
NCT02688556	III/completed	Feb-16	745	Dec-16	Double masked, placebo controlled study of safety and efficacy of 0.09% OTX-101
NCT02845674	III/completed	29-Jul-16	165	15-Aug-17	Safety extension enrolling subjects participating in Study OTX-101-2016-001

Source: FDA, clinicaltrials.gov, Edelweiss research

Commercial opportunity

Dry eye affects ~20mn people in the US and is one of most common reasons that people visit their eye doctor. It is often a progressive disease that remains a significant underserved medical need. An effective, well-tolerated product with relatively rapid onset of action would address the large underserved segment of the dry eye population who do not respond to available therapies. *Seciera* has the potential to be a best in class product and the first treatment for dry-eye syndrome that addresses tear production and inflammation of the ocular surface.

Restasis/*Restasis Multidose* labels claim statistical improvements in six months, and hence *Seciera* could have a label advantage. The addressable market size is growing rapidly and is expected to reach ~USD5bn by 2020. During an investor interaction, SUNP indicated that it expects *Seciera* to expand the Rx market rather than just compete with existing products.

Table 27: Peak sales of ~USD80mn

Seciera Revenues	FY17	FY18	FY19E	FY20E	FY21E	FY22E	FY23E
US Market Size (mn Rx/ annum)	20	21	21	22	23	23	24
YoY Growth (%)		*3.0*	*3.0*	*3.0*	*3.0*	*3.0*	*3.0*
Mkt. Share, (Rx %)				0%	0%	0%	0%
Market share gain/ loss (bps)				5 bps	15 bps	10 bps	0 bps
Seciera ('000s Rx/ annum)				11	45	70	72
Pricing (USD/ Rx/ annum)				1,000	1,050	1,103	1,158
Seciera revenue (USD mn)				11	47	77	83
YoY Growth (%)					*332.6*	*62.2*	*8.2*

Source: Edelweiss research

Therapy: Xelpros (BAK-free latanoprost formulation)

Status: Under review (approval held for SUNP's Halol resolution)

Indication: Glaucoma

Mechanism: Prostaglandin analogues

Peak sales potential: USD50 mn

Upcoming Newsflow: Halol resolution and subsequent final approval and launch (Plan A), or approval from alternate site (Plan B)

Xelpros

Background

Xelpros is a SPARC (Sun Pharma Advanced Research Company) product out licensed to SUNP for manufacturing and commercialisation in 2015. In a BSE filing dated December 2016, SPARC updated that the company had received a complete response letter citing issues with the regulatory compliance status of SUNP's Halol plant. SPARC believes Halol's resolution offers the shortest path to approval for *Xelpros*. It has also explored site transfer, and with the recent delays in Halol clearance, company may go ahead with this approach. The site transfer will require additional stability data and bridging bioequivalence studies.

Glaucoma

Glaucoma is a group of eye diseases which result in damage to the optic nerve and vision loss. It's often linked to a build-up of pressure inside the eye. This happens when the liquid in the front part of the eye does not circulate the way it should. Normally, the fluid, called aqueous humor, flows out of the eye through a mesh-like channel. If this channel gets blocked, the liquid builds up and causes glaucoma. The increased pressure, called intraocular pressure, can damage the optic nerve, which transmits images to brain. If the damage continues, glaucoma can lead to permanent vision loss. Without treatment, glaucoma can cause total permanent blindness within a few years.

Treatment paradigm

Prostaglandin analogs (*latanoprost*, *bimatoprost* and *travoprost*) increase outflow of aqueous humor and make up ~55% of prescriptions. Other agents include beta blockers, carbonic anhydrase inhibitors, alfa agonists, miotics and combination products.

Proprietary technology summary

Benzalkonium Chloride (BAK) is a preservative which is commonly used in eye drops. ~10-16% patients on *Xalatan* and other BAK containing products develop Ocular Surface Disease symptoms over long period of administration. *Xelpros* ophthalmic emulsion is a preservative (BAK) free, once a day formulation of *latanoprost*, which utilises a novel Swollen Micelle Microemulsion technology. This platform technology has been developed by SPARC, for dissolving ophthalmic drugs with limited or no solubility. This technology does not require the use of quaternary ammonium preservative/surfactant like BAK. Unlike conventional glaucoma eye drops, *latanoprost* BAK-free does not cause or aggravate Ocular Surface Disease on chronic use.

Mechanism of action

Latanoprost is a prostanoid selective FP receptor agonist that is believed to reduce the intraocular pressure by increasing the outflow of aqueous humor. Studies in animals and man suggest that the main mechanism of action is increased uveoscleral outflow.

Competition

Glaucoma is the largest segment in ophthalmic market with >2.2mn diagnosed patients (~22mn prescriptions). The product sales in US are ~USD2bn. Prostaglandins lead the market with ~55% share, of which *latanoprost* is the largest selling molecule with ~65% volume share (12mn prescriptions).

Intellectual property

Two phase III clinical trials supported the NDA filing. The pivotal data was generated with a trial involving 590 patients in efficacy and safety study (***Link***, ***Link***). *Xelpros* could meet the non-inferiority criteria of 1.5 mmHg at all time intervals and 1mmof Hg at four time intervals. The reduction in pressure from baseline for *Xelpros* was approximately 6 to 7 mm of Hg at all twelve time intervals, comparable to *Xalatan*. Since *Xelpros'* approval will entail this clinical trial, it will be eligible to receive 3 years of new product exclusivity.

Commercial opportunity

Prostaglandin analogues for glaucoma comprise USD1.4bn market. Typically drugs like *Xelpros* are put in a Tier-III reimbursement program. Peak sales will be reached in the fourth or fifth year, because sales force will need to drive prescriptions and to get managed care access and also have the product in all the formulary (that usually takes around two years) so that the generated prescriptions get reimbursed.

Table 28: Peak sales of ~USD50mn

Xelpros Revenues	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
US Market Size (mn Rx/ annum)	22	23	23	24	25	26	26
YoY Growth (%)		*3.0*	*3.0*	*3.0*	*3.0*	*3.0*	*3.0*
Latanoprost market share (Rx %)	55%	55%	55%	54%	54%	54%	54%
Xelpros market Share, (Rx %)	0%	0%	0%	0%	1%	2%	2%
Market share gain/ loss (bps)				30 bps	70 bps	60 bps	0 bps
Xelpros ('000s Rx/ annum)		-	-	72	248	408	420
Pricing (USD/ Rx/ annum)		100	105	110	116	122	128
Xelpros revenue (USD mn)		-	-	8	29	50	54
YoY Growth (%)					*261*	*73*	*8*

Source: Edelweiss research

Intrexon (S & I Ophthalmic)

Therapy: Details not available yet

Status: IND filed (end of 2016)

Indication: Wet AMD

Mechanism: Gene therapy

Upcoming Newsflow: IND filing for wet AMD

Background

In September 2013, Intrexon formed a joint-venture with SUNP, called S&I Ophthalmic, to develop controllable gene-based therapies for the treatment of ocular diseases that cause partial or total blindness in millions of people worldwide. These gene-based therapies would utilize the RheoSwitch platform which may address limitation of current approaches by enabling patients to receive a targeted biologic therapy without enduring a lifetime of injections. Initial targets include dry age-related macular degeneration (AMD), glaucoma and retinitis pigmentosa. The companies intend to further expand the future pipeline of targeted ocular diseases to potentially include wet AMD, macular edema, non-infectious uveitis and diabetic retinopathy.

Beginning on the seventh anniversary of the effective date of agreement, and upon second anniversary thereafter, Intrexon, as well as SUNP may make a cash offer to purchase all of the other party's interest in the JV. Upon receipt of such an offer, the other party must either agree to tender its interests at the offered price or submit a counteroffer at a price higher than the original offer. Such offer and counteroffer may continue until one party agrees to the other's price.

Wet AMD

Macular degeneration, also known as age-related macular degeneration (AMD or ARMD), is a medical condition which may result in blurred or no vision in the center of the visual field. Age-related macular degeneration (AMD) is the leading cause of blindness in the US, with more than 1.6mn people affected. Wet AMD is a more severe progression of AMD, affecting 10-15% of patients with AMD. It however accounts for 90% of the severe vision loss caused by macular degeneration. The "wet" form of advanced AMD, causes vision loss due to abnormal blood vessel growth.

Proprietary technology summary: RheoSwitch platform

Through an Exclusive Channel Collaboration (ECC), the JV will have access to Intrexon's full suite of proprietary synthetic biology technologies, including the RheoSwitch Therapeutic System (RTS) platform. A potential downside of gene therapy is that, in most cases, it will not be possible to end or turn off the therapy once it is delivered into the eye. RTS offers transcriptional control of a wide variety of therapeutic genes by regulating the timing and dose of an oral activator ligand.

Treatment paradigm

Lucentis (*ranibizumab*) and *Eylea* (*aflibercept*) are approved for wet AMD. However, *Avastin* (*bevacizumab*) is also used off label.

Commercial opportunity

Preclinical studies have shown a positive reduction in laser-induced CNV area of ~50%. Gene therapy offers a potential long-term solution to treat wet AMD with one injection, and there is a strong rationale for combination therapy to become the standard of care in wet AMD. There are a few early stage clinical trials that are evaluating gene therapy in wet AMD by companies like ***Sanofi*** and ***Avalanche Biotechnologies***.

Neurology

Therapy: Elepsia XR (Levetiracetam extended release formulation)

Status: Under review (approval held for SUNP's Halol resolution)

Indication: Epilepsy

Mechanism: Anti-convulsant

Peak sales potential: USD25 mn

Upcoming Newsflow: Halol resolution and subsequent final approval and launch (Plan A), or approval from alternate site (Plan B)

Elepsia XR

Background

Elepsia XR (*levetiracetam* extended-release) is a SPARC (Sun Pharma Advanced Research Company) product out licensed to SUNP for manufacturing and commercialisation. While *Elepsia XR* was granted final approval in 2015, it was rescinded by FDA citing issues with the regulatory compliance status of SUNP's Halol plant. SPARC believes, Halol's resolution offers the shortest path to approval for *Elepsia XR*. It has also explored site transfer, and with the recent delays in Halol clearance, company may go ahead with this approach. The site transfer will require additional stability data and bridging bioequivalence studies.

Epilepsy

Epilepsy is a group of neurological diseases characterised by epileptic seizures. Epileptic seizures are episodes that can vary from brief and nearly undetectable to long periods of vigorous shaking. These episodes can result in physical injuries including occasionally broken bones. In epilepsy, seizures tend to recur, and have no immediate underlying cause.

Proprietary technology summary:

Usually, controlled release dosage forms of very high concentrations and high solubility products are either, very large and difficult to swallow, or tend to release its entire drug at the same time (dose dumping). A combination of instant and long-term release is also tough to achieve in the same tablet. With SPARC's proprietary Wrap Matrix technology, a multi-layered matrix-based tablet of such drugs offers controlled release with just once a day dosing without creating too bulky a tablet for products requiring a large daily dose.

Treatment paradigm

The mainstay treatment of epilepsy is anticonvulsant medications, possibly for the person's entire life. The choice of anticonvulsant is based on seizure type, epilepsy syndrome, other medications used, other health problems, and the person's age and lifestyle.

Mechanism of action

The precise mechanism by which *levetiracetam* exerts its antiepileptic effect is unknown. The antiepileptic activity of *levetiracetam* was assessed in a number of animal models of epileptic seizures. *Levetiracetam* did not inhibit single seizures induced by maximal stimulation with electrical current or different chemoconvulsants and showed only minimal activity in sub maximal stimulation and in threshold tests. Protection was observed, however, against secondarily generalised activity from focal seizures induced by pilocarpine and kainic acid, two chemoconvulsants that induce seizures that mimic some features of human complex partial seizures with secondary generalisation. *Levetiracetam* also displayed inhibitory properties in the kindling model in rats, another model of human complex partial seizures, both during kindling development and in the fully kindled state. The predictive value of these animal models for specific types of human epilepsy is uncertain.

Competition

UCB Pharma received approval for *Briviact* (*brivaracetam*) in May 2016. However, *levetiracetam* remains front-line treatment in the management of epilepsy due to physicians' acceptance of a long term track record. There will be gradual conversion from *levetiracetam* to *brivaracetam* as it has a dosing advantage, but it will need to be proven in clinical setting that it works better than available treatment options for physicians.

Intellectual property

Since *Elepsia XR's* approval will not entail any clinical trials, it will be not be eligible to receive three years of new product exclusivity.

Commercial opportunity

For a majority of epilepsy patients, pill burden remains high. Over 80% patients on levetiracetam require dose exceeding 1000mg/day. Over 50% patients need more than six pills per day. Extended release, once daily dosing and reducing the pill burden are seen as major advantages by neurologists. *Elepsia XR* will provide a new therapeutic option to patients and physicians to reduce pill burden and help improve patient compliance. Around 720mn tablets were sold last year and the market is expanding by 10-11%. This product will take market share largely from <1,000 mg IR tablets.

Chart 8: Levetiracetam use by daily dosage

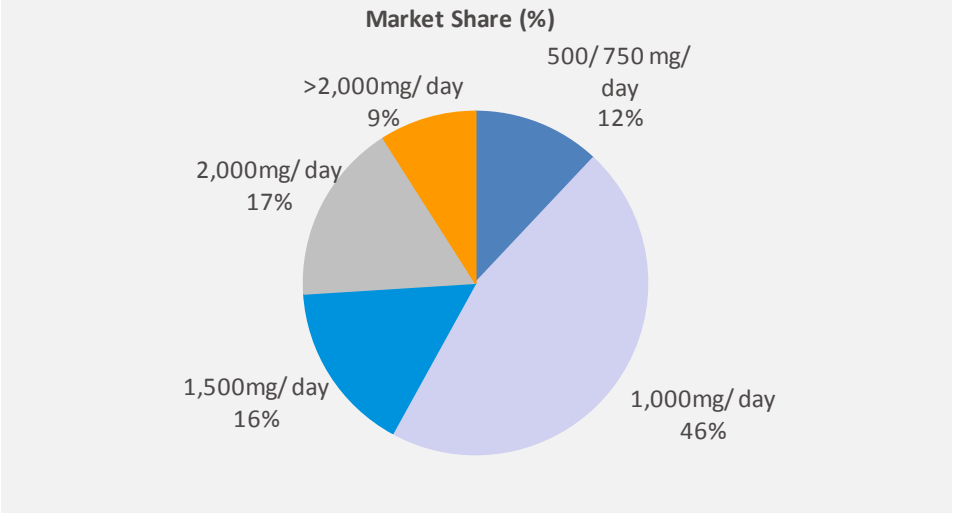


Table 29: Peak sales of ~USD25mn

Elepsia XR Revenues	FY17	FY18E	FY19E	FY20E	FY21E	FY22E	FY23E
US Market Size (mn Rx/ annum)	720	742	764	787	810	835	860
YoY Growth (%)		*3.0*	*3.0*	*3.0*	*3.0*	*3.0*	*3.0*
Levetiracetam <1,000mg market share (Rx %)	12.0%	12.0%	12.0%	11.5%	11.5%	11.5%	11.5%
Elepsia XR market Share, (Rx %)			0%	1%	1%	1%	1%
Market share gain/ loss (bps)				50 bps	25 bps	10 bps	0 bps
Elepsia XR ('000s Rx/ annum)				3,934	6,078	7,095	7,308
Pricing (USD/ Rx/ annum)			3	3	3	3	3
Elepsia XR revenue (USD mn)				12	19	23	25
YoY Growth (%)					*59.1*	*20.2*	*6.1*

Source: Edelweiss research

Therapy: MM-II

Status: Phase II (November 2012)

Indication: Symptomatic relief of mild-to-moderate osteoarthritis pain.

Mechanism: Novel liposomal non-opiod

Upcoming Newsflow: Phase III trial announcement

MM-II

Background

SUNP entered into an exclusive deal with Israel-based Moebius Medical to further develop *MM-II*, a novel pharmaceutical candidate for the treatment of pain in osteoarthritis. The company will fund further development of Moebius Medical's lead product, *MM-II*, and undertake its global commercialisation. Moebius Medical will conduct requisite pre-clinical studies, and will assume responsibility for product development and manufacturing through the end of phase II studies. SUNP will assume responsibility for further clinical studies, regulatory submissions and product commercialisation. Moebius Medical will receive an upfront payment, development-based and sales-based milestone payments, and tiered royalties on sales from SUNP.

Osteoarthritis

Osteoarthritis is one of the most common chronic health conditions and a leading cause of pain and disability among adults. It is the most common form of joint disease, characterised by articular cartilage degradation with an accompanying periarticular bone response and a synovial membrane inflammation. Clinical manifestations of osteoarthritis in the knee include pain in & around the joint, stiffness of the joint after rest, crepitus on motion and limited joint. *MM-II* medical device was designed to reduce wear and lower friction in knees of osteoarthritis patients by creating a lubricating layer onto cartilage surfaces upon injection.

Treatment paradigm

Lifestyle modification (such as weight loss and exercise) and analgesics are the mainstays of treatment. Acetaminophen (paracetamol) is recommended first line with NSAIDs being used as add on therapy only if pain relief is not sufficient. Hyaluronic acid injection is used in patients who have already been treated with pain relievers and other treatments that did not work well.

Mechanism of action

MM-II leverages the physical properties of proprietary liposomes by facilitating cartilage surface gliding to lubricate the joint and reduce friction and wear, thus leading to joint pain reduction.

Competition

A number of hyaluronic acid injection brands are sold in the US – *Euflexxa*, *Gel-One*, *Hyalgan*, *Hyalgan LL*, *Monovisc*, *Orthovisc*, *Supartz* and *Supartz FX*. There are a large number of therapies under clinical evaluation for osteoarthritis at the moment. ***Clinicaltrials.gov*** shows 89 phase II/III knee osteoarthritis trials, which are either open or ongoing.

Intellectual Property

A first-in-man, randomised, controlled, double-blinded study was conducted in mild to moderate symptomatic knee OA patients comparing *MM-II* to *hyaluronic acid* (HA), the standard of care (***Link***). A single injection of *MM-II* showed faster and better improvement in pain and activity than *Durolane* (*hyaluronic acid*). Daily acetaminophen intake was lower in the MM-II group, with a reduction of more than 50% in the number of days and total dose of rescue medication consumption seen following *MM-II* administration, compared with HA injection. Intra-articular injections of *MM-II* were found to be safe and effective. The pain-

reduction action was more rapid and sustained up to three months compared with HA. Larger randomised controlled trials are needed to confirm these encouraging results.

Chart 9: Mean relative % change in knee pain (WOMAC A) over time

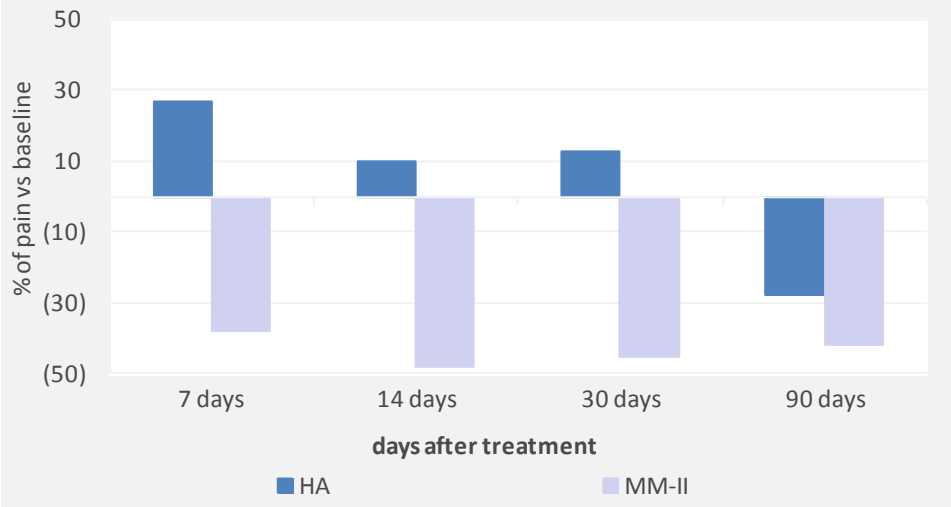
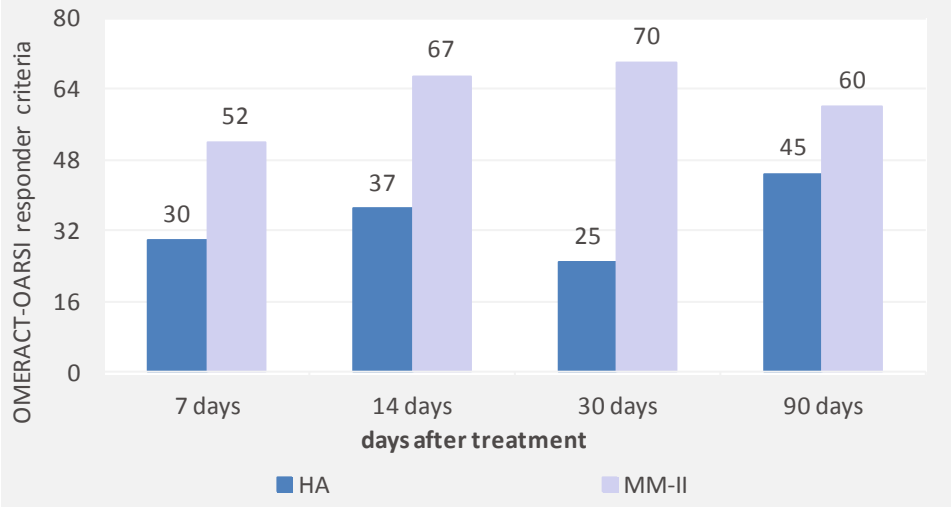


Chart 10: Percent of Participants Responding to Treatment



Source: FDA, Edelweiss Research

Commercial opportunity

Global estimates reveal that more than 100mn people are affected by osteoarthritis. More than 20mn people in the US suffer from knee osteoarthritis. Global market for products used for symptomatic relief of knee osteoarthritis pain (like intra-articular *hylauronic acid*) is about USD 2bn with 6.5% CAGR. Of this, US alone accounts for ~USD900mn comprising *hyaluronic acid* injections.

Neurology + Oncology

Therapy: glutamate-oxaloacetate transaminase

Status: Animal studies

Indication: Brain stroke, Brain cancer

Mechanism: Blood glutamate scavenger

Brain therapies research collaboration

Background

In December 2015, SUNP entered into a tripartite research and option agreement with Israel-based Weizmann Institute of Science and Spain's Health Research Institute of Santiago de Compostela (IDIS) to develop *glutamate-oxaloacetate transaminase (GOT)* for the treatment of neurological diseases like brain stroke; as well as glioblastoma, a lethal brain cancer. Product will bring about a better quality of life for the patient by enabling doctors to make crucial decisions and offer immediate treatment in high-risk medical emergencies.

Brain stroke

A stroke occurs when the blood supply to the brain is interrupted or reduced. This deprives the brain of oxygen and nutrients, which can cause brain cells to die. A stroke may be caused by a blocked artery (ischemic stroke) or the leaking or bursting of a blood vessel (hemorrhagic stroke). Currently the major challenge in treating neurological diseases like stroke is the need for a definitive diagnosis of the type of stroke: Until physicians have verified whether the stroke is ischemic or hemorrhagic, specific treatment cannot be started. However, the initial few hours are critical, from the prognostic point of view. The delay between the occurrence of the stroke and the diagnosis could mean a life and death scenario, or lifelong disability for the patient. If successful, *GOT* could enable the immediate administration of the treatment by a paramedic while a patient is in transit to the hospital. The enzyme could make a significant difference to the patient, as it can prevent the significant loss of brain function and avoid the debilitating consequences of stroke, while promising an improved quality of life for the patient. Thus the enzyme is expected to overcome this unmet gap in current medical treatments.

Mechanism of action

Research has shown that Ischemic stroke patients' chance of recovery may be significantly boosted by decreasing their blood glutamate levels to about 50% of the normal values (from ~200 µmol/L to ~100 µmol/L)) by bolus intravenous administration of *GOT*, that is, to a level of 150 U/L, which is around 3 times the normal range of *GOT* in clinical labs. This should bring about a decrease in glutamate in the extracellular fluids within and surrounding the infarcted brain region. By adding a single test for *glutamate/GOT* in the routine clinical lab analysis, physicians could gain a new tool for diagnosing stroke and regulating its treatment. Some of the research also shows the therapeutic effectiveness of blood glutamate scavenging in experimental models of brain cancer, and in experimental models of sporadic and familial amyotrophic lateral sclerosis.

Oncology

Therapy: p50 + KPC1 proteins

Status: Early stage

Indication: Cancers in digestive system and bone

Mechanism: Ubiquitination

Technion research collaboration

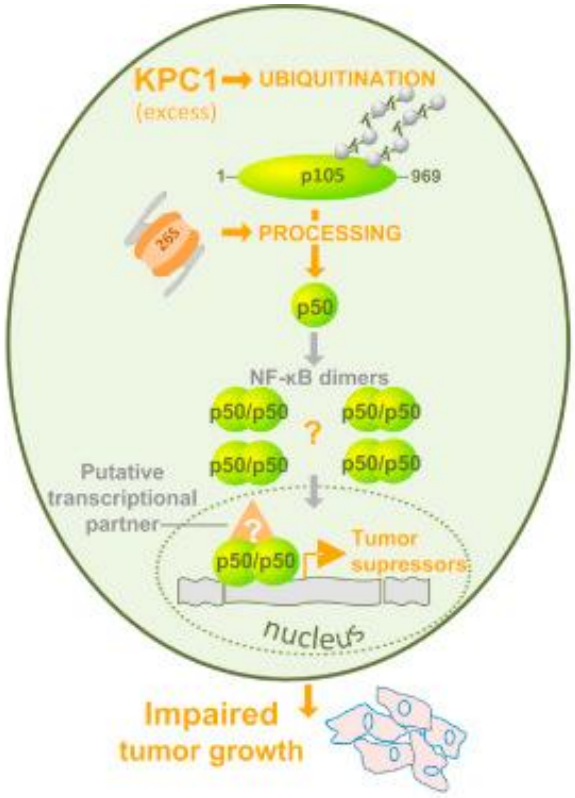
Background

In April 2015, SUNP and the Technion – Israel institute of technology announced exclusive worldwide research and license agreement aimed at the joint development of novel oncology drugs. Under the agreement, researchers from the Technion and Sun will conduct studies on how high concentrations of two proteins can protect tissue from tumors. The first is p50, which is produced in many body cells and is recognised as a factor that encourages inflammation – and which has been proven to be a factor in numerous cancer studies. p50 is produced by another protein called NF-κB, which was discovered nearly 30 years ago and has been linked in numerous studies to the development of malignancies in the prostate, breast, lungs, head and neck, colon, brain, and more. The second protein is called KPC1, and it, too, is involved in the production of p50. A study has revealed that in high concentrations, p50 is capable of having the opposite effect – of suppressing cancerous cells.

Mechanism of action

Ubiquitin is a small regulatory protein that has been found in almost all tissues. The addition of ubiquitin to a substrate protein is called ubiquitination or ubiquitylation. Ubiquitin is the key factor in deciding when and how a cell should regenerate. It attaches to other proteins, and marks them for destruction or degradation. Imbalance in ubiquitin can cause cancer and neuro-degenerative disorders.

Fig. 3: Mechanism of action



Source: Company

Table 30: Change in estimates

	FY18E			FY19E			FY20E		
P&L	**New**	**Old**	***Change %***	**New**	**Old**	***Change %***	**New**	**Old**	***Change %***
Net revenues	2,59,893	2,60,075	*(0.1)*	2,81,821	2,87,494	*(2.0)*	3,11,860	3,18,034	*(1.9)*
EBITDA	52,335	59,089	*(11.4)*	63,827	73,095	*(12.7)*	77,801	88,126	*(11.7)*
EBIT	38,201	45,977	*(16.9)*	50,656	59,924	*(15.5)*	64,270	74,596	*(13.8)*
PBT	24,871	38,566	*(35.5)*	52,121	63,692	*(18.2)*	67,523	81,108	*(16.7)*
Adjusted PAT	28,743	36,333	*(20.9)*	39,145	48,633	*(19.5)*	51,194	60,711	*(15.7)*
Adjusted EPS	11.9	15.1	*(20.9)*	16.3	20.2	*(19.5)*	21.3	25.2	*(15.7)*

Source: Company, Edelweiss research

Company Description

Sun Pharmaceuticals (SUNP) is the largest Indian Pharma company with an impressive track record of organic and inorganic growth. Various US acquisitions augment SUNP's pipeline with differentiated products, where SUNP has turned around business in a highly profitable manner – Taro/ TDPL/Natco's brands/etc. It has one of the highest return ratios amongst global peers.

Chart 11: SUNP revenue by business segment (FY18E)

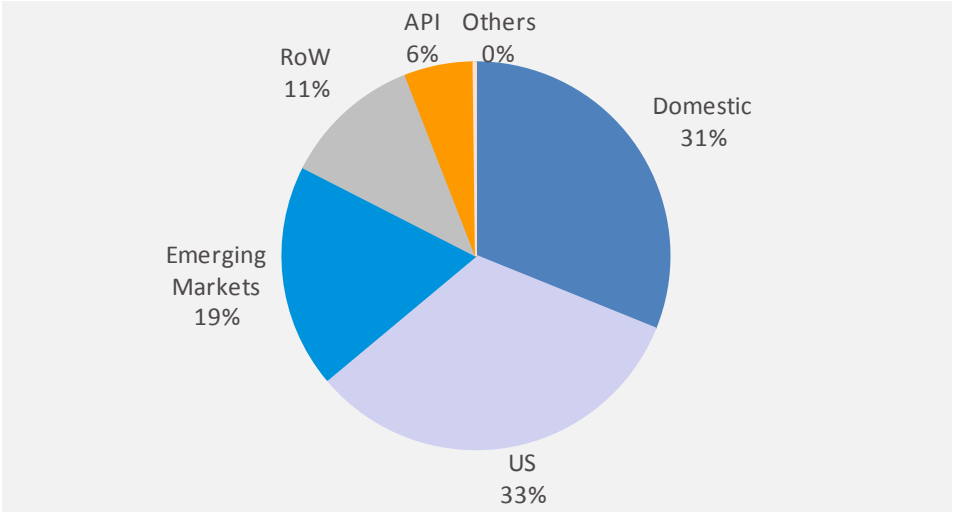


Chart 12: Revenue stagnant for the last 4 years

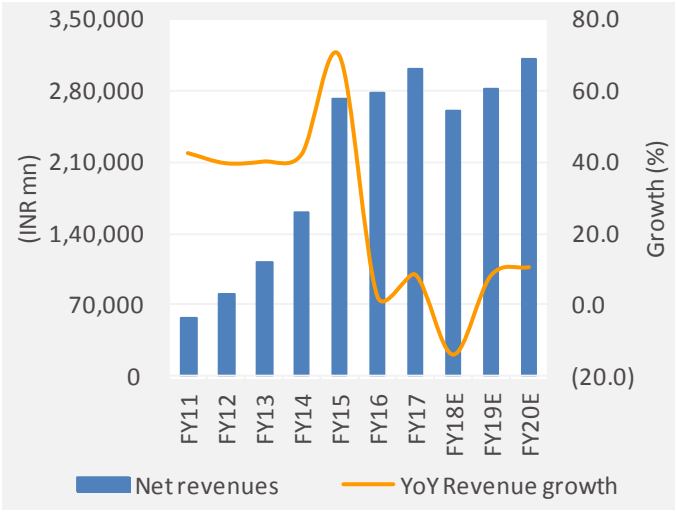
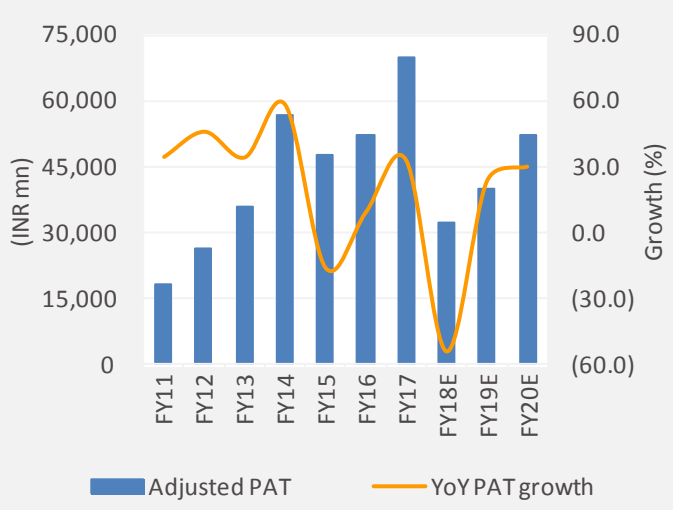


Chart 13: Profit has declined by ~60%



Source: Company, Edelweiss research

Investment Theme

Challenging macro environment, regulatory woes and the endeavour to create a specialty business in the US are exerting significant pressure on the business. We believe the two growth triggers from here are: 1) up take for tildrakizumab and Seciera in FY19; 2) clearance of Halol facility. We believe the risk-reward is unfavourable.

Key Risks

1) Better than expected pick up in tildrakizumab; 2) Competition failing to take-off in Levulan and Absorica; 3) Surprise launch of product not considered in our forecasts.

Financial Statements

Key Assumptions

Year to March	FY17	FY18	FY19E	FY20E
Macro				
GDP(Y-o-Y %)	6.6	6.5	7.1	7.6
Inflation (Avg)	4.5	3.8	4.5	5.0
Repo rate (exit rate)	6.3	6.0	6.0	6.5
USD/INR (Avg)	67.1	64.5	65.0	66.0
Sector				
IPM growth (Y-o-Y) %	12.0	12.0	12.0	12.0
Company				
India sales (INR mn)	77,491	80,921	91,232	104,745
US generics (USD mn)	2,051	1,323	1,352	1,467
Growth (YoY)%	(0.7)	(35.5)	2.2	8.5
EBITDA margins (%)	31.9	21.6	22.7	24.9
R&D (% of sales)	6.7	7.8	8.0	8.0
USD/INR (Avg)	67.1	64.5	65.0	66.0
Capex (INR mn)	35,904	10,000	10,000	8,000
Net debt to equity (x)	(0.2)	(0.3)	(0.3)	(0.4)

Income statement (INR mn)

Year to March	FY17	FY18	FY19E	FY20E
Gross revenues	302,642	260,075	281,644	311,534
Profit Before Tax	90,479	33,822	53,124	68,575
Less: Provision for Tax	12,116	6,932	9,562	12,343
Diluted shares o/s (mn)	2,407	2,407	2,407	2,407
Dividend per share (DPS)	3.5	1.3	1.7	2.2
Dividend Payout Ratio(%)	12.1	10.0	10.0	10.0
Net revenue	302,642	260,075	281,644	311,534
Other Operating Income	13,142	3,400	4,000	5,000
Income from operations	315,784	263,475	285,644	316,534
Materials costs	81,307	72,787	75,964	84,014
Employee costs	49,023	53,925	59,318	65,250
R&D Cost	21,024	20,551	22,852	25,323
EBITDA	100,893	56,785	64,829	78,841
Operating profit	100,893	56,785	64,829	78,841
EBIT	88,245	43,674	51,659	65,310
Add: Other income	6,231.5	6,125.95	6,737.94	7,337.54
Less: Interest Expense	3,998	6,473	5,273	4,073
Add: Exceptional items	-	(9,505)	-	-
Less: Minority Interest	8,719	4,047	3,594	4,175
Reported Profit	69,644	22,842	39,967	52,056
Exceptional Items	-	(9,505)	-	-
Adjusted Profit	69,644	32,347	39,967	52,056
Shares o /s (mn)	2,407	2,407	2,407	2,407
Adjusted Basic EPS	28.9	13.4	16.6	21.6
Adjusted Diluted EPS	28.9	13.4	16.6	21.6
Adjusted Cash EPS	34.2	18.9	22.1	27.3

Common size metrics

Year to March	FY17	FY18	FY19E	FY20E
Operating expenses	68.1	78.4	77.3	75.1
Materials costs	25.7	27.6	26.6	26.5
Staff costs	15.5	20.5	20.8	20.6
R & D cost	6.7	7.8	8.0	8.0
Depreciation	4.0	5.0	4.6	4.3
Interest Expense	1.3	2.5	1.8	1.3
EBITDA margins	31.9	21.6	22.7	24.9
Net Profit margins	24.8	13.8	15.3	17.8

Growth ratios (%)

Year to March	FY17	FY18	FY19E	FY20E
Revenues	8.5	(14.1)	8.3	10.6
Adjusted Profit	33.1	(53.6)	23.6	30.2
EBITDA	23.7	(43.7)	14.2	21.6
PBT	37.7	(62.6)	57.1	29.1
EPS	33.1	(53.6)	23.6	30.2

Balance sheet				(INR mn)
As on 31st March	**FY17**	**FY18**	**FY19E**	**FY20E**
Share capital	2,399	2,399	2,399	2,399
Reserves & Surplus	363,997	382,958	418,129	463,939
Shareholders' funds	366,397	385,357	420,528	466,338
Minority Interest	37,909	41,956	45,550	49,726
Total Borrowings	80,910	80,910	65,910	50,910
Long Term Liabilities	13,418	13,418	13,418	13,418
Def. Tax Liability (net)	(21,780)	(21,780)	(21,780)	(21,780)
Sources of funds	**476,853**	**499,861**	**523,627**	**558,611**
Gross Block	189,302	199,302	209,302	217,302
Net Block	121,390	118,278	115,108	109,577
Capital work in progress	28,014	28,014	28,014	28,014
Intangible Assets	55,362	55,362	55,362	55,362
Total Fixed Assets	204,766	201,654	198,484	192,953
Non current investments	9,610	9,610	9,610	9,610
Uses of funds	**476,853**	**499,861**	**523,627**	**558,611**
BVPS (INR)	152.2	160.1	174.7	193.8
Short term borrowings	66,549	66,549	56,549	46,549
Long term borrowings	14,361	14,361	9,361	4,361
Depreciation	12,648	13,111	13,171	13,531
Cash and Equivalents	153,717	195,057	213,516	245,540
Inventories	68,328	50,335	73,507	63,459
Sundry Debtors	72,026	58,314	63,221	70,057
Loans & Advances	35,465	35,465	35,465	35,465
Current Assets (ex cash)	175,819	144,114	172,193	168,981
Trade payable	43,954	27,468	47,071	35,368
Other Current Liab	68,367	68,367	68,367	68,367
Total Current Liab	112,321	95,836	115,438	103,735
Net Curr Assets-ex cash	63,498	48,278	56,755	65,246

Free cash flow				(INR mn)
Year to March	**FY17**	**FY18**	**FY19E**	**FY20E**
Reported Profit	69,644	22,842	39,967	52,056
Add: Depreciation	12,648	13,111	13,171	13,531
Interest (Net of Tax)	3,463	5,146	4,324	3,340
Others	7,479	25,294	(21,277)	(20,323)
Less: Changes in WC	22,411	15,220	(8,477)	(8,491)
Operating cash flow	70,822	51,174	44,661	57,095
Less: Capex	35,904	10,000	10,000	8,000
Free Cash Flow	**34,918**	**41,174**	**34,661**	**49,095**

Cash flow metrics				
Year to March	**FY17**	**FY18**	**FY19E**	**FY20E**
Operating cash flow	70,822	51,174	44,661	57,095
Investing cash flow	(42,216)	(10,000)	(10,000)	(8,000)
Financing cash flow	(22,854)	166	(16,202)	(17,072)
Net cash Flow	5,752	41,340	18,459	32,024
Capex	(35,904)	(10,000)	(10,000)	(8,000)
Dividend paid	(2,920)	(3,882)	(4,796)	(6,247)

Profitability and efficiency ratios				
Year to March	**FY17**	**FY18**	**FY19E**	**FY20E**
ROAE (%)	20.2	8.8	9.8	11.5
ROACE (%)	20.3	10.1	11.3	13.3
Debtors Days	84	91	79	78
Payable Days	179	179	179	179
Cash Conversion Cycle	203	210	197	197
Current Ratio	2.9	3.5	3.3	4.0
Gross Debt/EBITDA	0.8	1.4	1.0	0.6
Gross Debt/Equity	0.2	0.2	0.1	0.1
Adjusted Debt/Equity	0.2	0.2	0.1	0.1
Net Debt/Equity	(0.2)	(0.3)	(0.3)	(0.4)
Interest Coverage Ratio	22.1	6.7	9.8	16.0

Operating ratios				
Year to March	**FY17**	**FY18**	**FY19E**	**FY20E**
Total Asset Turnover	0.7	0.5	0.6	0.6
Fixed Asset Turnover	1.8	1.5	1.6	1.9
Equity Turnover	0.8	0.6	0.6	0.6

Valuation parameters				
Year to March	**FY17**	**FY18**	**FY19E**	**FY20E**
Adj. Diluted EPS (INR)	28.9	13.4	16.6	21.6
Y-o-Y growth (%)	*33.1*	*(53.6)*	*23.6*	*30.2*
Diluted P/E (x)	18.0	38.7	31.3	24.0
P/B (x)	3.4	3.2	3.0	2.7
Dividend Yield (%)	0.7	0.3	0.3	0.4
Adjusted Cash EPS (INR)	34.2	18.9	22.1	27.3
EV / Sales (x)	4.0	4.5	4.1	3.6
EV / EBITDA (x)	12.1	20.8	17.7	14.0

Peer comparison valuation

	Market cap	Diluted P/E (X)		EV / EBITDA (X)		ROAE (%)	
Name	**(USD mn)**	**FY18E**	**FY19E**	**FY18E**	**FY19E**	**FY18E**	**FY19E**
Sun Pharmaceuticals Industries	19,207	38.7	31.3	20.8	17.7	8.8	9.8
Cipla	7,162	29.8	24.3	16.6	14.1	11.6	12.8
Dr.Reddys Laboratories	5,568	29.4	14.9	15.5	9.6	9.6	17.4
Lupin	5,438	24.7	22.0	13.1	11.8	10.2	10.5
Median	-	29.6	23.1	16.0	12.9	9.9	11.6
AVERAGE	-	30.7	23.1	16.5	13.3	10.0	12.6

Source: Edelweiss research

Additional Data

Directors Data

Israel Makov	Chairman	Dilip S. Shanghvi	Managing Director
Sudhir Valia	Executive Director	Sailesh T. Desai	Executive Director
Hasmukh S. Shah	Non-Executive Independent Director	Keki M. Mistry	Non-Executive Independent Director
Ashwin Dani	Non-Executive Independent Director	S. Mohanchand Dadha	Non-Executive Independent Director
Rekha Sethi	Non-Executive Independent Director		

Auditors - Deloitte,Haskins and Sells

*as per last annual report

Holding – Top10

	Perc. Holding		Perc. Holding
Life Insurance Corporation of India	5.53	SBI Funds Management	1.15
ICICI Prudential Asset Management	2.90	UTI Asset Management	0.68
Vanguard group	1.58	FMR LLC	0.56
Blackrock	1.57	Reliance Capital	0.55
GIC Private Limited	1.25	ICICI Prudential Life Insurance	0.50

*in last one year

Bulk Deals

Data	Acquired / Seller	B/S	Qty Traded	Price
No Data Available				

*in last one year

Insider Trades

Reporting Data	Acquired / Seller	B/S	Qty Traded
22 Feb 2018	Jayant S Sanghvi	Sell	24200.00
06 Feb 2018	Jayant S Sanghvi	Sell	1079855.00
31 Jan 2018	Pratham Investments	Sell	1220669.00
15 Jun 2017	K Shivramchandra	Sell	25000.00

*in last one year

Company	Absolute reco	Relative reco	Relative risk	Company	Absolute reco	Relative reco	Relative Risk
Aurobindo Pharma	HOLD	SP	H	Cadila Healthcare	BUY	SO	M
Cipla	HOLD	SP	L	Divi's Laboratories	REDUCE	SU	H
Dr.Reddys Laboratories	BUY	SP	M	Glenmark Pharmaceuticals	HOLD	SU	H
Ipca Laboratories	BUY	SO	H	Lupin	HOLD	SP	M
Natco Pharma	BUY	SO	M	Sun Pharmaceuticals Industries	HOLD	SU	M
Torrent Pharmaceuticals	HOLD	SP	M				

ABSOLUTE RATING

Ratings	Expected absolute returns over 12 months
Buy	More than 15%
Hold	Between 15% and - 5%
Reduce	Less than -5%

RELATIVE RETURNS RATING

Ratings	Criteria
Sector Outperformer (SO)	Stock return > 1.25 x Sector return
Sector Performer (SP)	Stock return > 0.75 x Sector return
	Stock return < 1.25 x Sector return
Sector Underperformer (SU)	Stock return < 0.75 x Sector return

Sector return is market cap weighted average return for the coverage universe within the sector

RELATIVE RISK RATING

Ratings	Criteria
Low (L)	Bottom 1/3rd percentile in the sector
Medium (M)	Middle 1/3rd percentile in the sector
High (H)	Top 1/3rd percentile in the sector

Risk ratings are based on Edelweiss risk model

SECTOR RATING

Ratings	Criteria
Overweight (OW)	Sector return > 1.25 x Nifty return
Equalweight (EW)	Sector return > 0.75 x Nifty return
	Sector return < 1.25 x Nifty return
Underweight (UW)	Sector return < 0.75 x Nifty return

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Date: 2018.04.05 15:30:30 +05'30'

Coverage group(s) of stocks by primary analyst(s): Pharmaceuticals

Aurobindo Pharma, Cadila Healthcare, Cipla, Divi's Laboratories, Dr.Reddys Laboratories, Glenmark Pharmaceuticals, Ipca Laboratories, Lupin, Natco Pharma, Sun Pharmaceuticals Industries, Torrent Pharmaceuticals

Recent Research

Date	Company	Title	Price (INR)	Recos
03-Apr-18	**Pharma**	Tough times to continue; *Q4FY18 Result Preview*		
16-Feb-18	**Torrent Pharma**	Unichem portfolio overlap to outweigh synergies; *Result Update*	1,423	Hold
14-Feb-18	**IPCA Laboratories**	Overhangs behind, rebound on the horizon; *Result Update*	640	Buy

Distribution of Ratings / Market Cap

Edelweiss Research Coverage Universe

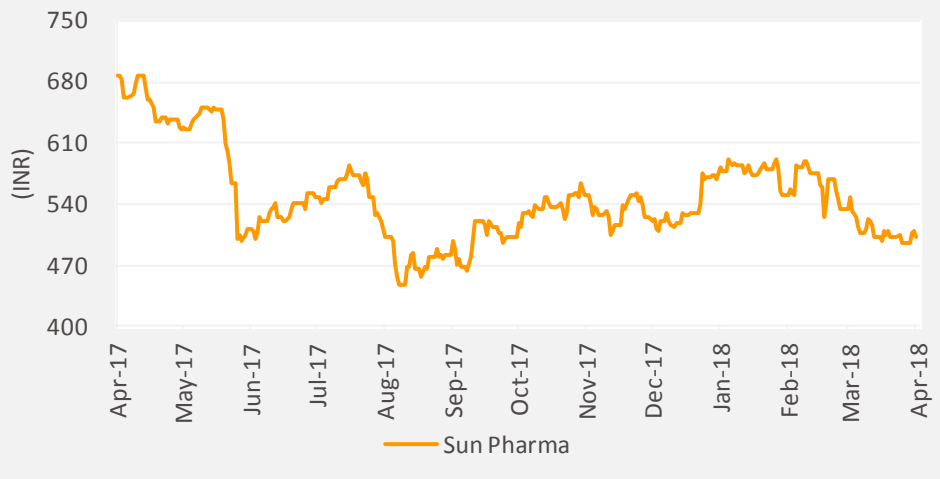
	Buy	Hold	Reduce	Total
Rating Distribution*	161	67	11	240
* 1stocks under review				

	> 50bn	Between 10bn and 50 bn	< 10bn
Market Cap (INR)	156	62	11

Rating Interpretation

Rating	Expected to
Buy	appreciate more than 15% over a 12-month period
Hold	appreciate up to 15% over a 12-month period
Reduce	depreciate more than 5% over a 12-month period

One year price chart



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