

Dollars in for dermatology

Exploration by biopharma companies of new biological pathways underlying skin disorders is leading to the entry of potential blockbusters into the dermatology market, and fueling high-value deals.

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BioPharma Dealmakers

Indications such as psoriasis and atopic dermatitis have taken center stage in the dermatology market, leading to a surge of deals as biopharma companies explore novel targets such as interleukin (IL)-17, IL-4/IL-13 and IL-31, often with monoclonal antibody (mAb) therapeutics. These drugs may provide important new treatment options—particularly for patients with more severe disease or for those who do not respond to standard therapies—and some are anticipated to become blockbusters.

Poised for growth

The atopic dermatitis market in particular is on the cusp of a major breakthrough: the highly anticipated approval of the injectable IL-4/IL-13 inhibitor dupilumab from Regeneron and Sanofi, which could become the first biologic in the United States for this indication in 2017. Analysts at Datamonitor Healthcare have predicted that annual sales for drugs for atopic dermatitis in seven major markets (the United States, Japan, Germany, France, the United Kingdom, Spain and Italy) could grow from ~\$580 million in 2015 to ~\$2.1 billion in 2024 (Fig. 1), largely driven by the entry of dupilumab. This mAb is forecast to have annual sales of ~\$1.3 billion in 2024, as it could provide a new

option for patients with more severe disease that is not controlled adequately with current treatments such as topical corticosteroids. Eucrisa (crisaborole), which Pfizer gained through its \$5.2 billion acquisition of Anacor Pharmaceuticals in mid-2016, is also expected to contribute substantially to US market growth. This topical small-molecule phosphodiesterase-4 inhibitor was approved for atopic dermatitis by the US Food and Drug Administration (FDA) in December 2016, and it is forecast to have annual sales of ~\$210 million in the United States alone in 2024.

Targeting cytokines in psoriasis

Psoriasis has also been a major focus of R&D in the dermatology area over the past decade, and several biologics have already achieved substantial clinical and commercial success for this indication. Humira (adalimumab; AbbVie), a mAb that targets tumor necrosis factor (TNF), leads the market, with global sales of ~\$2 billion in 2014. This represents 27% of a total market of ~\$7.5 billion, according to data from IMS Health (*Nat. Rev. Drug Discov.* **14**, 745–746, 2015).

Recent efforts to target other cytokines involved in the pathogenesis of psoriasis have focused on IL-17, as well as its upstream regulator

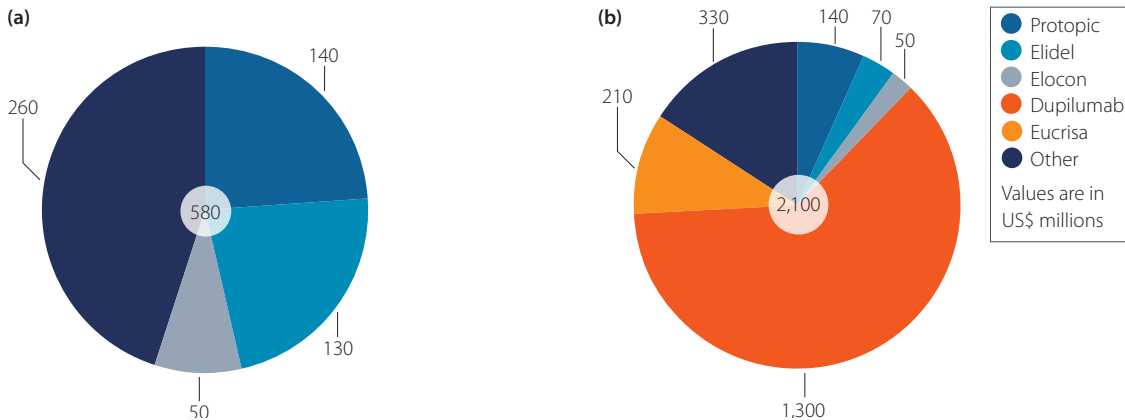


Figure 1: The market for atopic dermatitis. (a) Sales of drugs for atopic dermatitis (the most common form of eczema) in the seven major markets in 2015 were worth \$580 million. Major products included the current market-leading calcineurin inhibitors Protopic (tacrolimus; Astellas/Leo Pharma/Maruho/Roche) and Elidel (pimecrolimus; Valeant/Meda), as well as topical corticosteroids such as Elocon (mometasone furoate;

Merck & Co./Shionogi). **(b)** The anticipated entry of dupilumab (developed by Regeneron/Sanofi) in 2017 has been projected to drive the market to expand to \$2.1 billion in 2024, with sales of the recently approved Eucrisa (crisaborole; Pfizer) also making a substantial contribution. Note: sales of Eucrisa represented here are from the US market alone. Source: Datamonitor Healthcare | Pharma Intelligence, 2016.

IL-23. Stelara (ustekinumab; Janssen Biotech), a mAb that targets the shared p40 subunit of IL-12 and IL-23, had global sales of ~\$1.9 billion in 2014. In January 2015, Cosentyx (secukinumab; Novartis), a mAb that targets IL-17A, was approved by the FDA to treat psoriasis, and was closely followed by Lilly's Taltz (ixekizumab), another mAb that targets IL-17A, in March 2016.

Janssen are also hot on the trail with guselkumab, a mAb that targets the unique p19 subunit of IL-23, which is expected to be approved in

2017 after submission to the FDA in late 2016. Sun Pharma is pursuing the same target with tildrakizumab, the focus of a recent deal with Almirall (Table 1). Companies are also pursuing other approaches that have catalyzed deals, such as Allergan's 2016 acquisition of Vitae Pharmaceuticals, through which it gained the small-molecule ROR γ t antagonist VTP-43742. Overall, sales of new drugs are projected to lead to the global psoriasis market, reaching \$9 billion by 2019 (*Nat. Rev. Drug Discov.* **14**, 745–746, 2015).

Table 1: Selected major dermatology deals since 2015

Date	Companies	Indication	Value	Deal summary
May 2015	LEO Pharma, arGEN-X	Skin conditions	\$116 million (including \$5 million in pre-investigational new drug (IND) and up-front payments)	LEO Pharma signs a deal with arGEN-X to develop its mAb therapeutic for skin conditions.
June 2015	Allergan, Kythera Biopharmaceuticals	Double chin	\$2.1 billion	Allergan acquires Kythera Biopharmaceuticals, including its double-chin drug Kybella (deoxycholic acid)—which has recently been approved by the FDA—to strengthen its position in the skin cosmetics field.
November 2015	LEO Pharma, Astellas Pharma	Acne, atopic dermatitis and skin infection	\$725 million	LEO Pharma signs an asset purchase agreement for Astellas' dermatology business, including the marketed atopic dermatitis drug Protopic (tacrolimus), a topical immunosuppressant.
March 2016	Dr Reddy's Laboratories, Xenoport	Psoriasis	\$490 million (including a \$47.5 million up-front fee)	Dr Reddy's enters into an agreement with Xenoport to gain exclusive rights to XP 23829, an oral prodrug of monomethyl fumarate that has reached phase 2 trials for psoriasis.
March 2016	AbbVie, Boehringer Ingelheim	Psoriasis	\$595 million up front and undisclosed milestone and royalty payments from AbbVie	AbbVie teams up with Boehringer Ingelheim to develop and commercialize BI 655066, an anti-IL-23 mAb, which is currently in phase 3 development for psoriasis.
May 2016	Pfizer, Anacor Pharmaceuticals	Atopic dermatitis	\$5.2 billion	Pfizer to acquire Anacor Pharmaceuticals, including its lead compound crisaborole, a topical PDE4 inhibitor under FDA review for atopic dermatitis.
July 2016	Galderma Pharmaceuticals, Chugai Pharmaceutical Company	Atopic dermatitis, pruritus	Undisclosed; Galderma to pay up-front, milestone and royalty payments to Chugai	Galderma licenses the mAb nemolizumab, which targets IL-31 receptor A, from Chugai Pharmaceutical. If the mAb is approved, Galderma will gain the rights to develop and market it globally apart from in Japan and Taiwan.
July 2016	LEO Pharma, AstraZeneca	Atopic dermatitis	\$115 million up front and up to \$1 billion in commercially related milestones and product royalty sales	LEO Pharma gains an exclusive licence to tralokinumab from AstraZeneca. The anti-IL-13 mAb has completed phase 2b trials for atopic dermatitis.
July 2016	LEO Pharma, AstraZeneca	Psoriasis	Undisclosed	LEO Pharma will gain the European rights to brodalumab, an IL-17-receptor-targeted mAb from AstraZeneca, which is under regulatory review in Europe for patients with psoriasis.
July 2016	Almirall, Sun Pharmaceutical Industries Ltd	Psoriasis	Almirall will pay Sun Pharma an initial up-front payment of \$50 million. Sun will be eligible to receive development and regulatory milestone payments.	Sun Pharma and Almirall partner to develop and commercialize tildrakizumab in Europe. The anti-IL-23 mAb has completed phase 3 trials.
September 2016	Allergan, Vitae Pharmaceuticals	Atopic dermatitis, psoriasis	\$639 million	Allergan to acquire Vitae Pharmaceuticals, including VTP-43742, an orally active ROR γ t-selective antagonist that has reached phase 2 trials for psoriasis, and a topical LXR β -selective agonist that has reached phase 2 trials for atopic dermatitis.
November 2016	LEO Pharma, MorphoSys	Skin diseases	Potential \$120 million milestone payments per program	LEO Pharma partners with MorphoSys to develop antibody therapeutics for dermatological diseases.
December 2016	Novartis, Ziarno Group Limited	Atopic dermatitis	Undisclosed	Novartis agrees to acquire dermatology-focused Ziarno Group Limited, including its orally available histamine H4 receptor antagonist ZPL-389, which has reached phase 2 trials for atopic dermatitis.
December 2016	Purdue Pharma, Exicure	Psoriasis	Exicure could receive up to \$790 million, including an up-front payment, regulatory and commercial milestones and equity investment	Purdue Pharma to collaborate with Exicure to develop treatments for psoriasis and other diseases using Exicure's SNA technology. The lead compound AST-005, a topically applied SNA that targets TNF, has completed a phase 1 trial.

IL, interleukin; LXR, liver X receptor; mAb, monoclonal antibody; PDE, phosphodiesterase; ROR, retinoic acid receptor; SNA, spherical nucleic acid; TNF, tumor necrosis factor.