Table 2 Approved antibody therapies for allergic disease

Company	Molecule	Target	Licensed indications	First FDA approval
Roche	Xolair (omalizumab)	Immunoglobulin E (IgE)	Allergic asthma; chronic idiopathic urticaria	6/20/2003
GlaxoSmithKline	Nucala (mepolizumab)	IL-5	Severe asthma with an eosinophilic phenotype	11/4/2015
Teva (Petach Tikva, Israel)	Cinqair (reslizumab)	IL-5	Severe asthma with an eosinophilic phenotype	3/26/2016
AstraZeneca	Fasenra (benralizumab)	Alpha subunit of IL-5 receptor	Severe asthma with an eosinophilic phenotype	11/14/2017

Source: Company websites, FDA

IL-5 (**Table 2**). Individuals may respond to one or another depending on their allergic profile: those with a high eosinophil count respond to IL-5-directed therapy, whereas patients with an allergic phenotype, which is characterized by high IgE levels, tend to respond to Xolair (omalizumab), Roche's IgE-directed antibody.

Dupixent has attracted multi-billion-dollar sales forecasts on the strength of its efficacy in eczema and asthma, but it will face competition from newer agents as well as these established therapies. UCLA's Corren was principal investigator on a phase 2 trial of AMG 157 (also called MEDI9929), an antibody which Amgen, of Thousand Oaks, California, and AstraZeneca's MedImmune arm are jointly developing. In a dose-ranging study, it reduced patients' annualized exacerbation rates by about 60–70% compared to those on placebo, while also improving lung function (*N. Engl. J. Med.* **377**, 936–946, 2017). "The data look astonishing," Wenzel says. What's more, it appeared to work across different phenotypes. "It really seems to be a very homogenously effective treatment," she says. The antibody targets thymic stromal lymphopoietin (TSLP), a cytokine that acts upstream from IL-4 and IL-13, and which plays a central role in initiating and amplifying T_H2 responses by acting on dendritic cells, as well as other types of immune effector cells. "When airway dendritic cells are exposed to TSLP, subsequent interaction of these dendritic cells with naive $CD4^+$ T cells leads these T cells to adopt a T_H2 phenotype," says Corren. "These cells play an important role in promoting airway inflammation in patients with asthma."

The long saga of solo IL-13 inhibition is not over yet, but it is entering its final chapter. Failures in dermatology indications would most likely finish off a therapeutic class that has never managed to meet expectations. But Dupixent's story is just beginning—and it is likely to have a significant impact in several allergic conditions. Its clinical success underscores the importance, however incompletely understood, of IL-4, as well as IL-13, in T_H2-mediated disease.

Cormac Sheridan *Dublin*

AI for your heart, on your wrist

Add to the dizzying number of Apple Watch accessories the first FDA-cleared medical device made for Apple's hot-selling smartwatch. KardiaBand is an Apple Watch strap that lets users capture their electrocardiogram (ECG) anytime by touching their thumb to an integrated sensor. Results are displayed on the face of Apple Watch and allow the detection of normal sinus heart rhythms and atrial fibrillation, the most common heart arrhythmia. KardiaBand sells for $199, about twice as much as its previous smartphone-based incarnation. Its manufacturer, Mountain View, California–based AliveCor, has also launched an Apple Watch app, SmartRhythm, that taps a deep autoregressive neural network using heart rate, activity and ECG data from healthy and sick populations and alerts the user to record an ECG if their heart rate differs from the neural network—for example, if it rises while they are resting, by comparing their heartbeat with the user's location and speed provided by the watch's built-in accelerometer.

alivecor

First *in vivo* human genome editing trial

The first patient dosed with an *in vivo* gene editing therapy was treated at UCSF Benioff Children's Hospital Oakland as part of Sangamo Therapeutics' clinical trial. The phase 1/2 CHAMPIONS study launched in November is an open-label trial that will evaluate single ascending IV doses of Sangamo's SB-913, a zinc finger nuclease (ZFN)-mediated gene editing therapy for treating mucopolisaccharidosis II (MPS II) or Hunter's syndrome. MPS II is a progressive inherited lysosomal storage disorder caused by mutations in the gene encoding iduronate-2-sulfatase enzyme, which degrades glycosaminoglycans. Depending on the severity of the mutation and the degree of residual enzyme activity, children with this may experience delays in cognitive development, enlarged organs, cardiovascular disorders, hearing loss, stunted growth and skeletal abnormalities, owing to a buildup of toxic carbohydrates in cells throughout their body. One in 100,000–170,000 people are estimated to be born with MPS II. The current standard of care is enzyme replacement therapy that requires regular infusions. The open-label trial will test for safety, vector clearance and the change from baseline in urinary glycosaminoglycans. Sangamo aims to use genome editing to insert a corrective gene into the precise location within the albumin gene using adeno-associated virus vectors that specifically target the liver. The ability to introduce the therapeutic gene permanently could enable a patient's liver to produce a stable supply of the missing enzyme. Sangamo's *in vivo* genome editing approach allows the therapeutic gene to integrate precisely into the genome, whereas conventional AAV cDNA gene therapy and lenti- or retroviral-based approaches insert randomly. SB-913 has Fast Track, Orphan Drug and rare pediatric disease designations in the US to treat MPS II. Two additional clinical trials are underway in the US to evaluate Sangamo's *in vivo* genome editing therapeutics for hemophilia B and MPS I, also known as Hurler or Hurler-Scheie syndrome.

"The last gift any of us want to give away this holiday season is our most personal and sensitive information," US Senator Chuck Schumer of New York, commenting on DTC genomics companies slashing of prices as part of holiday promotions, leading at least this member of Congress to question whether privacy protections are adequate. (*NBC News*, 26 November 2017)

"It was so normal in the company. It was like a fact of life that everyone had to accept. Sam [Isaly] just did what he could get away with." Yanping Ren was one of several women who complained of inappropriate behavior by Isaly, founder of OrbiMed, the largest biotech hedge fund. After this was reported by *STAT*, Isaly stepped down. (*STAT*, 7 December 2017)