

Zolgensma heads up spate of US approvals



[Madeleine Armstrong](#)



The US FDA granted seven approvals in two days last week, including an eagerly awaited thumbs-up for Novartis's gene therapy Zolgensma.

Friday evening saw the US approval of the new poster child for pricey products, Novartis's spinal muscular atrophy gene therapy Zolgensma. Although the company did its best to play down the headline \$2.1m price tag, this was understandably the focus for many. Zolgensma is now the world's most expensive treatment, and then some.

Even so, it was not as bad as many had feared – Novartis prepped the market well by [previously insisting that it could justify a \\$4-5m price tag](#), something that, in reality, had probably never been on the cards.

And the company also stated that, over five years, Zolgensma would cost \$425,000 per year. Notably, Biogen's rival marketed SMA therapy, Spinraza, costs \$750,000 for the first year of treatment and \$375,000 per year thereafter.

This puts the cost of Spinraza at around \$4m over 10 years, Novartis was quick to point out. Put this way, Zolgensma starts to look more reasonable. Still, a lot depends on how long-lasting the gene therapy's effects turn out to be.

Ahead of the approval, there were questions about whether Zolgensma would be limited to the most severe type 1 SMA population, but in the end the FDA granted a broad label, covering patients aged under two years with bi-allelic mutations in the SMN1 gene. This could also include type 2 disease, and it will be interesting to see whether this will be covered by payers.

The US pricing watchdog Icer concluded that Zolgensma was too expensive, but only just. To hit a standard cost-effectiveness threshold of \$150,000 per quality-adjusted life year, Zolgensma would need to cost \$1.9m, the organisation said in an addendum to a previous report.

Novartis also said it was working with payers on five-year outcomes-based agreements, as well as options to pay over time.

After lacklustre uptake of other gene therapies, Novartis will need to buck the trend to justify its \$8.7bn outlay on Zolgensma's developer, Avexis.

Keeping abreast

Meanwhile, Novartis also got the green light for its breast cancer therapy alpelisib, now branded Piqray. The

PI3K inhibitor is indicated for hormone receptor-positive, Her2-negative patients with a PIK3CA mutation, based on positive data from the Solar-1 trial ([Esmo 2018 - In breast cancer Novartis hopes to succeed where Roche failed, October 20, 2018](#)).

Around 40% of these patients have the mutation, according to Novartis; a companion diagnostic developed by Qiagen has also been approved to identify them. The company will hope Piqray will do better than its other recent breast cancer entrant, the CDK4/6 inhibitor Kisqali, which has had a disappointing launch. *EvaluatePharma* sellside consensus forecasts Piqray sales of \$713m by 2024.

Incyte also got some good news on Friday with the approval of a new use for its Jak inhibitor Jakafi, steroid-refractory acute graft-versus-host disease (GVHD), which can develop after stem cell transplant.

This represents a new mechanism for the disorder nearly two years after Abbvie and Johnson & Johnson's Imbruvica [got the US go-ahead](#) for the treatment of second-line chronic GVHD. Incyte expects more GVHD data with Jakafi later this year from the [Reach 2](#) and [Reach 3](#) trials in steroid-refractory acute and chronic disease respectively.

EvaluatePharma consensus puts Jakafi's GVHD sales at \$216m in 2024, well behind its approved uses of myelofibrosis and polycythaemia vera.

A new field

The FDA has also approved several innovative medical devices. One of these approvals was done under a humanitarian device exemption – a type of approval that does not require the applicant to submit evidence of effectiveness. The device must be intended for a rare condition that affects fewer than 8,000 people in the US each year.

Novocure's NovoTTF-100L system, which uses electric fields to shrink tumours, has been approved, in combination with Lilly's Alimta and platinum-based chemotherapy, for the first-line treatment of unresectable locally advanced or metastatic malignant pleural mesothelioma. Novocure claims this is the first FDA-approved treatment for this form of mesothelioma in more than 15 years.

The approval was based on [data from a phase II trial, Stellar](#), which reported in April 2018. The FDA has been surprisingly tardy – analysts had expected the approval to come through around six months ago. NovoTTF-100L is already approved in glioblastoma, where it is branded Optune; it is forecast to have sales of more than \$1bn in this indication in 2024, according to *EvaluateMedTech's* consensus data.

Novocure's forecast sales								
Indication	WW annual sales (\$m)							CAGR
	2018	2019e	2020e	2021e	2022e	2023e	2024e	
Glioblastoma multiforme	331	437	542	638	733	844	1,000	+20%
Mesothelioma	-	3	29	59	90	124	168	N/A
Other indications	-	-	-	-	61	127	208	N/A
Total sales	331	440	571	697	883	1,096	1,376	+27%

Source: EvaluateMedTech.

Hide and Zika

A couple of innovative in vitro diagnostics have also been waved through. The agency granted the first non-emergency approval to a Zika virus test – and is considering revoking the clearances of some of the others.

So far the FDA has cleared 19 Zika virus tests under its [Emergency Use Authorization protocol](#). The ZIKV Detect 2.0 developed by Inbios International was one of five antibody-based blood tests in this group. The agency has now given it formal de novo clearance, and is now considering whether to revoke the EUAs of the other four similarly-acting tests, developed by Chembio Diagnostic Systems, Siemens, Diasorin and the CDC.

In 2017 there were 452 cases of Zika in the US and a further 666 in its overseas territories, including Puerto Rico and the US Virgin Islands. Since then Zika cases have declined sharply and it is not clear exactly how much of a market Inbios's test can drum up.

Another test to have won a de novo clearance was Synovasure PJI, the first test to assess periprosthetic joint infection. This was developed by CD Diagnostics, which was bought by orthopaedics giant Zimmer Biomet in 2016.

The assay detects, within 10 minutes, human alpha defensins – proteins released by neutrophils in response to infection – in the synovial fluid of patients with inflammation at the joint replacement site. Previously surgeons would have sought to detect infection using X-rays or lab tests that take several days to return results, and might have opted for revision surgery if infection status remained unclear.

[More from Evaluate Vantage](#)

Evaluate HQ
[44-\(0\)20-7377-0800](tel:44-020-7377-0800)

Evaluate Americas
[+1-617-573-9450](tel:+1-617-573-9450)

Evaluate APAC
[+81-\(0\)80-1164-4754](tel:+81-080-1164-4754)

© Copyright 2021 Evaluate Ltd.