Table 1 Selected clinical stage drugs for spinal muscular atrophy

Company (location)	Agent	Stage
Ionis/Biogen	Nusinersen, SMN2 antisense splicing modifier	Phase 3
Cytokinetics/Astellas (S. San Francisco, California/ Northbrook, Illinois)	CK-2127107 (CK-107), skeletal muscle troponin activator	Phase 2
Roche	Olesoxime, neuroprotectant	Phase 2
AveXis	AVXS-101, scAAV9-SMN1 gene therapy	Phase 1
Roche	RG7800, small-molecule SMN2 splicing modifier	Phase 1 on clinical hold
Roche	RG7916, small-molecule SMN2 splicing modifier	Phase 1
Novartis	LM1070, small-molecule SMN2 splicing modifier	Phase 1/2, enrollment paused

she says, if nusinersen works better on motor neurons that innervate leg and arm muscles than on the muscles that control respiration. Anecdotal in patients, “some muscles seem to respond really well, and others less well,” says Sumner.

The unreleased data also raise the question, do infants who are treated earlier do better on nusinersen? This would be consistent with SMA mouse models, where there is a developmental window during which treatment is critical.

Another question is whether just injecting nusinersen into the CNS will be enough. In SMA mouse models, systemic treatment is necessary for long-term success (*Nature* 478, 123–126, 2011), but whether this applies to humans is unknown. Although intrathecal nusinersen obviously works well in type 1 infants, Krainer worries that nusinersen CNS-only treatment will unmask previously unseen problems elsewhere in the body as the babies mature beyond the age they now normally die with the disease. Krainer hopes that Biogen will launch trials incorporating systemic treatment once the drug is approved.

One theoretical issue for systemic treatment is thrombocytopenia. Ionis’s Phase 3 trials of two other antisense oligonucleotides in other indications led to declines in platelet levels, leading to fears that the company’s 2’MOE chemistry was causing off-target toxicity. Ionis dismisses these concerns. “We have not seen serious platelet declines with over a dozen other 2’MOE antisense drugs that we have tested in human clinical trials,” says Ionis spokesperson Wade Walke. Company data indicate the recent problems were “unique to these drugs and/or patient populations.”

Other companies are trying systemic treatments for SMA, including small-molecule SMN2 splice modifiers from Roche and Novartis (Table 1). “Those are both brain-penetrant compounds, and delivered orally, which is obviously a great advantage,” says

Sumner. “The challenge [of small molecules] has been the specificity, minimizing off-target effects.” In 2011 Roche in Basel, Switzerland, licensed South Plainfield, Illinois-based PTC Therapeutics’s orally bioavailable RG7800 (*Science* 345, 688–693, 2014), but suspended dosing in a Phase 2 SMA trial in April 2015 owing to unexpected toxicity in animal studies, says Roche spokesperson Catherine Dürr. A backup compound, which completed Phase 1, will soon begin two trials in SMA. Novartis in Basel developed a similar compound (*Nat. Chem. Biol.* 11, 511–517, 2015), but enrollment in a Phase 1/2 SMA trial was paused in May following a review of animal toxicology safety data, says Novartis spokesperson Jeff Lockwood.

Meanwhile, AveXis in Bannockburn, Illinois, in August reported promising Phase 1 interim data for its systemic SMA gene therapy product, an adeno-associated virus vector carrying *SMN1*. All 15 babies showed improvements in motor function, including several in the normal range, compared to baseline. And all remained alive as of late August, several beyond 2 years of age, very rarely achieved by SMA infants, all but one without need of permanent ventilation. Further trials are planned, and the company is also moving forward in type 2 SMA, using intrathecal delivery. Unlike SMN2 induction therapies like nusinersen, “AVXS-101 addresses the root cause of SMA, by replacing the lost or defective *SMN1* gene,” says AveXis CSO Brian Kaspar.

Other drugs working by mechanisms unrelated to SMA genetics are also progressing (Table 1). But nusinersen, once approved, will make it hard to design ethical placebo-controlled, single-agent pivotal trials. “Anything that comes after nusinersen,” says Schmidt, “anything that might also work, will probably find its way into the treatment paradigm more likely in combination with nusinersen than displacing nusinersen.”

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Bayer bids \$66 billion for Monsanto

German pharma and chemical giant Bayer agreed to buy US biotech seed developer Monsanto for a whopping \$66 billion, the companies announced September 14. The deal marks the third high-profile consolidation in the agbiotech industry in the last year. It follows a proposed merger between Midland, Michigan-based Dow Chemical and Wilmington, Delaware-based DuPont worth a combined \$130 billion, and a \$43-billion acquisition of Syngenta by China National Chemical, a state-run chemical giant in Beijing. All three deals face antitrust reviews in multiple countries. Regulators will assess whether the consolidations will unfairly lead to higher prices for farmers and consumers, and any chilling effects on innovation. In the Bayer–Monsanto deal, the companies aim to pair Leverkusen-based Bayer’s crop protection business with St. Louis-based Monsanto’s seeds and traits portfolio. Bayer is best known, however, as the maker of aspirin, Alka Seltzer and other healthcare products—a business that represented 67% of the company’s sales in 2015. Consuming Monsanto will reshape Bayer’s focus, putting crop science on an equal footing with healthcare in terms of projected sales, according to the company. That might pull resources away from Bayer’s pharmaceutical research pipeline, weakening its capacity to grow in that sector, analysts say. Bayer’s offer represents a 44% premium to Monsanto’s share price before takeover talk was first reported in May, and is the largest acquisition of 2016 in any sector. Bayer said it would pay Monsanto \$2 billion if the deal falls apart on antitrust grounds.

Emily Waltz

“We’re seeing increases all the time in drug prices—so the key here is whether the issue can excite an audience’s passion. For some companies, it blows up. For other companies, it goes completely under the radar,” notes Peter LaMotte, senior vice president of crisis management firm Chernoff Newman of Columbia, South Carolina. (*STAT*, 26 August 2016)

“Stem cell scientists include the best and the brightest doing great work, and I admire them. At the other end of the scale, there’s snake oil.” Janice Mulligan, a San Diego attorney working on a potential class-action lawsuit against unnamed stem cell clinics. (*Los Angeles Times*, 19 August 2016)

“Onboard sequencing makes it possible for the crew to know what is in their environment at any time. That allows us on the ground to take appropriate action—do we need to clean this up right away, or will taking antibiotics help or not?” NASA’s Sarah Castro-Wallace describes the rationale for DNA sequencing, performed for the first time by molecular biologist Kate Rubins using Oxford Nanopore Technologies’ MinION on the international space station. (*nasa.gov*, 29 August 2016)