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ACC - Savara shrugs as Mast fades into the past



[Madeleine Armstrong](#)

The last remnant of Mast Therapeutics, the inhaled nitrite Aironite, has failed in a phase II trial in heart failure, delivering a blow to Mast's acquirer, Savara Pharmaceuticals.

But Savara appears to have avoided the worst: though its shares were off 23% in premarket trading this morning they were later down just 2%, suggesting that investors had not put too much stock in Mast's asset. Maybe Savara's assertion that the discontinuation of Aironite would have no impact on its core orphan lung disease business, where it has two late-stage assets, did the trick (see table below).

Savara's reverse acquisition of Mast in January 2017 was a relative bargain - the former did not have to part with any cash in an all-stock deal that valued Mast at just \$36.5m. This gave Savara a Nasdaq listing as well as a shot at heart failure with preserved ejection (HFpEF), an underserved disorder where drugs have so far failed to make a mark.

A win, however unlikely, could have allowed Savara to mix it up with the big boys: the likes of Novartis and Bayer are also looking at HFpEF.

Into thin AIR

This dream is now over after the phase II Indie trial of Aironite, also known as AIR001, failed on its primary endpoint of improvement in peak exercise capacity, assessed by cardiopulmonary exercise testing, and secondary endpoints. [The data were presented](#) at the American College of Cardiology meeting in Orlando yesterday.

Aironite is in another phase II study, Inable-Training, which was due to be completed in 2020, but whose status is now unclear; Savara says it does not plan to support any new development of the project.

The big readout in HFpEF this year is that of the Paragon trial of Novartis's Entresto, interim data from which are expected in the second half.

Entresto is approved in heart failure with reduced ejection fraction. A win in HFpEF would double its market, Leerink analysts believe, and Novartis reckons that Entresto sales in HFpEF alone could surpass \$1bn ([Novartis investors put faith in new chief, January 24, 2018](#)).

Meanwhile Bayer's neladenoson bialanate is in a phase II study in HFpEF, which is due to conclude this year. As an adenosine A1 receptor agonist this has a different mechanism than Entresto so could be used in combination with Novartis's drug, Bayer's innovation chief, Kemal Malik, previously told *EP Vantage*.

For its part, Savara's hopes now rest on Molgradex and AeroVanc; the former was gained through the July 2016 acquisition of Serendex.

Savara's pipeline

Project	Pharma class	Indication	Status	Originator	Trial(s)
Molgradex	Inhaled GM-CSF	Pulmonary alveolar proteinosis	Phase III	Serendex	Impala - expected to complete enrolment Q3 2018 (NCT02702180)
		Non-tuberculous mycobacteria lung infection	Phase II		Phase IIa trial to begin Q1 2018 (NCT03421743)
AeroVanc	Inhaled vancomycin	MRSA infection in cystic fibrosis	Phase III	Savara	Avail - expected to complete enrolment Q1 2019 (NCT03181932)
Aironite	Inhaled inorganic nitrite	Heart failure with preserved ejection fraction	Discontinued	Mast	Indie - failed (NCT02742129); Inable-Training - ongoing (NCT02713126)

Source: Company website; Clinicaltrials.gov.

Molgradex's lead indication is pulmonary alveolar proteinosis, a lung disorder characterised by the build-up of lung surfactant in the alveoli that affects around 2,500 people in the US. The Impala trial has a primary completion date of October 2018, according to Clinicaltrials.gov.

The project is also set to go into phase II development this year in non-tuberculous mycobacteria lung infection - but a 30-patient trial, slated to start in February, does not appear to have begun recruiting yet. Meanwhile, AeroVanc's ongoing pivotal Avail trial in MRSA in patients with cystic fibrosis should be completed by June 2019.

Mast's erstwhile investors, who have had to endure a string of failures including the demise of vepoloxamer in 2016, will be glad of these new chances. Savara's might be wondering why the company took a gamble on Mast, but should ultimately be relieved that they did not get more badly burnt.

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