Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	AGY
Price (p)	12.5
12m High (p)	29.0
12m Low (p)	7.3
Shares (m)	636.2
Mkt Cap (£m)	79.5
EV (£m)	28.9
Free Float*	39%
Market	AIM

**As defined by AIM Rule 26*

Description

Allergy Therapeutics (AGY) provides information to professionals related to prevention, diagnosis and treatment of allergic conditions, with a special focus on allergy vaccination. The emphasis is on treating the underlying cause and not just the symptoms.

Company information

CEO	Manuel Llobet
CFO	Nick Wykeman
Chairman	Peter Jensen
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Key shareholders

Directors	0.7%
Abbott Labs	37.8%
Southern Fox	22.7%
Odey	6.9%
Blackrock	5.3%
Invesco	4.5%

Diary

1H'20	Ph.1 Polyvac Peanut trial to begin
2H'20	Phase III Grass Trial to begin

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ALLERGY THERAPEUTICS

House dust mite vaccine – clinical progress

AGY is a long-established specialist in the prevention, diagnosis and treatment of allergies. The Pollinex Quattro (PQ) platform, an ultra-short-course subcutaneous allergy immunotherapy (SCIT), continues to gain market share despite its availability in the EU on a 'named-patients' (NP) basis only. The aim of ongoing trials is to move the platform to full registration under the new regulatory framework. Following the success of 'Acarovac Plus' in NP, the 'Acarovac MPL' vaccine for house dust mite allergy is in clinical development to provide a registered vaccine. Results from the Phase I trial of Acarovac MPL were positive, demonstrating safety and tolerability.

- **Strategy:** AGY is a fully-integrated pharmaceutical company focused on the treatment of allergies. There are three parts to its strategy: continued development of its European business via investment or opportunistic acquisitions; the US PQ opportunity; and further development of its pipeline.
- **Phase I trial:** AM101 was an open-label, exploratory trial investigating the safety and tolerability of Acarovac MPL in 16 adult patients with rhinoconjunctivitis due to house-dust mite (HDM) allergy. Seven injections of the SCIT were administered as a 6- to 12-week treatment course.
- **Successful endpoints:** Both the primary and secondary endpoints were positive. The vaccine was well tolerated and the safety profile was satisfactory – there were adverse events reported, but these were consistent with similarly formulated allergy vaccines. This allows progression to Phase II development.
- **Regulatory process:** Under the regulatory framework, there is a strong desire to have 'named-patient' products moved to full marketing approval. In addition to the primary aim of tolerability, strong secondary endpoints indicated a sustained immune response, which should prove helpful in subsequent regulatory discussions.
- **Investment summary:** The market has started to recover from the overly pessimistic view of the PQ Birch trial primary endpoint failure in March. However, AGY is still trading on a 2019E EV/sales of only 0.7x, which is well below the multiples commanded by its direct competitors. All future trial designs are being improved as a consequence of the PQ Birch trial experience in the expectation of enhancing the prospects of gaining full regulatory approval.

Financial summary and valuation

Year-end Jun (£m)	2016	2017	2018	2019E	2020E	2021E
Sales	48.5	64.1	68.3	74.0	80.0	88.0
R&D investment	-16.2	-9.3	-16.0	-16.0	-20.0	-15.0
Underlying EBIT	-12.3	-2.9	-6.4	-7.2	-9.0	-1.9
Reported EBIT	-12.5	-2.6	-7.4	-8.2	-10.0	-2.9
Underlying PBT	-12.5	-3.0	-6.5	-7.4	-9.3	-2.3
Statutory PBT	-12.2	-2.7	-7.5	-8.4	-10.3	-3.3
Underlying EPS (p)	-2.4	-0.5	-1.1	-1.1	-1.6	-0.5
Statutory EPS (p)	-2.3	-0.4	-1.3	-1.3	-1.6	-0.5
Net (debt)/cash	20.0	18.8	12.5	12.8	0.4	-30.5
Capital increase	11.0	0.0	0.0	10.4	0.3	0.3
P/E (x)	-5.3	-26.6	-11.4	-11.1	-7.9	-25.3
EV/sales (x)	1.0	0.8	0.7	0.7	0.6	0.6

Forecasts have not been revised following this trial result and may be subject to change
Source: Hardman & Co Life Sciences Research

Phase I Acarovac MPL trial

Background

AGY has 10 allergy vaccines submitted to TAV for consideration…

…with the AM101 trial aimed at moving Acarovac MPL to full marketing approval

In 2008, under the direction of the Paul Ehrlich Institute (PEI) and based on European legislation, the Therapieallergene-Verordnung (TAV, Therapy Allergy Ordinance) in Germany commenced a process to have allergy vaccines fully regulated. At the beginning of the process, documentation for 123 vaccines was submitted to the TAV for consideration, including 10 from AGY. By the end of 2018 (as announced at the PEI seminar in September), the number of products remaining in the process had been reduced to 58 (ca.47%) either through withdrawal of applications or being turned down by the PEI. All of AGY's products remain in the process to become fully regulated.

AM101 trial

The Phase I AM101 trial protocol recruited 16 patients…

…suffering from HDM induced rhinoconjunctivitis

The AM101 Phase I HDM study was designed to support AGY's development of a fully-approved HDM allergy vaccine (Acarovac MPL) that builds on the success of the named-patient HDM allergy vaccine (Acarovac Plus) in Portugal and Austria. HDMs are a major cause of allergic rhinitis and allergic asthma, and sensitisation to HDM allergens occurs in as many as 130m people worldwide. The Acarovac MPL formulation consists of a triple combination of HDM allergoids from the two most commonly occurring HDM species, plus AGY's proprietary MCT (microcrystalline tyrosine) depot-forming and MPL adjuvant technologies.

Primary endpoint: tolerability

AM101 evaluated the safety and tolerability of Acarovac MPL in 16 patients with allergic rhinoconjunctivitis in a 6- to 12-week course of treatment involving seven injections. The seven injections were spaced one to two weeks apart, and were found to be well tolerated. The occurrence of adverse events was consistent with similar formulations and the safety profile was satisfactory for further development.

Secondary endpoints: efficacy

Secondary endpoints in the trial assessed the efficacy of the vaccine. This included an assessment of symptom score improvements following nasal provocation tests (NPT), the international standard for monitoring allergic rhinitis. Patients' total symptom scores, as assessed by clinicians, improved significantly at 12-weeks. Patients also reported high satisfaction with the new treatment approach in a survey.

Objective measurement of efficacy

Achieving primary endpoints in late stage allergy trials is notoriously difficult…

…because they are based on subjective symptom scores

In addition, although objective endpoints are not required for ongoing development or even for regulatory approval, AGY takes the prudent decision to include them within its protocols, quantifying the presence of immune biomarkers after treatment.

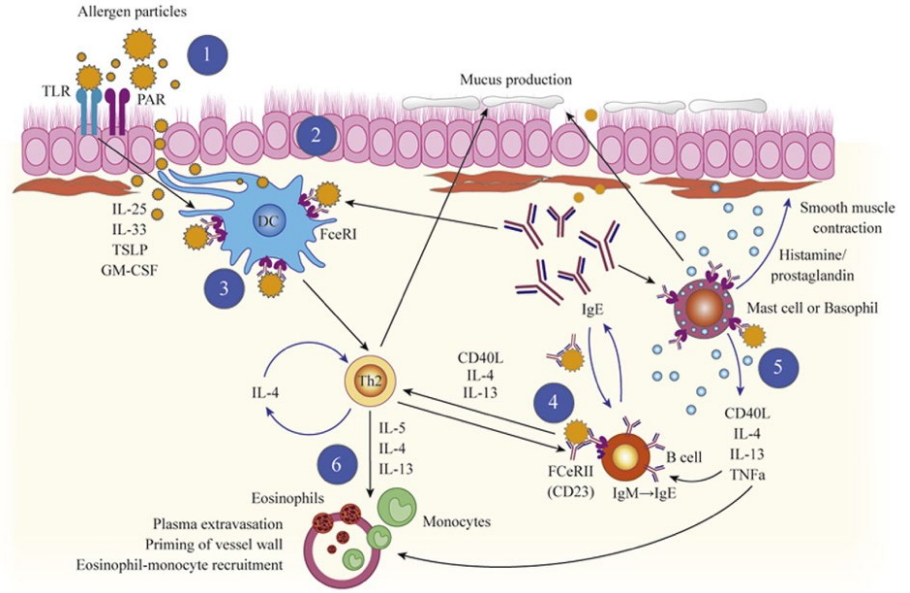
Inhaled dust mite aeroallergens are able to activate both the innate and adaptive immune systems, leading to symptoms particularly in the upper and lower airways. The immunity pathways are still being elucidated; however, it is understood that stimulation of the innate immune system by allergens causes chronic inflammation that is mediated in part by the production of cytokines such as IL-4. Cytokines also stimulate the activation of B cells and the production of immunoglobulins/antibodies that can cause an immediate allergic response via histamine production. Therefore, quantification of cytokines and immunoglobulins is a surrogate of the size of the immune response, and changes before and after treatment in these surrogates allowed AGY to assess the efficacy of Acarovac MPL objectively.

Prudently, AGY did measure immunoglobulins…

…to provide a secondary biomarker endpoint of immune response…

…even though it is not required for clinical progression or even final approval

Model for effect of HDM allergens on the immune response



IL-4 and Ig (immunoglobulin) were measured by AGY as a secondary endpoint in the AM101 study
Source: Calderon M. A. et al Allergy Clin Immunol (2017) 136:1

The secondary, objective, assessment of immune biomarkers showed that there was a significant improvement to the immune response at 12 weeks. There was a statistically significant increase in immunoglobulin markers, indicating a sustained immunological protection against HDM allergic reactions. In addition, a reduction in IL-4 was observed, suggesting desensitisation through a reduction in the inflammatory response and an associated reduction in symptoms.

Clinical and regulatory outlook

The objective endpoint of immune response may help to generate a stronger protocol for the upcoming Phase II trial

In addition to safety and efficacy, a new treatment regimen was tested in the AM101 study. The positive safety, tolerability, efficacy, and patient satisfaction with the treatment approach provides a straightforward path to the next stage of development. They should allow generation of a strong Phase II trial protocol, which would advance the company closer to another fully-approved allergy SCIT in Europe.

Significance

The underlying life history of the *Dermatophagoides spp*. means that HDM allergy epidemiology has patterns at the local and population levels, with perennial allergy having an annual peak in July to November. Acarovac MPL is well positioned to be a leading treatment in the $1.5bn per year (company data) HDM allergy vaccine market, being based on two adjuvants, and given the success of Acarovac Plus, which uses the same allergoids. AGY intends to focus initially on launching Acarovac in the EU, US and Chinese markets.

Investment conclusion

Despite the setback received from the PQ Birch trial results in March, AGY remains at the forefront of SCIT companies attempting to move products from 'named patient' to full regulatory approval. Although there has been some recovery in the share price from the overly pessimistic stance taken by the market in March, the stock remains trading on a 2019E EV/sales of only 0.4x. This trial result should further boost market confidence.

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