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Pharmaceuticals & Biotechnology

Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	**AGY**
Price (p)	25.5
12m High (p)	39.5
12m Low (p)	23.0
Shares (m)	594.1
Mkt Cap (£m)	151.5
EV (£m)	128.9
Free Float*	37%
Market	AIM

**As defined by AIM Rule 26*

Description

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	0.9%
Abbott Labs	40.5%
Southern Fox	21.4%
Odey	7.4%
Invesco	4.8%

Diary

2H'18	Ph.III PQ Birch trial
Sep'18	Finals
Nov'18	AGM

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Allergy Therapeutics

Opening the door to registration

AGY is a long-established specialist in the prevention, diagnosis and treatment of allergies. Pollinex Quattro (PQ) Grass, the subcutaneous allergy immunotherapy (SCIT), continues to gain market share despite being available in the EU only on a 'Named Patient' basis. As part of a programme designed to get PQ Grass formally approved in both Europe and the US, AGY has announced positive results from its Phase II dose-ranging clinical trial. It has identified the optimum dose as needed to move forward into the final Phase III efficacy trials, and to become the first SCIT product to be registered in these important pharmaceutical markets.

- **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.
- **G205 trial:** As part of an agreed programme with both the Therapieallergene-Verordnung (TAV) and the US Food and Drug Administration (FDA), AGY has undertaken a Phase II dose-ranging study with Modified Allergen Tyrosine Absorbed (MATA) MPL (PQ Grass) to identify the optimal dose for Phase III.
- **Results:** Headline data provided everything that AGY could have hoped for: a strong dose-response relationship ($p<0.001$); extremely well tolerated; and an excellent adherence rate (>95%). Results also allowed the company to identify the optimal dose for Phase III trials, subject to regulatory discussions.
- **Next steps:** This trial was extremely important because it was a required step in the programme towards regulatory approval of PQ Grass in both Europe and the US. Although overall protocols for the Phase III trials in the EU and US might be slightly different, they are likely to use the same dose, and start in 1H 2019.
- **Investment summary:** Success in the Phase II G205 trial was important for moving PQ Grass to the next stage. The resounding results will make upcoming discussions with the respective regulators somewhat easier, paving the way for commencement of the final Phase III trials which, in turn, open the door to PQ Grass becoming the first registered ultra-short-course allergy immunotherapy product in both Europe and the US.

Financial summary and valuation

Year-end June (£m)	2015	2016	2017	2018E	2019E	2020E
Sales	43.23	48.51	64.14	68.0	77.0	86.5
R&D investment	-3.12	-16.22	-9.30	-18.0	-16.0	-8.0
Underlying EBIT	2.91	-12.34	-2.89	-9.7	-5.9	8.1
Reported EBIT	1.41	-12.53	-2.60	-10.4	-6.6	7.4
Underlying PBT	2.84	-12.45	-2.97	-9.8	-6.0	8.0
Statutory PBT	0.65	-12.21	-2.67	-10.5	-6.7	7.3
Underlying EPS (p)	0.48	-2.36	-0.47	-1.7	-1.0	1.2
Statutory EPS (p)	0.02	-2.29	-0.42	-1.8	-1.1	1.2
Net (debt)/cash	20.14	20.04	18.80	8.5	3.2	14.0
Capital increase	20.08	10.97	0.03	0.3	0.3	0.3
P/E (x)	56.4	-11.5	-58.1	-15.4	-26.3	21.1
EV/sales (x)	3.2	2.9	2.2	2.0	1.8	1.6

Source: Hardman & Co Life Sciences Research

Paving the way to Phase III trials

Background

Pollinex Quattro was originally approved for use on a 'Named Patient' basis in Europe in 1999. Whilst this was positive and allows AGY to make sales and garner experience with the product – it has been used in 250,000 patients to date – this limited approval prevents universal marketing. Therefore, with the backing of more clinical trials, AGY has sought full product approval in Europe and the US.

Once the regulatory position had been clarified in both Europe (with the TAV via the Paul Ehrlich Institut) and the US (FDA), AGY embarked on a series of clinical trials to underpin a clear pathway leading to full regulatory approval as a biological product in Europe and for a Biologics License Application (BLA) in the US.

In the US, there is a tremendous drive by both the FDA and the US Pharmacopeial Convention (USP) to introduce new regulations and move the allergy vaccine market from its current 'unlicensed' position to one that is fully regulated, with fit-for-purpose approved biologicals based on clinical outcomes.

Drawbacks of conventional SCIT in US

- Variability of supply
- Variability of quality of formulations
- Variability of dose/regimen
- Non-GMP manufacturing
- Long courses of treatment with slow emergence of clinical benefit
- Lack of safety and efficacy data
- Low patient compliance

Source: Allergy Therapeutics (adapted); Hardman & Co Life Sciences Research

In June 2016, AGY suffered a setback when its US dose-ranging study (G204) with Pollinex Quattro/ MATA MPL Grass to identify an optimal dose for late-stage efficacy trials produced an inconclusive result. Given that AGY had already achieved successful outcomes in an 'equivalent' PQ Birch trial in Europe, this was a surprise. However, it should be noted that G204 used a mobile challenge chamber which is very different to conjunctival provocation tests (CPT) used in the European trial.

Therefore, following discussions with the FDA, AGY was allowed to undertake a larger (more doses) dose ranging study (G205) in Europe, which would be acceptable to both the European and US regulators. Results from this trial have been announced today, paving the way for the final push with Phase III efficacy studies in 2019.

G205 results

G205 was a multi-centre (>50), double-blind, placebo-controlled, Phase II trial that recruited 447 patients in Germany, Poland and Austria. Patients received four increasing doses of PQ Grass via subcutaneous injections administered once a week over a six-week period. The aim of the trial was to evaluate the dose-response and safety of PQ Grass and to identify the optimal dose that could be used in Phase III efficacy studies.

Headline results were positive and provided the best possible outcome that could have been expected with this subcutaneous immunotherapy (SCIT). Publication in a scientific journal or presentation at a scientific conference of the complete set of data is likely later in 2018.

Headline results

- The trial met its primary end-point showing a strong dose-dependent relationship ($p<0.0001$) for PQ Grass.
- PQ Grass was extremely well tolerated, with few reported side effects at any dose level.
- In the CPT to evaluate the change in allergic symptoms, there was a significant improvement in in total symptom score (TSS), allowing the identification of the optimal dose.
- Unusually with this type of trial, largely because it is not a regulatory requirement, AGY also collected objective data through the measurement of immunoglobulin (total IgE, grass specific IgE, and grass specific IgG) levels. Early analysis indicated that the levels of immunoglobulin were dose dependent.
- Adherence to the trial was excellent, with 95% of patients completing the course of six weekly injections.

Observations

Headline results provided everything that the company could have hoped for. The key objective was to see a dose response and to identify the optimal dose that will be taken forward into the Phase III efficacy studies. Subject to agreement with the regulators, both of these objectives were achieved.

Current SCIT programmes, particularly in the US, involve multiple (50-100) injections over a period of up to three years, making adherence to schedules very poor; the majority of patients fail to complete the treatment course, resulting in highly variable clinical outcomes. In contrast, PQ is an ultra-short-course SCIT normally involving four, weekly, injections. Therefore, it was very reassuring to see that over 95% of patients adhered to the protocol, suggesting that patients are likely to be compliant with the dosing schedule once the product is approved.

Most companies involved in this therapeutic area do not assess any objective criteria as part of the study, largely because such data is not demanded by the regulatory authorities. Therefore, it was very reassuring to note that AGY had undertaken, by design, measurement of immunoglobulin levels in these patients, which has provided powerful objective data that can be related to the dose of PQ Grass given. Full analysis of this data will be available later in the year.

Conclusion

These positive subjective and objective results will pave the way for constructive discussions with the regulators about the optimal dose and trial design for the Phase III PQ Grass trials. Commencement of trials in 2019 will open the door towards the final push for EU and US registration of the first-to-market ultra-short-course SCIT.

This would leave AGY very well positioned in both Europe and the US, where there is a massive drive, as highlighted earlier, to introduce new regulations to move the allergy vaccines market away from its current ‘unlicensed’ position to one that is fully regulated.

Newsflow

Results from the pivotal Phase efficacy III trial with PQ Birch in Europe as part of the TAV process are due to be released in 2H 2018.

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The fact that we are commissioned to write the research is disclosed in the disclaimer, and the research is widely available.

The full detail is on page 26 of the full directive, which can be accessed here: http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf

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