

## Update on progress in cystic fibrosis programs

- Positive results with FLAMINGO study
  - C1 corrector GLPG2222 as monotherapy in homozygous Class II F508del CF patients
  - Study over-recruited within 5 months in the US and Europe
  - GLPG2222 was well tolerated when dosed once daily for 28 days
  - Dose dependent decrease in sweat chloride observed
- Start of Phase 1 study with backup novel C1 corrector GLPG2851, triggering \$10 M milestone payment to Galapagos from AbbVie
- First dosing of PELICAN Phase 2 study of C2 corrector GLPG2737 in combination with Orkambi<sup>®1</sup> in homozygous Class II F508del CF patients
- Dosing of first patient with first investigational triple combination expected in Q1 2018, interim readout mid-2018
- First dosing in Phase 1 study with second investigational triple combination therapy in healthy volunteers with combination of GLPG3067+GLPG2222+GLPG2737

**Mechelen, Belgium; 2 January 2017, 22.01 CET – Galapagos NV (Euronext & NASDAQ: GLPG) provided an update on several aspects of its cystic fibrosis (CF) programs: Galapagos started three new clinical studies, concluded the FLAMINGO study in CF patients, and expects to report patient data with a first proprietary investigational triple combination therapy in mid-2018. Galapagos, together with collaboration partner AbbVie, stays on track to deliver a competitive triple combination therapy to target 90% of the CF patient population that have the Class II mutation.**

### Positive topline results from FLAMINGO Phase 2 study

The FLAMINGO study included 59 cystic fibrosis (CF) patients with two copies of the Class II F508del mutation and who had not received prior treatment with Orkambi or tezacaftor-ivacaftor<sup>®2</sup> for four weeks prior to dosing of GLPG2222. The FLAMINGO study was over-recruited within five months. This is the first Galapagos CF patient study conducted in the United States as well as in Europe.

Primary objectives of this randomized, double-blinded, placebo controlled study were to evaluate the safety and tolerability of novel C1 corrector GLPG2222. Once daily doses of GLPG2222 or placebo were administered for a total of four weeks on treatment. All patients completed the full treatment course.

Overall, GLPG2222 was well tolerated, with observed treatment emergent adverse events being predominantly mild or moderate and typical for a CF patient population. A total of four Serious Adverse Events (SAEs) were reported in three patients. Of these, two patients were on placebo, each experiencing pulmonary exacerbations due to infection. One patient was on Dose B of GLPG2222 and experienced two pulmonary exacerbations, both with onset during the follow up period; this patient had a significant sweat chloride decrease up to Day 29. There were no discontinuations due to adverse events.

The study doses achieved the targeted GLPG2222 exposure levels. These will provide support to dose modelling and dose selection for the first investigational triple combination. Consistent with the ALBATROSS patient study, exposures achieved in patients were in line with those observed in healthy volunteers.

A statistically significant dose-dependent decrease in sweat chloride concentration was observed with a maximum decrease of 18.3 mmol/L in the Dose C cohort. Mean percent predicted FEV1 (ppFEV1)

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<sup>1</sup> Orkambi<sup>®</sup> is a marketed product of Vertex Pharmaceuticals.

<sup>2</sup> Ivacaftor<sup>®</sup> is a marketed product of Vertex Pharmaceuticals. Tezacaftor has been submitted for approval by Vertex.



levels overall were 63.4% at screening (prior to treatment with GLPG2222). Consistent with expectation and similar prior VRTX studies, there was no significant impact on ppFEV1 levels.

	<b>Placebo (n=11)</b>	<b>Dose A (n=10)</b>	<b>Dose B (n=10)</b>	<b>Dose C (n=14)</b>	<b>Dose D (n=14)</b>
<b>Sweat chloride, mean change Day 15 vs baseline, in mmol/L</b>	-5.0 (2.93 <sup>^</sup> )	-9.6 (3.24)	-7.7 (3.46)	-16.2 (2.62)*	-12.5 (2.62)
<b>Sweat chloride, mean change Day 29 vs baseline, in mmol/L</b>	-2.5 (2.79)	-5.8 (3.08)	-6.6 (3.29)	-18.3 (2.49)*	-8.8 (2.49)

\* = p<0.05 (pairwise comparison with Placebo)

<sup>^</sup>= LS-means (SE) from an ANCOVA model with treatment as factor and baseline as covariate with LOCF (Last Observation Carried Forward) method

"We are pleased to have recruited this relatively large study so rapidly during a time in which Vertex was recruiting for its Phase 3 with tezacaftor and ivacaftor. The FLAMINGO results, coming on the back of the positive ALBATROSS patient study findings, further support that GLPG2222 was well tolerated in CF patients. In addition, the exposures achieved, coupled with the activity observed on sweat chloride, support our dose selection plans for the triple combination therapy," said Dr. Piet Wigerinck, CSO of Galapagos. "C1 corrector GLPG2222 is the most validated component for all our investigational triple combination therapies planned."

#### **Start of Phase 1 study with GLPG2851, \$10 million milestone payment**

A Phase 1 study with backup novel C1 corrector GLPG2851 for cystic fibrosis (CF) has started, triggering a \$10 million milestone payment from its collaboration partner AbbVie for this achievement.

The aim of the Phase 1 study is to evaluate the safety, tolerability and pharmacokinetics of GLPG2851 in healthy volunteers. The randomized, double-blind, placebo controlled, single center study is being conducted in Belgium. Topline results from this Phase 1 study are expected to be disclosed at a future medical conference.

In order to bring a more effective therapy to the majority of CF patients, Galapagos and AbbVie have a large portfolio of candidates addressing three complementary components for a potential combination therapy. GLPG2851 is the second C1 corrector, chemically distinct from the same series as the first C1 corrector. It will be a back-up corrector for the triple combo's expected to be tested in patients in the future. Both C1 and C2 series of correctors have different modes of action.

#### **First dosing of PELICAN Phase 2 study with GLPG2737 in combination with Orkambi**

First dosing of a CF patient has taken place in the PELICAN study, which is being run in 10 sites in Germany. The aim of the double-blind, placebo-controlled Phase 2 study is to evaluate the safety and tolerability of novel C2 corrector GLPG2737 in adult CF patients who are homozygous for the Class II F508del mutation. Patients will remain on their stable dose of Orkambi and will receive treatment with GLPG2737 over a period of 4 weeks, with up to 3 weeks' follow up. Secondary endpoints include measurements of sweat chloride, ppFEV%, and CFQ-R. Topline results are expected in H1 2018.

#### **Expected first dosing of CF patient with investigational triple combination therapy**

Galapagos announces that discussions with the UK MHRA are ongoing and Galapagos expects to dose the first patient with an investigational triple combination therapy - comprising potentiator GLPG2451, C1 corrector GLPG2222, and C2 corrector GLPG2737 - in Q1 2018. An interim readout from this first triple combination patient study is expected in the summer of 2018.

#### **First dosing in Phase 1 study with second triple combination**



The first healthy volunteer was dosed with novel investigational triple combination therapy comprising potentiator GLPG3067, C1 corrector GLPG2222, and C2 corrector GLPG2737 in a Phase 1 study in Belgium. The aim of the Phase 1, randomized, double-blinded, placebo-controlled study is to evaluate the safety, tolerability and pharmacokinetics of multiple ascending doses of this second investigational triple combination therapy in up to 16 healthy volunteers. Topline results from this Phase 1 study are expected to be presented at a future medical conference.

GLPG2222, GLPG2451, GLPG2737, GLPG2851, GLPG3067 are investigational therapies; their safety and efficacy have not been established.

### **About Galapagos**

Galapagos (Euronext & NASDAQ: GLPG) is a clinical-stage biotechnology company specialized in the discovery and development of small molecule medicines with novel modes of action. Galapagos' pipeline comprises Phase 3 through to discovery programs in cystic fibrosis, inflammation, fibrosis, osteoarthritis and other indications. Our target discovery platform has delivered three novel mechanisms showing promising patient results in, respectively, inflammatory diseases, idiopathic fibrosis and atopic dermatitis. Galapagos is focused on the development and commercialization of novel medicines that will improve people's lives. The Galapagos group, including fee-for-service subsidiary Fidelta, has approximately 578 employees, operating from its Mechelen, Belgium headquarters and facilities in the Netherlands, France, and Croatia. More information at [www.glpj.com](http://www.glpj.com).

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### **Forward-looking statements**

*This release may contain forward-looking statements, including statements regarding the potential activity of GLPG2222, GLPG2851, GLPG2451, GLPG2737, or GLPG3067 (or any combinations thereof), the anticipated timing of clinical studies with, and plans related to, GLPG2222, GLPG2851, GLPG2451, GLPG2737, or GLPG3067 (or any combinations thereof), the timing, progression and/or results (including the reporting thereof) of such studies and plans, statements regarding potential triple combination therapies and statements regarding interactions with regulatory authorities. Galapagos cautions the reader that forward-looking statements are not guarantees of future performance. Forward-looking statements involve known and unknown risks, uncertainties and other factors which might cause the actual results, financial condition and liquidity, performance or achievements of Galapagos, or industry results, to be materially different from any historic or future results, financial conditions and liquidity, performance or achievements expressed or implied by such forward-looking statements. In addition, even if Galapagos' results, performance, financial condition and liquidity, and the development of the industry in which it operates are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. Among the factors that may result in differences are the inherent uncertainties associated with competitive developments, clinical trial and product development activities and regulatory approval requirements (including that data from the ongoing and planned clinical research programs in CF may not support registration or further development of GLPG2222, GLPG2851, GLPG2451, GLPG2737, GLPG3067, or potential triple combination therapies, due to safety, efficacy or other reasons), Galapagos' reliance on collaborations with third parties (including its collaboration partner for CF, AbbVie), and estimating the commercial potential of Galapagos' product candidates. A further list and description of these risks, uncertainties and other risks can be found in Galapagos' Securities and Exchange Commission (SEC) filings and reports, including in Galapagos' most recent annual report on Form 20-F filed with the SEC and subsequent filings and reports filed by Galapagos*



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