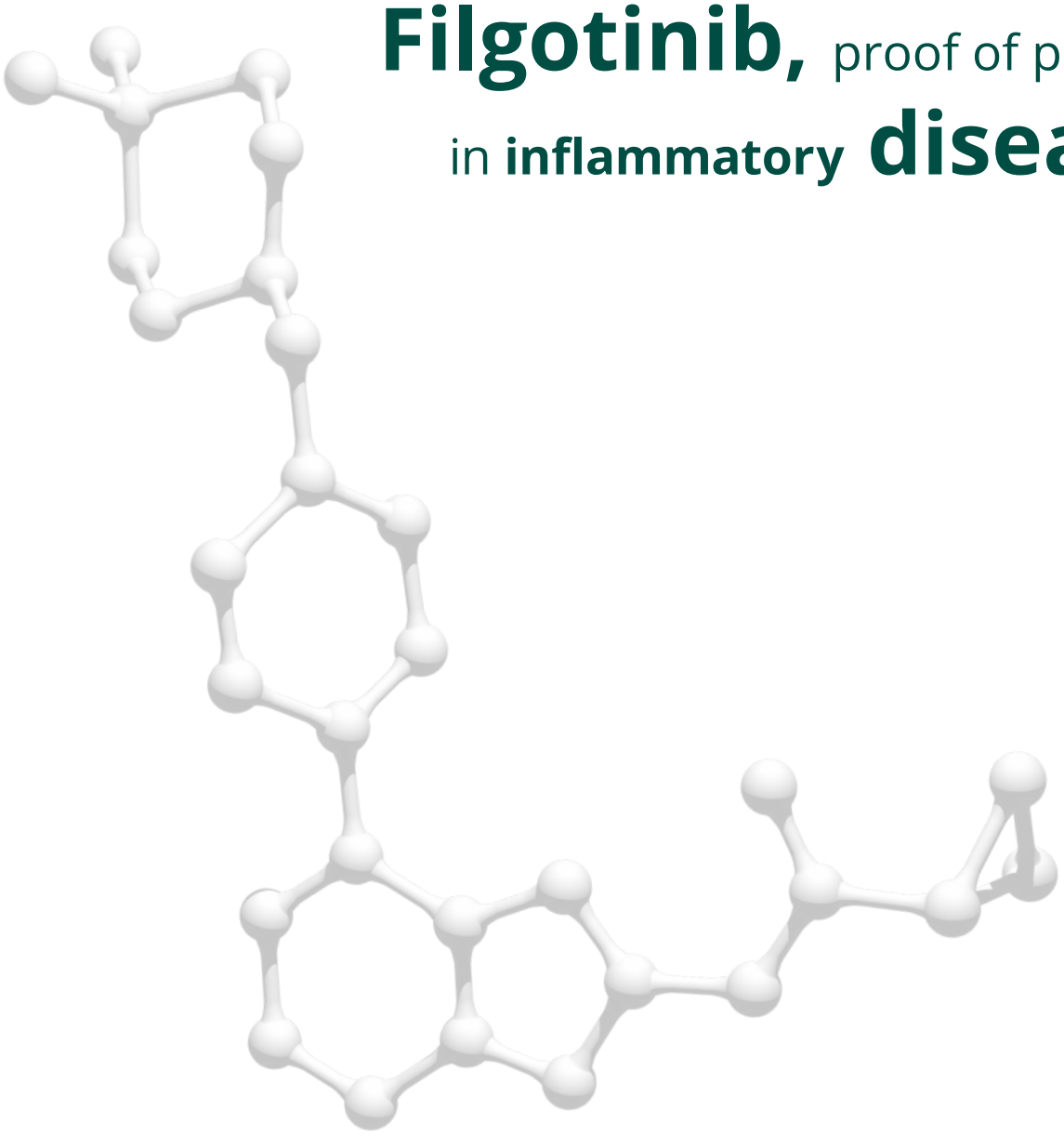
R&D

Research &
Development

Filgotinib, proof of platform in **inflammatory diseases**



Filgotinib, a selective JAK1-inhibitor which has shown activity and favorable tolerability in inflammatory diseases.

The Galapagos pipeline

We aim to discover, develop, and prepare for future commercialization of medicines with novel modes of action, addressing disease areas of high unmet medical need. Our pipeline includes programs ranging from discovery to Phase 3 clinical trials in inflammation, fibrosis, cystic fibrosis (CF), and other indications. Our target discovery platform is applicable across many therapeutic areas. Our clinical late stage programs include: filgotinib, which is currently in Phase 3 trials in rheumatoid arthritis (RA) and Crohn's disease (CD), in Phase 2/3 in ulcerative colitis (UC) and in Phase 2 in multiple additional indications; GLPG1690, our fully proprietary autotaxin inhibitor, which is expected to initiate pivotal trials for idiopathic pulmonary fibrosis (IPF) in 2018; our CF portfolio of drugs aimed at a triple combination therapy for 90% of CF patients, for which we plan to report interim results from a first triple combination therapy in a Phase 2 clinical trial in 2018; GLPG1972 for osteoarthritis (OA), which is expected to be dosed in a global Phase 2 trial in OA patients in 2018; and MOR106, which is expected to be dosed in a Phase 2 trial in atopic dermatitis (AtD) patients in 2018. Most of these programs are based on inhibiting targets which were identified using our target discovery platform.

We have collaborations with Gilead for filgotinib, with AbbVie for CF, with Servier for GLPG1972, and with MorphoSys for MOR106. The following table highlights key aspects of our development programs at the start of 2018:

Area	Pre-clinical	Ph1	Ph2	Ph3
Filgotinib	10+ indications evaluated in Ph2 and Ph 3, pivotal trial completion as of 2018			
IPF	Multiple late stage trial to start in H1'18			
CF	Ph2 to start Q1 '18			
AtD	Ph2 to start H1 '18			
OA	Ph2 to start H1 '18			
Inflammation & fibrosis	>20 programs			

Proprietary target discovery platform

Our target discovery platform provides a significant and substantial competitive advantage in our portfolio of novel mode of action product candidates as it:

- closely mimics the *in vivo* situation through the use of primary human cells with relevant trigger and readout for a specific disease phenotype
- identifies the optimal point to intervene in a disease pathway by knocking down of a given protein in these assays
- enables us to analyze rapidly all of the drugable genome and select pharmaceutically tractable protein targets directly by their ability to regulate key disease biology

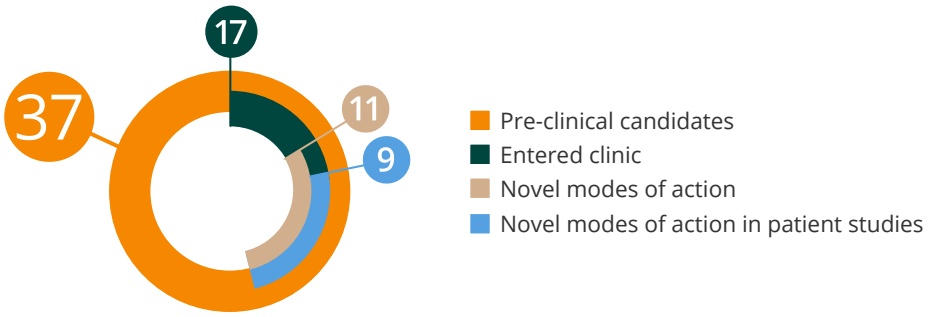
Our product candidate filgotinib acts on a target whose role in the specific disease was discovered by us using our discovery platform and we believe is a proof of success of this approach. Filgotinib acts on JAK1 and we believe has potential for a best-in-class profile. We believe that further proof of this approach was shown in 2017 with autotaxin inhibitor GLPG1690 in IPF patients, and with fully human monoclonal antibody MOR106 directed toward IL-17C in AtD patients. Autotaxin and IL-17C are targets we discovered for these diseases.

The human genome is made up of tens of thousands of genes which code for the proteins that make up the human body. Nearly all chronic diseases and disorders are caused by a disruption in the normal function of certain proteins. The main goal of the industry is to develop molecules that alter the activity of these proteins so that normal function returns and the cause of the disease is minimized or eliminated. One of the main obstacles in discovering new drugs is to understand exactly which of the body's thousands of proteins play a key role in a particular disease. Once these proteins are discovered, they become targets for drug discovery and development. Finding these targets is one of the critical steps in the drug discovery process. Our approach to target discovery is unique as our discovery platform focuses on target identification using primary human cells, which provides a good system to study the effect that a protein might have on the disease in the human body.

In order to study proteins in human cells, we take advantage of the distinctive properties of adenoviruses. Adenovirus is the virus that causes the common cold and has the capability to infect almost every type of human cell. The adenoviruses we work with have been engineered to act as a shuttle vehicle, allowing the delivery of specific pieces of DNA into human cells. Additionally, these viruses have been made replication incompetent, meaning they do not replicate in the human cell they infect, and so do not interfere with the processes in the cell. We engineered the viruses to carry small pieces of DNA, specific for individual human genes. When the virus enters the cell, this DNA piece leads to the production of a short sequence of RNA that is processed in the cell to become "short interfering RNA," or siRNA, which specifically interferes with the mRNA of the protein it was designed for. By using these viruses, we can cause the cells to block, or "knock-down," the production of a certain protein, mimicking what a small molecule drug does in the human body. We built a collection with these adenoviruses, now in excess of 20,000 viruses, that addresses around 6,000 drugable genes.

Our drug discovery research is based on the targets discovered using this technology. Once a target is validated, it is tested against large collections of chemical small molecules to identify chemical structures that interact with the target and block or activate protein production. These chemical structures are then optimized to obtain "drug-like" characteristics followed by testing of the product candidate in the clinic.

This discovery approach may increase the chances of success in bringing new mode of action drugs to the market. Since 2009, we have generated 37 pre-clinical candidates of which 27 have novel modes of action. Of these, 17 have entered the clinic, 11 with novel modes of action.

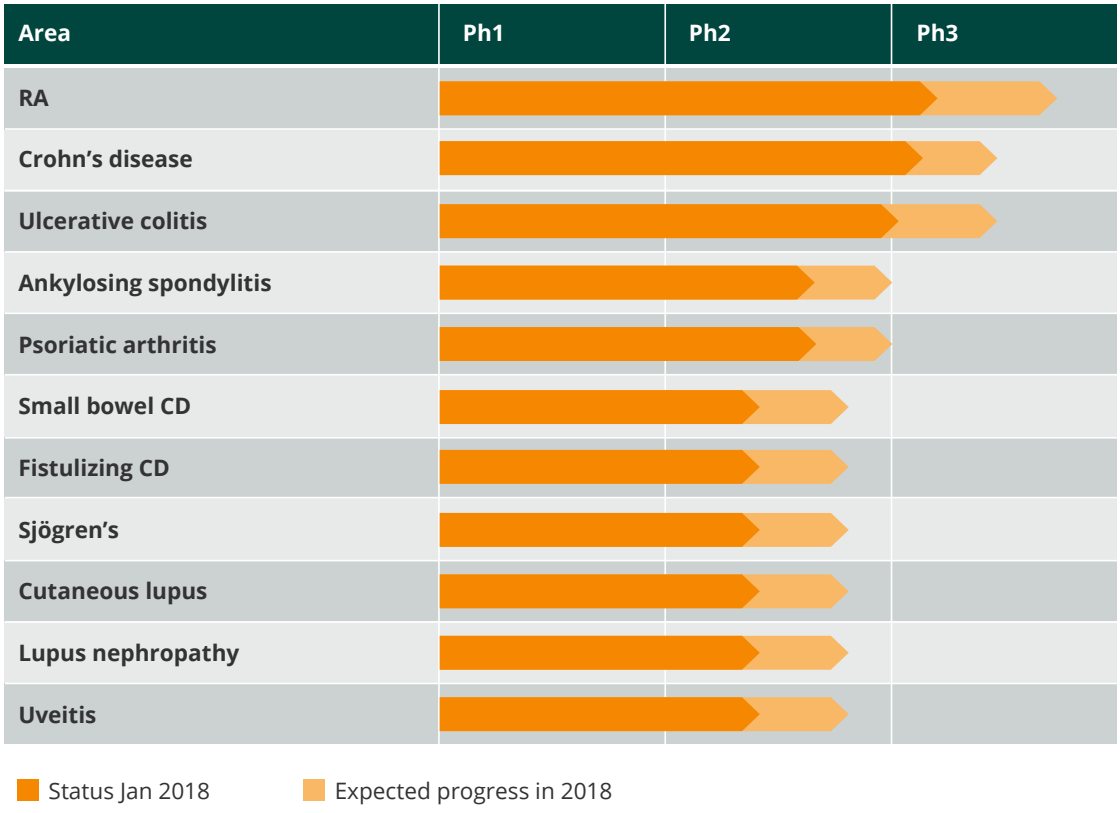


In addition to our pipeline of molecules in the clinic, we have multiple discovery programs which are advancing toward clinical development. We are exploring new modes of action in AS, psoriatic arthritis, IBD, AtD, lupus, IPF, systemic sclerosis, nonalcoholic steatohepatitis, type 2 diabetes, and hepatitis B.

Filgotinib: selective JAK1 inhibitor with a potential best-in-class product profile

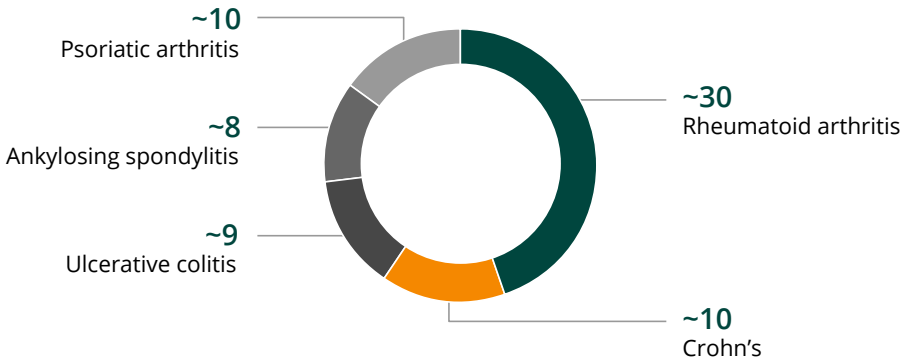
We believe that filgotinib is a promising candidate for the treatment of RA, CD and potentially other inflammatory diseases. We have an exclusive collaboration agreement with Gilead to develop and commercialize filgotinib in multiple diseases. Under the terms of the collaboration, Gilead is primarily responsible for development and seeking regulatory approval of the licensed product. We assist Gilead with certain development activities. Gilead initiated Phase 3 clinical programs in RA and CD and a Phase 2b/3 program in UC in 2016, and we and Gilead initiated multiple Phase 2 trials with filgotinib in additional indications in 2017:

Building the filgotinib franchise



Markets for inflammation drugs are considerable and growing. We estimate that the inflammation market could grow to ~$65 billion by 2027, driven by new drugs filling the current unmet need for oral, monotherapy treatments with a rapid response, and higher efficacy maintained over time. RA remains the largest market at approximately $30 billion in these forecasts, with the other main markets growing considerably as well:

Inflammation market in ~2027, $B



Based on the Phase 2 data observed with filgotinib in RA and CD thus far, we believe that filgotinib has the potential to improve treatment standards substantially in RA and inflammatory bowel diseases. Compared with biologic agents, filgotinib is orally administered, with a rapid onset, sustained response, and potential for monotherapy. ACR scores with filgotinib in Phase 2 trials in RA patients are encouraging, and CDAI remission and SES-CD50 scores are similarly promising with filgotinib in a Phase 2 trial in CD patients who are naïve to TNF therapy. Filgotinib is highly selective for JAK1, resulting in favorable tolerability so far, including low rates of infection.

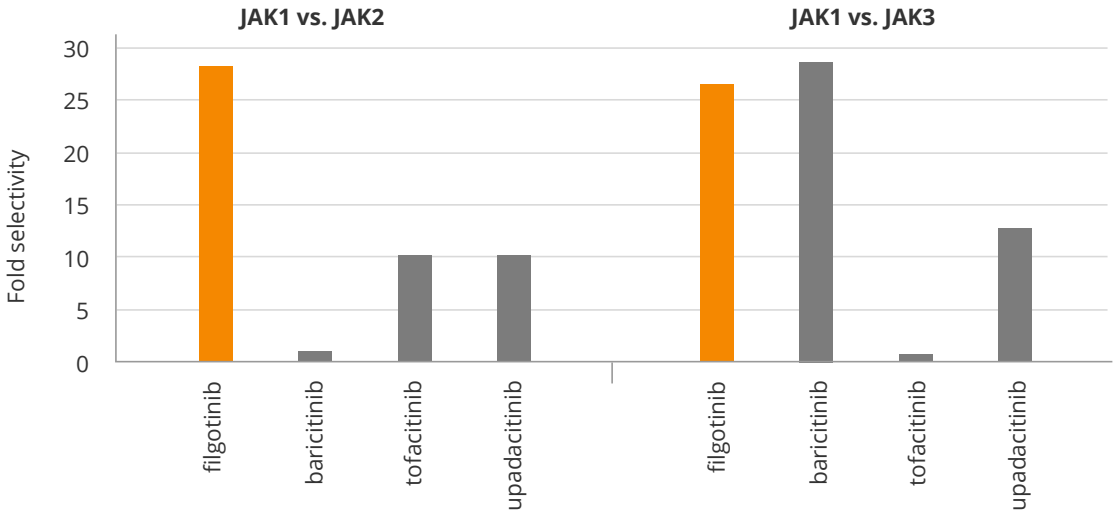
Our filgotinib program in RA

RA is a chronic autoimmune disease that affects ~3 million patients in the U.S. and the five largest European markets. RA is characterized by inflammation and degeneration of the joints. Patients suffer from pain, stiffness, and restricted mobility due to a persistent inflammation of multiple joints, ultimately resulting in irreversible damage of the joint cartilage and bone. According to GlobalData, sales of RA therapeutics across the 10 main healthcare markets was $21.7 billion in 2017, with the current market being dominated by injectable, biological therapies. Biologics, mostly TNF therapies, need to be injected and often lose their effect over time, so there continues to be a considerable unmet need with regard to efficacy, safety, and convenience of use with existing treatments.

New oral therapies that target the Janus kinase, or JAK, signaling pathway are emerging to treat inflammatory diseases; non-specific JAK inhibitors, however, have a range of side effects, including aberrations in low-density lipoprotein, or LDL, cholesterol and red blood and NK cell counts. We discovered JAK1 in an inflammation target discovery assay in 2003 and subsequently discovered filgotinib as a JAK1 specific inhibitor small molecule. In a human whole blood assay we demonstrated that filgotinib, with a nearly 30-fold selectivity for JAK1 over JAK2 and for JAK1 over JAK3, is more selective for JAK1 than any other JAK inhibitor known to us to be either approved for sale or in clinical development in inflammation; these findings were independently corroborated by Dr. Iain McInnes ("*Ex Vivo* Comparison of Baricitinib, Upadacitinib, Filgotinib, and Tofacitinib for Cytokine Signaling in Human Leukocyte Subpopulations," ACR 2017).

The high selectivity of filgotinib for JAK1 may allow for a positive efficacy profile, with an improved safety profile for filgotinib due to the improved selectivity over JAK2 and JAK3.

Filgotinib
Highly JAK1 selective



Source: Galapagos human whole blood assay

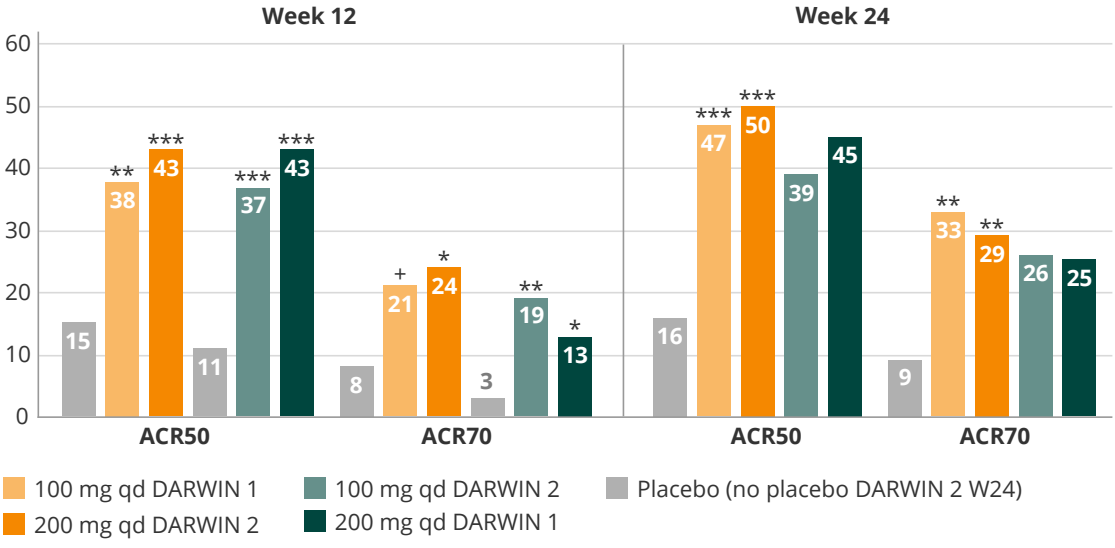
Source: Galapagos biochemical assay

Our clinical program for filgotinib for RA

Clinical trials to date have shown that filgotinib is well-tolerated, with atherogenic index improvement, absence of anemia, low infection rates and low incidence of deep venous thrombosis and pulmonary embolisms. We believe its once-a-day oral dosage and its low risk for drug-drug interactions make it convenient for patient use.

We reported final 24-week data from DARWIN 1 (594 patients, add-on to methotrexate) and DARWIN 2 (283 patients, monotherapy) Phase 2b dose-range finding clinical trials in insufficient methotrexate responders with moderate to severe RA in 2015. Both trials achieved the primary endpoints (ACR20). Below are the ACR50 and ACR70 scores at 12 and 24 weeks for 100 and 200 mg qd in both DARWIN 1 and DARWIN 2:

% responders



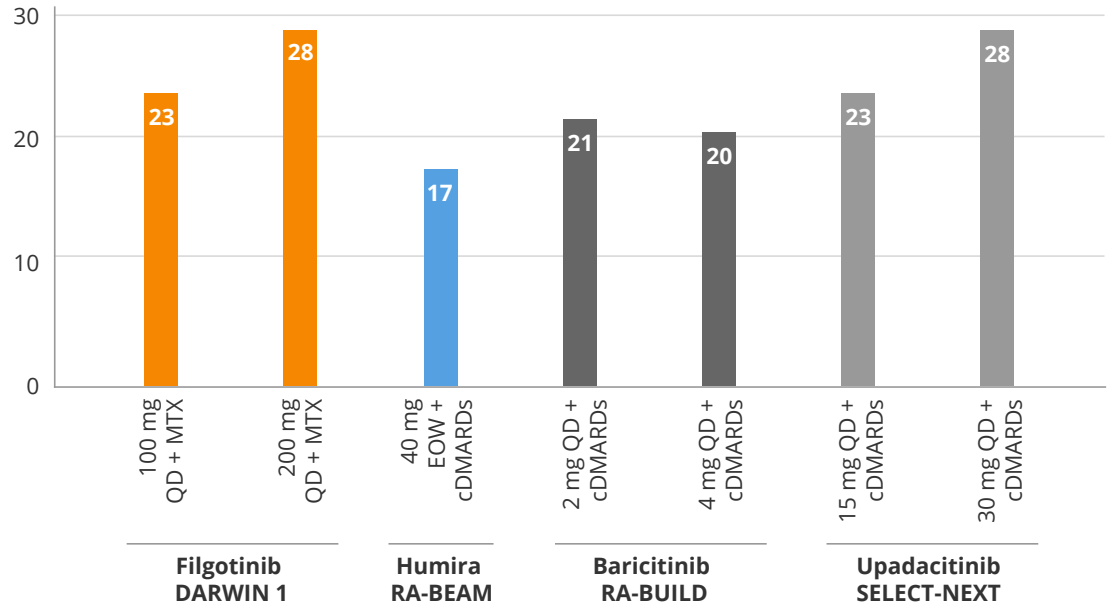
+: p<0.10; *: p<0.05; **: p<0.01; ***: p<0.001

Overall, there was no statistically relevant difference between the once-daily and twice-daily dosing regimens in DARWIN 1. Both trials showed a rapid onset of activity, as of week one for ACR and DAS28(CRP) responses. In DARWIN 1 (200 mg bid) and in DARWIN 2 (100 mg qd) up to 50% of the patients reached low disease activity or remission. The 100 mg and 200 mg qd doses achieved similar levels of activity overall.

Below follows information regarding activity of filgotinib, other JAKs, and another mechanism (anti-TNF) of RA treatment in separate patient trials; JAKs have scored higher on ACR50% in recent trials than the mechanism most often used today:

Superior activity JAK class in RA

ACR50% (W12, active delta), % responders

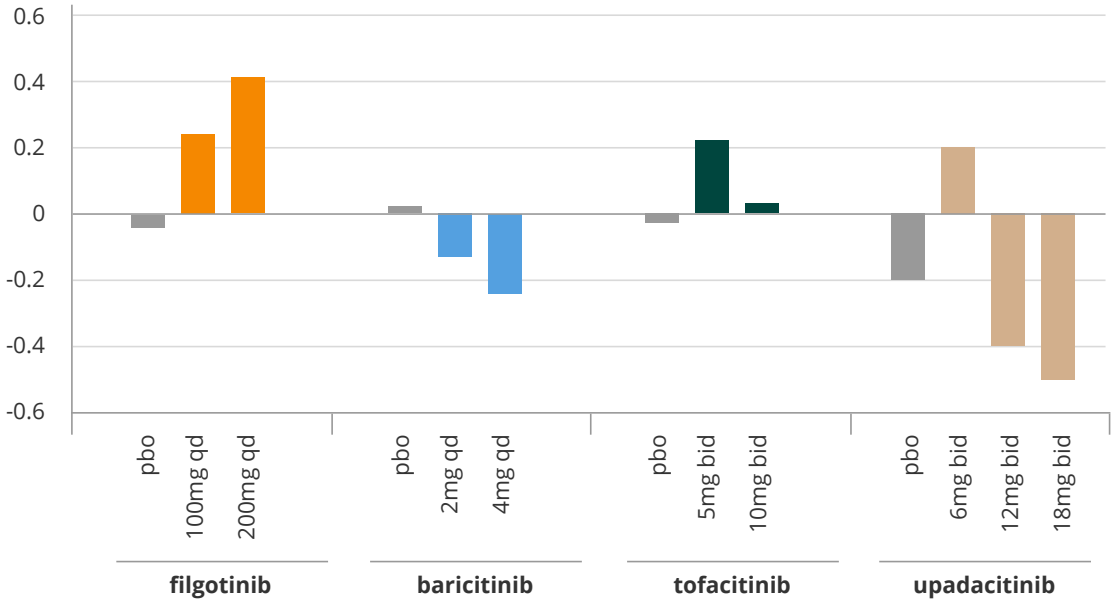


Note: data from separate studies not conducted by the Company

Filgotinib's improvement in hemoglobin shown in DARWIN 1 and 2 potentially differentiates it when compared to impact on hemoglobin shown by other JAK inhibitors in their respective RA trials:

Hemoglobin

Hb mean CFB (g/dL), W12

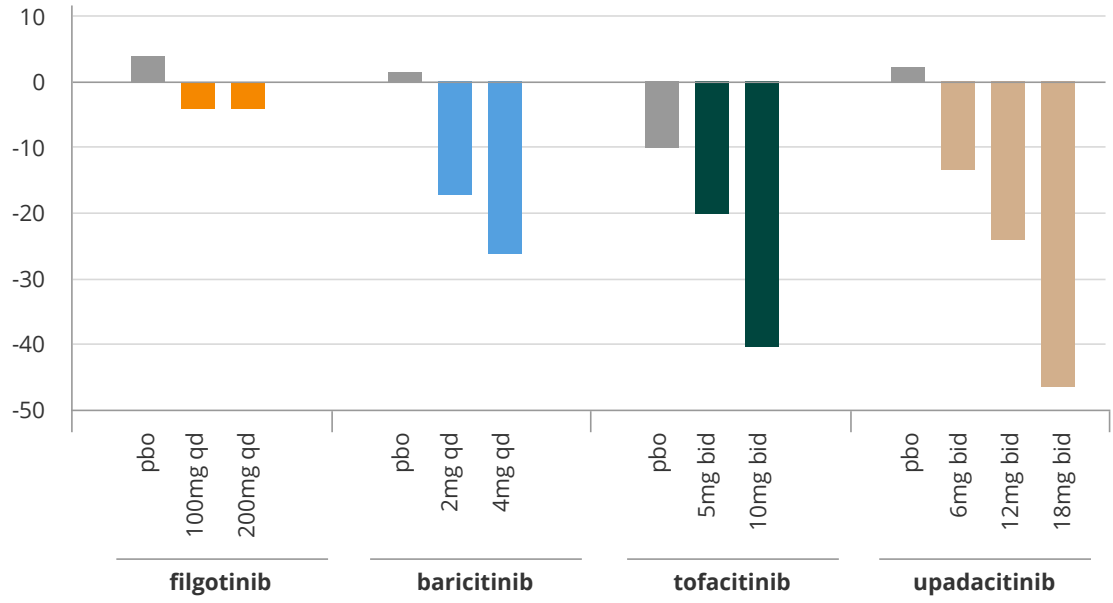


Note: data from separate RA studies not conducted by the Company. **filgotinib** – Westhovens *et al.*, and Kavanaugh *et al.*, ARD 2016; **baricitinib** – Dougados *et al.*, Annrheumdis 2016, RA-BUILD; **tofacitinib** – FDA AdComm briefing document May 2012; **upadacitinib** – Genovese *et al.* ACR 2017

Rheumatoid arthritis patients experience a decrease in natural killer (NK) cells as a consequence of their disease. Filgotinib's lack of impact on NK cells shown in DARWIN 1 and 2 potentially differentiates it when compared to the impact on NK cells shown by other JAK inhibitors in their respective RA trials:

NK cells

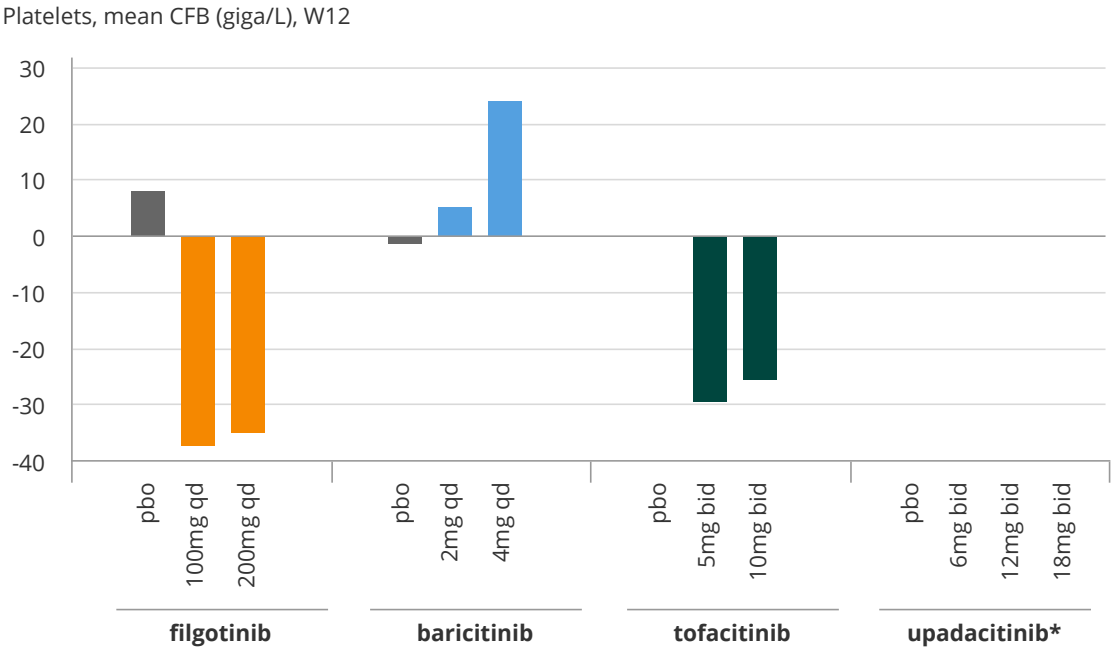
NK cells mean CFB (%), W12



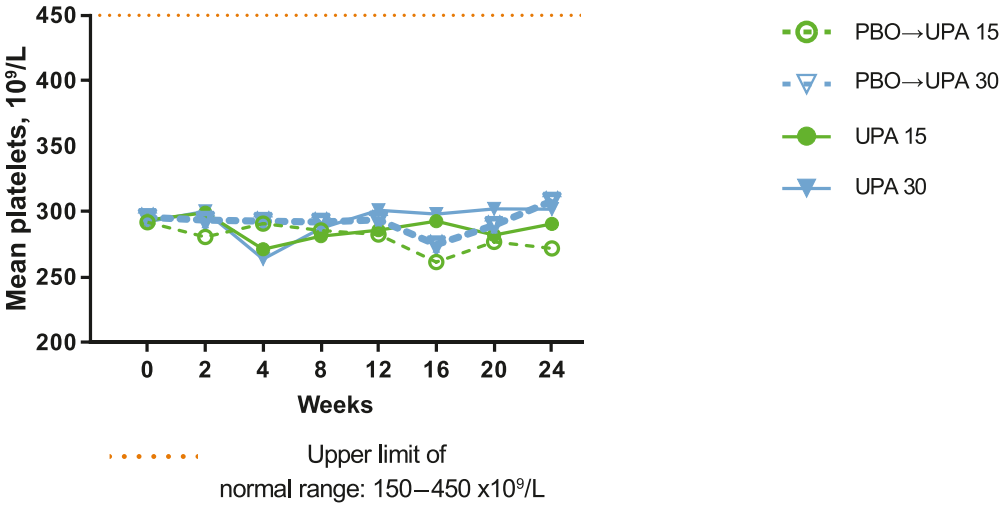
Note: data from separate RA studies not conducted by the Company. **filgotinib** – Westhovens *et al.*, and Kavanaugh *et al.*, ARD 2016; **baricitinib** – Dougados *et al.*, Annrheumdis 2016, RA-BUILD and Tanaka EULAR 2016 abstract RA-BEAM; **tofacitinib** – Van Vollenhoven abstract 2013, median CFB at W6; **upadacitinib** – Genovese *et al.* A&R 2016 BALANCE 2.

Rheumatoid arthritis patients experience platelet elevation as a consequence of their disease. Filgotinib's reduction of platelets to more normal levels, as shown in DARWIN 1 and 2, potentially differentiates it when compared to the impact on platelets shown by other JAK inhibitors in their respective RA trials:

Reduction of platelets



Note: data from separate RA trials and not conducted by the company. **filgotinib** – DARWIN 1 W12 results; **baricitinib** – Dougados *et al.*, Annrheumdis 2016; **tofacitinib** – FDA AdComm briefing document May 2012, ***upadacitinib*** – for data see graph below, Genovese *et al.* ACR 2017



Source: Genovese *et al.* ACR 2017

Also due to its high selectivity for JAK1, filgotinib has shown the lowest rates of infection, deep venous thrombosis (DVT), and pulmonary embolisms (PEs) per 100 patient year experience (PYE) versus other JAKs and other therapy types thus far in their respective trials in RA:

Low incidence DVT and infections

Event Per 100 PYE	filgotinib (50-)200mg daily DARWIN 3 Wk 84 Genovese, ACR2017	upadacitinib 6 and 12mg BID Genovese *et al.*, ACR2017	baricitinib 2 and 4mg QD Genovese *et al.*, ACR2017	tofacitinib 5mg bid Wollenhaupt *et al.*, ACR2017	tocilizumab 4 and 8 mg / kg Genovese *et al.*, ACR2012	adalimumab Burmester *et al.*, 2011
Patient year exposure	1,708	725	6,637	5,891	14,994	23,943
Serious infection	1.5	2.3	2.9	2.2	4.5	4.6
Herpes Zoster	1.2	3.7	3.2	3.6	NR	NR
DVT / PEs	2 / 1,708	5 / 725	31 / 6,754	3 / 1,849[1]	–	–
N cases / 100PY	0.1	0.7	0.5	0.2		

Note: data from separate RA studies not conducted by the Company.
(1) DVT / PE data on tofacitinib from Mease et al, ACR 2017, 5mg bid

DARWIN 3 is a multi-center, open-label, long-term follow-up safety and efficacy trial of subjects who have completed either DARWIN 1 or DARWIN 2. All subjects started the trial at the same dose level, either at 200 mg once per day or at 100 mg twice per day (except for males in the U.S. sites of these trials who receive a maximum daily dose of 100 mg), depending on the regimen administered during the preceding trial, with DARWIN 1 subjects continuing to use filgotinib in combination with MTX.

Galapagos and Gilead reported findings from DARWIN 3 at 60 and 84 weeks of treatment in the course of 2017. Promising activity levels were maintained and favorable findings relating to tolerability profile were reported; data from both time points in DARWIN 3 were consistent with the risk/benefit profiles reported in DARWIN 1 and 2, as presented by Dr. Mark Genovese at ACR 2017 ("Long-term Safety of Filgotinib in the Treatment of Rheumatoid Arthritis: Week 84 Data from a Phase 2b Open-Label Extension Study").

FINCH Phase 3 program with filgotinib in RA

In August 2016, Gilead initiated the FINCH global Phase 3 program investigating the efficacy and safety of 100 mg and 200 mg filgotinib once daily, in RA patient populations, ranging from early stage to biologic-experienced patients:

FINCH 1 is a 52-week, randomized, placebo- and adalimumab-controlled trial in combination with methotrexate (MTX) in an expected 1,650 patients who have had inadequate response to MTX. The primary endpoint is ACR20 at week 12. ACR20 response rate signifies a 20% or greater improvement in the number of swollen and tender joints as well as a 20% or greater improvement in three out of five other disease-activity measures. ACR50 and ACR70 reflect the same, respectively for 50% and 70% response rates. The trial will also include radiographic assessment at weeks 24 and 52. We expect Gilead to complete recruitment for FINCH 1 in Q2 2018.

FINCH 2 is a 24-week, randomized, placebo-controlled trial in an expected 423 patients who are on conventional disease-modifying anti-rheumatic drugs (cDMARD), and have had an inadequate response to biological treatment. The primary endpoint is ACR20 at week 12. We and Gilead expect to report topline findings from the FINCH 2 trial in H2 2018.

FINCH 3 is a 52-week, randomized trial in an expected 1,200 MTX-naïve patients to study filgotinib in combination with MTX, as well as monotherapy. The primary endpoint is ACR20 at week 24. Radiographic progression will also be assessed. We expect Gilead to complete recruitment for FINCH 3 in Q3 2018.

Gilead is performing a single dedicated male patient safety trial in UC patients concurrent to all Phase 3 programs.

Our filgotinib program in inflammatory bowel disease (IBD)

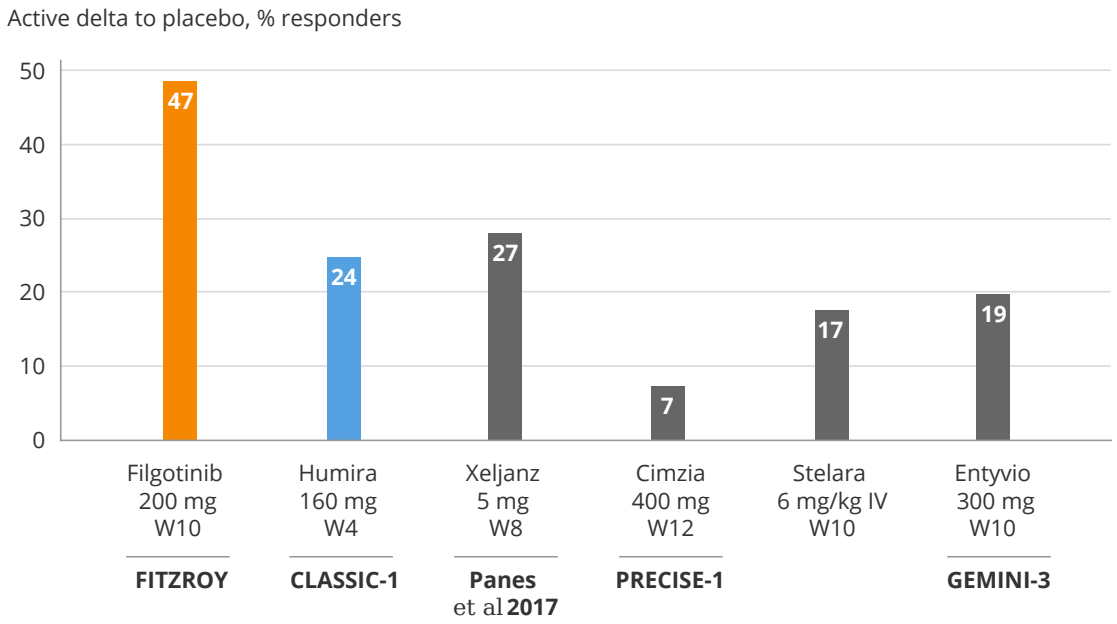
IBD includes CD and UC. We observed high activity and a favorable safety profile in a Phase 2 trial with filgotinib in CD, as reported in *The Lancet* (Vermeire *et al*) in 2016. The profile we saw with filgotinib in this CD patient trial leads us to believe the product candidate may show activity and tolerability in UC patient trials as well. IBD affects approximately 2 million patients (of which approximately 0.5 million are being treated with biologics) in the United States and Europe, and the market for IBD therapies is approximately $9 billion today, according to GlobalData. Current treatments are dominated by anti-TNF agents, with new biologic products gaining some ground in second line treatment.

CD is an IBD of unknown cause, resulting in chronic inflammation of the gastrointestinal tract with a relapsing and remitting course. Today, only 10% of CD patients achieve prolonged clinical remission. There are currently no highly effective oral therapies approved for CD and, similar to RA, treatment is dominated by injectable, biologic treatments including anti-TNF therapies. Anti-TNF agents have improved the management of CD; however, not all patients respond to these drugs, and secondary loss of response is reported in up to 50% of patients per year in placebo-controlled trials. There continues to be a considerable unmet need with these existing treatments. Dysregulation of the JAK signaling pathway has also been associated with CD, and we believe that filgotinib, with its high selectivity for JAK1, is a highly attractive candidate for the treatment of CD. By inhibiting JAK1 but not JAK2, unwanted effects such as anemia may be prevented. This absence of anemia is of particular importance to IBD patients, who frequently experience fecal blood loss.

Our clinical program with filgotinib in CD

Our FITZROY Phase 2 trial (174 patients) evaluated filgotinib once-daily versus placebo in patients with moderate to severely active CD and mucosal ulceration. Patients recruited were either anti-TNF naïve or anti-TNF failures. FITZROY was the first trial in CD to require endoscopic confirmation of lesions at entry, and also to include a placebo control on endoscopy. The trial comprised two parts, each of 10 weeks duration: the first part investigated the safety and efficacy of filgotinib 200 mg once daily versus placebo, while the second part of the trial investigated continued treatment through 20 weeks in an observational exploratory design. As reported in *The Lancet* (Vermeire *et al*), the FITZROY trial achieved the primary endpoint of clinical remission at 10 weeks: the percentage of patients overall achieving a Crohn's Disease Activity Index (CDAI) score lower than 150 was statistically significantly higher in patients treated with filgotinib (47%) versus patients receiving placebo (23%). The share of patients achieving 100-points clinical response (60%) also was significant versus those receiving placebo (41%). We believe that the activity observed with filgotinib in TNF naïve patients in FITZROY compared favorably to that seen with other treatments in other, separate trials:

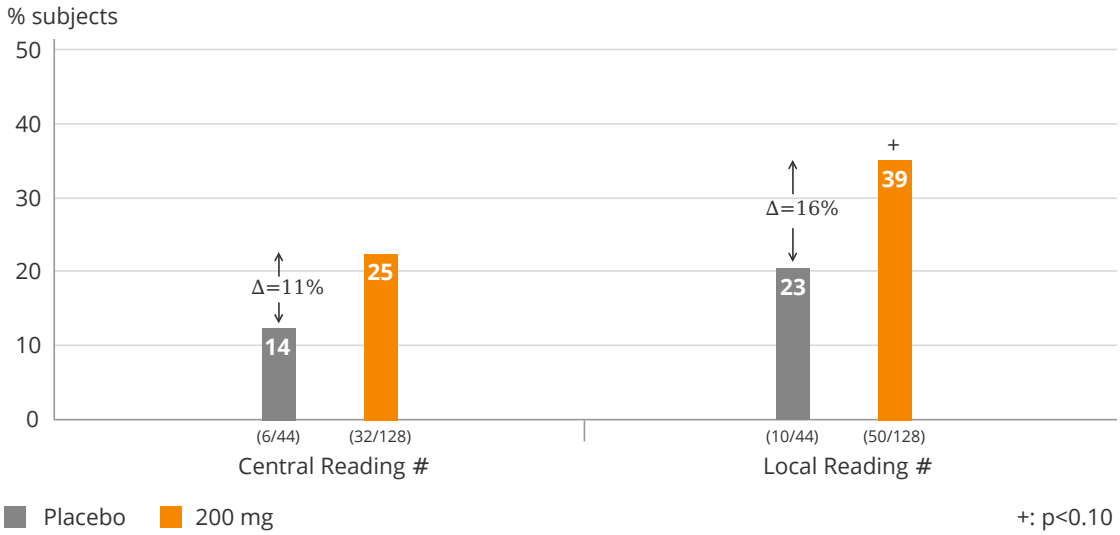
Activity readouts in CD, TNF naive
Clinical remission: induction



Note: data not from head-to-head studies

Improvement in quality of life, histopathology, endoscopy assessment and biomarkers of inflammatory activity were also observed at week 10. Overall mean change in histopathology scores at week 10 for patients treated with filgotinib (-3.5) versus placebo (-0.6) was significantly different, confirming the clinical responses in the tissues of patients. More patients on filgotinib showed >50% improvement in SES-CD (endoscopy) scores versus placebo patients at week 10:

SES-CD50 achievement in FITZROY at week 10



Only using segments explored at both baseline and week 10 (matching segments)

Vermeire *et al., The Lancet*, 2016

Clinical responses were maintained from week 10 to week 20. Non-responders in the placebo arm from the first ten weeks received filgotinib 100 mg in the second ten weeks and showed improvement in clinical remission during the second part of the trial.

Overall, in the FITZROY trial at 20 weeks of treatment, filgotinib demonstrated a favorable safety profile consistent with the DARWIN trials in RA. An increase in hemoglobin was also observed in FITZROY, without difference between filgotinib and placebo. No clinically significant changes from baseline in neutrophils or liver function tests were observed.

Gilead initiated a Phase 3 trial (DIVERSITY) with filgotinib in CD in November 2016. The DIVERSITY Phase 3 trial investigates efficacy and safety of 100 mg and 200 mg filgotinib once-daily compared to placebo in patients with moderately to severely active disease including those with prior antibody therapy failure. Gilead will recruit approximately 1,300 patients from the United States, Europe, Latin America, Canada, and Asia/Pacific regions. Men and women in the DIVERSITY trial will be randomized to receive placebo, 100 mg or 200 mg filgotinib. In the United States, males may receive 200 mg if they failed at least one anti-TNF and vedolizumab, a monoclonal anti-integrin antibody marketed by Takeda. Gilead expects to complete recruitment for DIVERSITY in the first half of 2019.

In March 2017, Gilead initiated a Phase 2 trial in small bowel CD and a Phase 2 trial in fistulizing CD.

Our clinical program with filgotinib in UC

UC is an inflammatory bowel disease resulting in ulcerations and inflammation of the colon and rectum. Unlike CD, UC involves damaging inflammation of only the colon and rectum. According to GlobalData, there were 1.2 million patients being treated for ulcerative colitis in the 7 major markets, for a combined total sales of just over $5 billion in 2017. Although the introduction of anti-TNF biologics has improved the treatment of some patients, only 33% of patients will achieve long-term remission, and many patients lose their response to treatment over time. The medical need for improved efficacy is high and likely could be achieved by a new mechanism of action.

Gilead initiated the SELECTION Phase 2b/3 trial in UC with filgotinib in December 2016. SELECTION investigates efficacy and safety of 100 mg and 200 mg filgotinib once-daily compared to placebo in patients with moderately to severely active disease including those with prior antibody therapy failure. Gilead will recruit approximately 1,300 patients from the United States, Europe, Latin America, Canada, and Asia/Pacific regions. The SELECTION Phase 2b/3 trial in UC will include a futility analysis, serving as the Phase 2b part of this integrated Phase 2b/3 trial. The outcome of the futility analysis is expected to be reported in 2018. Men and women in SELECTION will be randomized to receive placebo, 100 mg or 200 mg filgotinib. In the United States, males may receive 200 mg if they failed at least one anti-TNF and vedolizumab.

Other clinical programs with filgotinib

In the course of 2017, Gilead initiated clinical trials with filgotinib in Sjögren's disease, cutaneous lupus erythematosus, lupus membranous nephropathy, and uveitis. We initiated patient trials with filgotinib in psoriatic arthritis and ankylosing spondylitis, for which we expect to report topline results in 2018.

Psoriatic arthritis

Psoriatic arthritis is an inflammatory form of arthritis, affecting up to 30 percent of psoriasis patients. There are approximately 1 million patients in the U.S. and Europe today, with men and women being affected equally. Psoriatic arthritis can cause swelling, stiffness and pain in and around the joints, cause nail changes and overall fatigue. Studies show that delaying treatment for psoriatic arthritis as little as six months can result in permanent joint damage. Early recognition, diagnosis and treatment of psoriatic arthritis are critical to

relieve pain and inflammation and help prevent joint damage. Despite the availability of a number of treatment options, few current treatments effectively relieve the enthesitis (inflammation of the tendons or ligaments) and symptoms in the joints and the skin.

The EQUATOR Phase 2 trial is a multi-center, randomized, double-blind, placebo-controlled trial to assess the safety and efficacy of the selective JAK1 inhibitor filgotinib in adult patients with moderately to severely active psoriatic arthritis. Approximately 124 patients are planned to be randomized in the trial in a 1:1 ratio to receive 200 mg or placebo once-daily administered for 16 weeks. EQUATOR will recruit in 8 European countries. The EQUATOR trial is fully recruited, and we expect trial completion in the second quarter of 2018.

Primary goal of EQUATOR is to evaluate the effect of filgotinib compared to placebo on the signs and symptoms of psoriatic arthritis, as assessed by the ACR20 at Week 16. The trial also explores the effects of filgotinib on the skin manifestations (psoriasis) as well as other domains like fingers (dactylitis), tendon insertions (tendinitis), spine involvement (spondylitis) and nail involvement.

Ankylosing spondylitis (AS)

AS, a systemic, chronic, and progressive inflammatory arthritis, is one of the most common rheumatic diseases across the globe, affecting ~2 million patients in the U.S., Europe, and Japan today. AS primarily affects the spine and sacroiliac joints and progresses into severe inflammation that fuses the spine, leading to permanent painful stiffness of the back. Currently, there is no known cure for AS, but there are treatments and medications available to reduce symptoms and manage pain. Recent studies show that the newer biologic medications can potentially slow disease progression in some people, with varying responses.

The TORTUGA Phase 2 trial is a multi-center, randomized, double-blind, placebo-controlled trial to assess the safety and efficacy of the selective JAK1 inhibitor filgotinib in adult patients with moderate to severe active AS. Approximately 100 patients are planned to be randomized in the trial in a 1:1 ratio to receive 200 mg or placebo once-daily administered for 12 weeks. TORTUGA will recruit in 8 European countries. We expect to complete TORTUGA in the second half of 2018.

The primary goal of TORTUGA is to evaluate the effect of filgotinib compared to placebo on the signs and symptoms of AS, as assessed by the Ankylosing Spondylitis Disease Activity Score (ASDAS) at Week 12. The trial also explores signs & symptoms of AS, physical function, spinal mobility, enthesitis, spinal and sacroiliac joint inflammation, and safety.

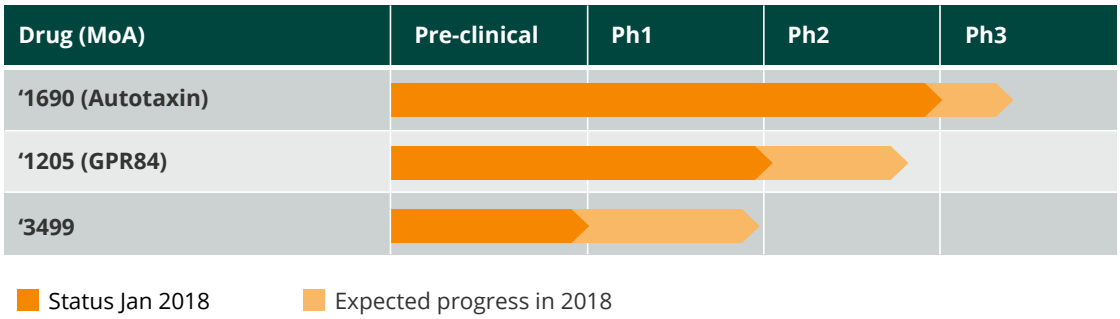
Our IPF programs

IPF is a chronic, relentlessly progressive fibrotic disorder of the lungs that typically affects adults over the age of 40. IPF affects approximately 200,000 patients in the United States and Europe and, as such, we have received orphan designation for our product candidate GLPG1690 in IPF from the European Commission and from the FDA. The clinical prognosis of patients with IPF is poor, as survival at diagnosis is two to four years. Currently, no medical therapies have been found to cure IPF. The medical treatment strategy aims to slow disease progression and improve quality of life. Lung transplantation may be an option for appropriate patients with progressive disease and minimal comorbidities.

Regulatory agencies have approved Esbriet®[3] and Ofev®[4] for the treatment of mild to moderate IPF. Both Esbriet and Ofev have been shown to slow the rate of functional decline in IPF and are gaining ground as the standard of care worldwide. Combined sales of both drugs reached $1.1 billion in 2016, with 74% of global revenues being in the United States. These regulatory approvals represent a major breakthrough for IPF patients; yet neither drug improves lung function, and the disease in most patients on these therapies continues to progress. Moreover, the adverse effects associated with these therapies are considerable (e.g., diarrhea, liver function test abnormalities with Ofev, nausea and rash with Esbriet). Therefore, there is still a large unmet medical need as IPF remains a major cause of morbidity and mortality. We estimate global sales of approved IPF drugs will grow to nearly $5 billion in 2025.

Our IPF portfolio

Building an IPF franchise



We have developed a portfolio of three candidate drugs, each with a distinct, novel mechanism of action aimed toward addressing the root causes of IPF. Having multiple mechanisms of action within our own portfolio of IPF candidates allows the possibility of exploring combinations of therapies as well. These candidates are fully proprietary to us, and we aim to commercialize successful drug candidates ourselves.

GLPG1690

GLPG1690 is a potent and selective inhibitor of autotaxin (ATX). We identified ATX as a potential target for IPF, using an inflammation assay in our target discovery platform. Pharmacology and translational studies published by other parties since then suggest that ATX may also play a role in metabolic disease, arthritic pain, oncology, and lung disease.

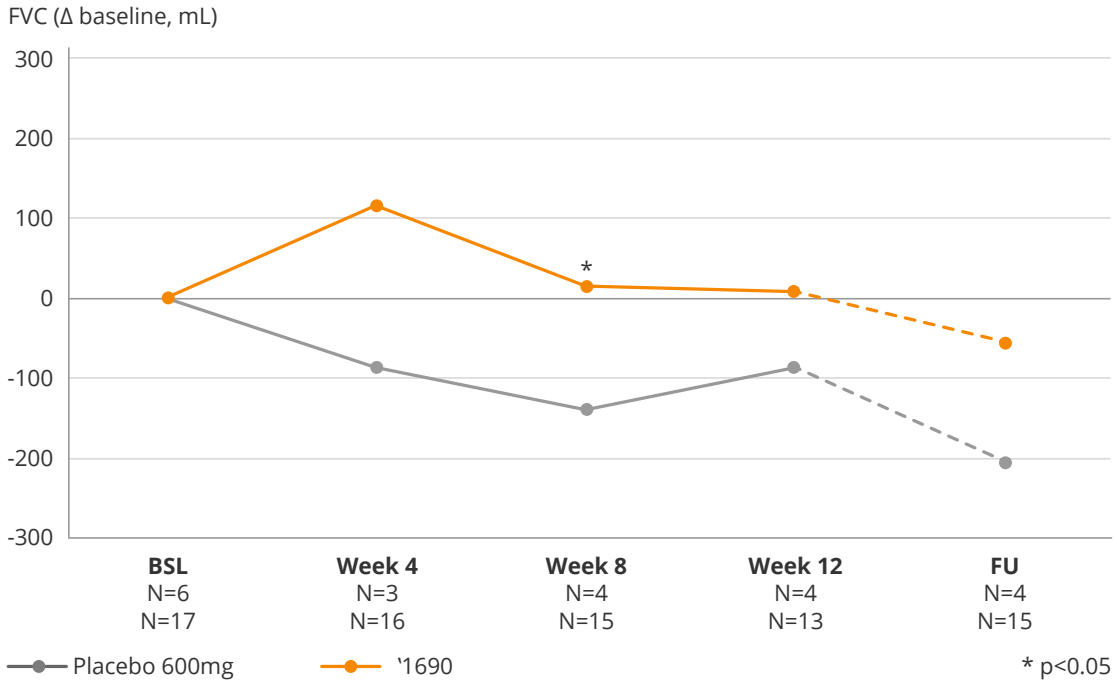
We completed a Phase 2a trial (called FLORA) in IPF patients and announced topline results in August 2017. FLORA was an exploratory, randomized, double-blind, placebo-controlled trial investigating a once-daily oral dose of GLPG1690. The drug candidate was administered for 12 weeks in 23 IPF patients, 17 of whom received GLPG1690 and 6 placebo.

[3] An approved drug (pirfenidone) for IPF, marketed by Roche.
[4] An approved drug (nintedanib) for IPF, marketed by Boehringer Ingelheim.

Primary objectives of the trial were to assess safety, tolerability, pharmacokinetics and pharmacodynamics of GLPG1690 in an IPF patient population. Secondary objectives included the evaluation of lung function, changes in disease biomarkers, FRI, and quality of life. The IPF diagnosis was confirmed by central reading.

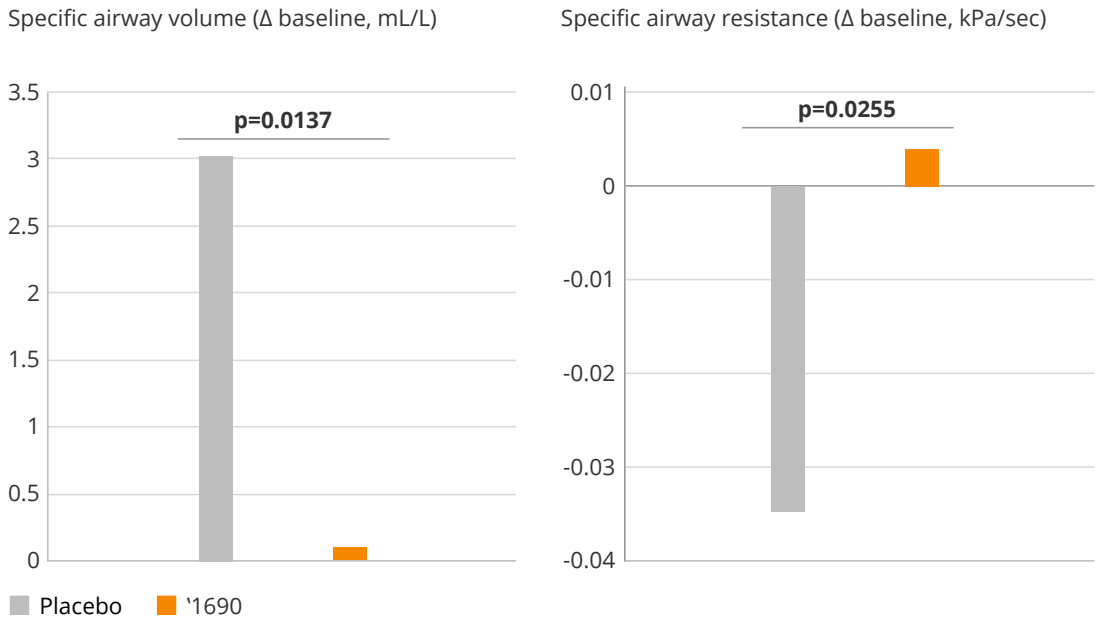
Over the 12-week period, patients receiving GLPG1690 showed stabilization of disease, with an FVC increase of 8 mL, while patients on placebo showed an FVC reduction of 87 mL (mean from baseline). Such reductions in FVC in the placebo arm were in line with expectations based on similarly conducted third-party trials in IPF patients.

FVC: stabilization by '1690



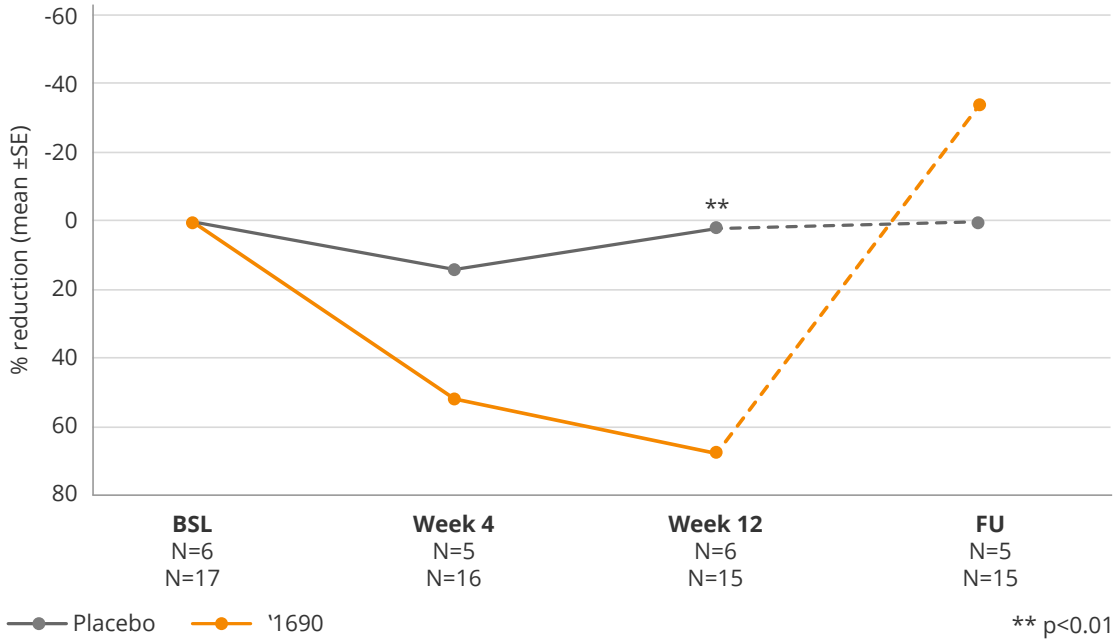
In addition to the demonstrated absence of lung function decline over the 12 week period, more sensitive functional respiratory imaging (FRI) confirmed disease stabilization in the GLPG1690 arm, versus disease progression in the placebo arm, reaching statistical significance on two specific parameters, despite the trial not being powered for significance.

FRI: airway volume & resistance
Significant difference between ‘1690 & placebo



Patients on GLPG1690 treatment showed a clear reduction of serum LPA18:2, a biomarker for ATX inhibition, as expected based on the mechanism of action of GLPG1690. Thus, the level of target engagement observed in Phase 1 with healthy volunteers was confirmed in IPF patients in FLORA.

Steep reduction of biomarker
Plasma LPA18:2 drops in ‘1690 arm



GLPG1690 was found to be generally well tolerated in this Phase 2 trial. Rates of discontinuation due to adverse events, as well as serious adverse event rates, were similar between patients on GLPG1690 and placebo.

Balanced safety endpoints
Between ‘1690 & placebo

Overview safety endpoints	Placebo (N=6)	‘1690 (N=17)
Treatment emergent adverse event	67% (4)	65% (11)
Serious TE AE	33% (2)	6% (1)
Mild TE AE	0% (0)	24% (4)
Moderate TE AE	50% (3)	35% (6)
Severe TE AE	17% (1)	6% (1)
Related TE AE	0% (0)	12% (2)
Temporarily stopped treatment	0% (0)	12% (2)
Permanently stopped treatment	17% (1)	6% (1)

Related TEAEs: headache (mild intensity, no change in treatment) & peripheral swelling of shin (moderate intensity, treatment temporarily stopped)
Discontinuations: 1 placebo SAE, 2 GLPG1690: withdrawal of consent and SAE
All AEs reported in subjects with ≥ 1 reported AE

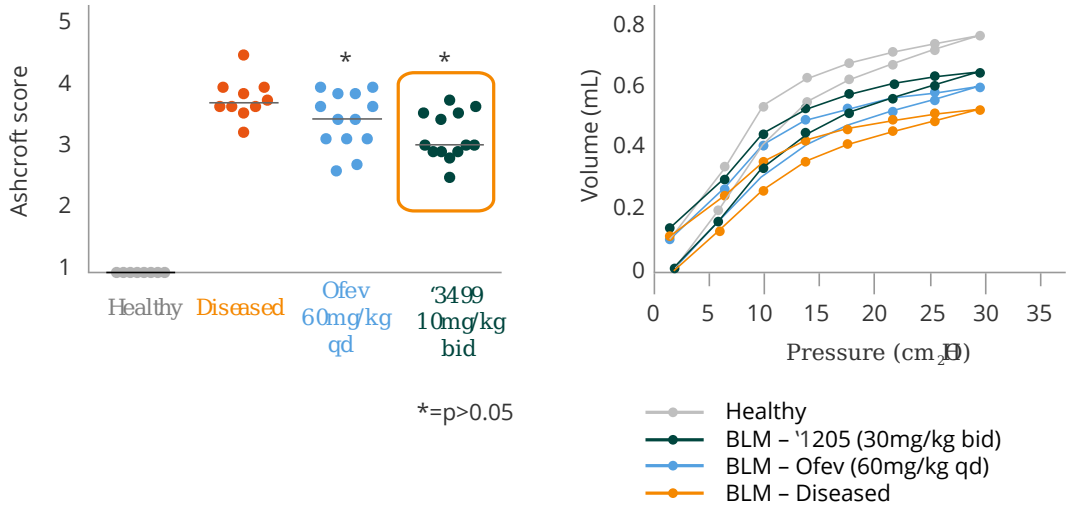
Following the promising results with GLPG1690 in the FLORA trial, we decided to pursue further development of the compound ourselves. We plan to progress GLPG1690 rapidly into a late stage trial and are in discussions with regulators regarding trial design.

GLPG3499 and GLPG1205

In June 2017, we nominated a new product candidate for IPF, GLPG3499. The novel mechanism of action of GLPG3499 remains undisclosed. This candidate is expected to enter Phase 1 trials in 2018. Pre-clinical data in a bleomycin mouse model for IPF show a numerical advantage with treatment with GLPG3499 over Ofev in reduction of fibrotic scores.

GLPG1205 is a GPR84 inhibitor discovered by us and we have shown favorable tolerability but no effect in UC patients in 2016. GLPG1205 will be tested in IPF patients starting in 2018. Pre-clinical data in a bleomycin mouse model for IPF show a numerical advantage with treatment with GLPG1205 over Ofev in improvement of respiratory capacity.

Additional novel mechanisms '3499 (left) and '1205 (right) in IPF



‘3499 and ‘1205 reduce IPF signs & symptoms in BLM model

Note: both experiments are 21 day therapeutic bleomycin lung fibrosis model in mice (BLM)

Our CF program

CF is a rare, life-threatening, genetic disease affecting the lungs and the digestive system, impacting approximately 80,000 patients worldwide. CF patients carry a defective CF transmembrane conductance regulator (CFTR) gene and are classified based on their specific mutation of the CFTR gene. The Class II mutation is present in approximately 90% of CF patients, with Orkambi®[5] and Symdeko®[6] being the only approved therapies for the underlying cause of CF in this mutation. Kalydeco®[7] is a disease-modifying treatment for Class III and several residual function mutations, representing about 8% of total CF patients. The market for CF therapies is robust and growing. According to Vertex Pharmaceuticals, approximately 9,000 patients were treated with Vertex therapies in 2016, and this they expect to grow to approximately 75,000 patients by 2024. Combined sales of Kalydeco and Orkambi were approximately $2.2 billion in 2017.

Despite the approval of Kalydeco, Orkambi, and Symdeko, there is need for better therapies to improve pulmonary function for a large majority of the patient population. Though many pediatric patients have normal lung function at the time of diagnosis, physicians generally believe that earlier treatments can have downstream benefits for the patient by slowing the deterioration in lung function.

CF drug developers are focused on two types of disease-modifying CFTR modulators. Potentiator molecules aim to restore the flow of ions through an activated CFTR by influencing the channel's opening. Corrector molecules aim to overcome defective protein processing by restoring proper folding of CFTR and allowing for increased cell surface expression. In order to improve CFTR function meaningfully for the largest patient group with Class II and other mutations, we believe a combination of medicines will be required, comprising a potentiator and two novel corrector (which we refer to as C1 and C2) molecules.

We believe that our candidate CF combination therapy may address the unmet need in CF patients with one or two copies of the F508del mutation. From 2005-2017, we focused on developing novel CF compounds to address the needs of Class II patients, and we believe we validated the potentiator and C1 corrector components in patient trials. In 2018 we expect to validate the final component, the C2 corrector, in a patient trial.

We aim to evaluate a once-daily, oral, triple combination CF therapy in patients starting in Q1 2018, with additional trials with novel CF compounds and triple combinations initiating throughout 2018. We developed a portfolio of lead and backup compounds from which to select the best potentiator and corrector molecules for our triple combination therapies. The first triple combination comprises GLPG2451, GLPG2222, and GLPG2737. The second comprises GLPG3067, GLPG2222, and GLPG2737.

1st triple combination

FALCON is a patient trial combining potentiator GLPG2451, C1 corrector GLPG2222, and C2 corrector GLPG2737 into a triple combination in CF patients homozygous for the Class II mutation.

2nd triple combination

The first healthy volunteer was dosed with a second novel investigational triple combination therapy comprising potentiator GLPG3067, C1 corrector GLPG2222, and C2 corrector GLPG2737 in a Phase 1 trial in Belgium. The aim of the Phase 1, randomized, double-blinded, placebo-controlled trial is to evaluate the safety, tolerability and pharmacokinetics of multiple ascending doses of this second investigational triple combination therapy in up

[5] A combination potentiator-corrector therapy marketed by Vertex Pharmaceuticals.
[6] A corrector-potentiator combination for CF patients with the Class II mutation; marketed by Vertex Pharmaceuticals.
[7] A potentiator drug (ivacaftor) marketed by Vertex Pharmaceuticals.

to 16 healthy volunteers. Topline results from this Phase 1 trial are expected to be presented at a future medical conference. We aim to evaluate this triple combination in patients, pending satisfactory completion of the Phase 1 trial.

3rd triple combination

We aim to evaluate a third triple combination comprising potentiator GLPG3067, C1 corrector GLPG2222, and C2 corrector GLPG3221 in both healthy volunteers and patients. We currently await the outcome of a Phase 1 trial with GLPG3221, which is expected in 2018.

Our clinical program for CF

Potentiators

We reported favorable tolerability and pharmacokinetics in Phase 1 trials for potentiator GLPG2451 and potentiator GLPG3067 at the North American Cystic Fibrosis Conference (NACFC) 2017. GLPG2451 and GLPG3067 have potential for once-daily dosing. GLPG2451 has an active metabolite with a half-life of one month. Both GLPG2451 and GLPG3067 were tested separately in combination with C1 corrector GLPG2222, showing favorable tolerability in healthy volunteers.

C1 correctors

GLPG2222

We reported that GLPG2222, the first early binding (C1) corrector, showed favorable safety and tolerability in Phase 1 trials in healthy volunteers in June 2016. GLPG2222 was tested in single ascending doses up to 800 mg, and in multiple ascending doses up to 600 mg qd for 14 days in a double-blind, randomized, placebo-controlled trial. The product candidate was shown to be well-tolerated and no emerging safety signals observed in the dose range studied. In 2017, we reported topline data for GLPG2222 from two Phase 1b clinical trials, our ALBATROSS and FLAMINGO trials.

ALBATROSS

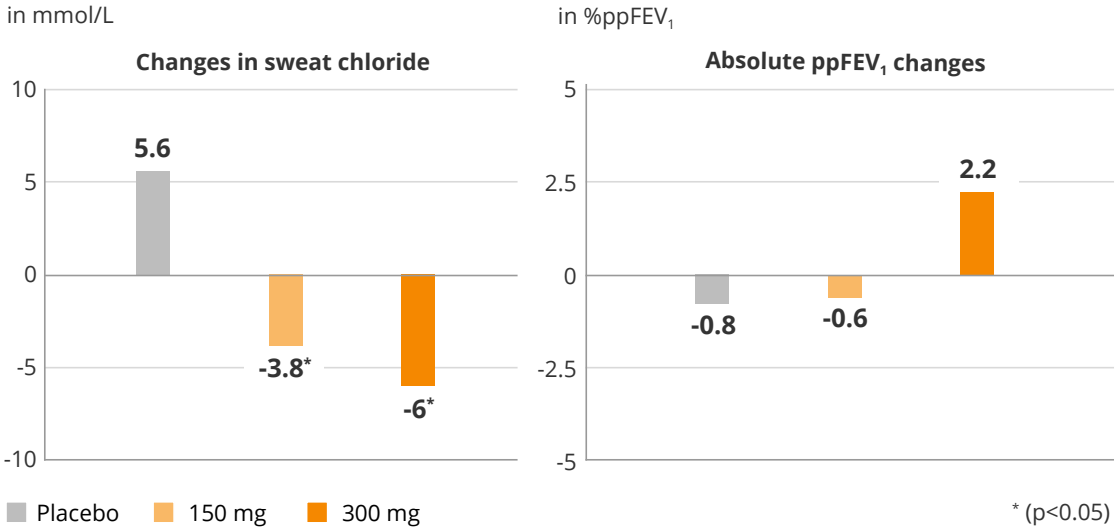
The ALBATROSS trial included 37 cystic fibrosis patients with a gating (Class III) mutation on one allele and F508del (Class II) mutation on the other allele. All patients were on long-term stable Kalydeco treatment (150 mg twice daily) at screening and continued their Kalydeco treatment throughout the trial. The ALBATROSS trial was fully recruited within five months.

Overall, GLPG2222 was well tolerated, with observed treatment emergent adverse events being predominantly mild or moderate, and typical for a CF patient population. There were no serious adverse events reported and no discontinuations due to adverse events.

The targeted exposures of GLPG2222 were achieved in this patient trial, further strengthening dosing modelling for the first investigational triple combination. Exposures achieved in patients were in line with those observed in healthy volunteers.

The additional activity observed with treatment with GLPG2222 on top of Kalydeco was in line with what was observed with tezacaftor combined with Kalydeco in a Phase 2 trial in this population. ALBATROSS showed dose-dependent decreases on sweat chloride; below is a summary of activity seen:

Clear activity profile GLPG2222
D29 vs. Baseline



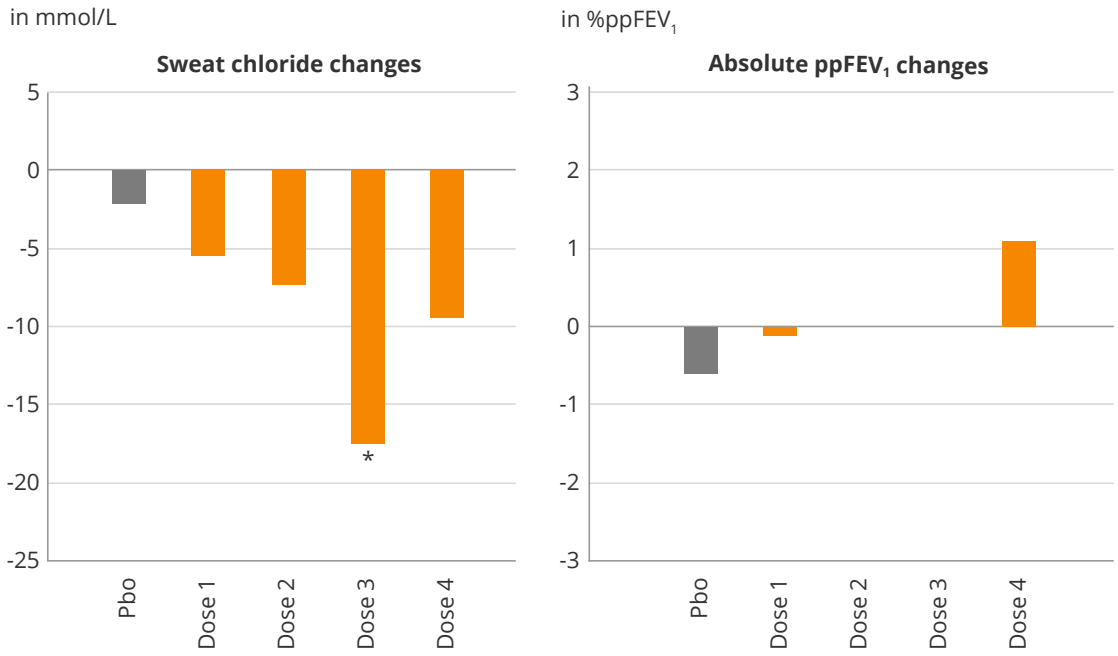
FLAMINGO

The FLAMINGO trial 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 Symdeko for four weeks prior to dosing of GLPG2222. The FLAMINGO trial was over-recruited within five months. This is our first CF patient trial conducted in the U.S. as well as in Europe. Once daily doses of GLPG2222 (ascending from dose 1 to dose 4) 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 were reported in three patients. Of these, two patients were on placebo, each experiencing pulmonary exacerbations due to infection. One patient on dose 2 of GLPG2222 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.

A statistically significant, dose-dependent decrease in sweat chloride concentration was observed. Consistent with our expectations and similar prior trials conducted by Vertex, there was no significant impact on ppFEV1 levels.

On target activity GLPG2222
Mean changes D29 vs. baseline



* LOCF values Mean ±SE

We believe that ALBATROSS and FLAMINGO validated our C1 corrector series in patients.

GLPG2851

A Phase 1 trial with backup novel C1 corrector GLPG2851 for cystic fibrosis (CF) started in late 2017; the aim of the trial is to evaluate the safety, tolerability and pharmacokinetics of GLPG2851 in healthy volunteers. The randomized, double-blind, placebo controlled, single center trial is being conducted in Belgium.

C2 correctors

GLPG2737

We reported favorable tolerability in a Phase 1 trial with our first late binding (C2) corrector GLPG2737, the final component needed for a triple combination therapy, at NACFC 2017.

PELICAN

PELICAN is a patient trial with C2 corrector GLPG2737 in combination with Orkambi, being run in 10 sites in Germany. The aim of the double-blind, placebo-controlled Phase 2 trial 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 and ppFEV%. We expect to report the results of PELICAN in 2018, and we look to this trial to validate our C2 corrector in patients.

GLPG3221

We reported the start of a Phase 1 trial with novel backup C2 corrector GLPG3221 in late 2017. The aim of the Phase 1 trial is to evaluate the safety, tolerability and pharmacokinetics of GLPG3221 in healthy volunteers. The randomized, double-blind, placebo controlled, single center trial is being conducted in Belgium.

Our OA program

Sometimes called degenerative joint disease or degenerative arthritis, OA is the most common chronic condition of the joints. OA can affect any joint, but it occurs most often in the small joints of the fingers, knees, hips, lower back and neck, and the bases of the thumb and big toe. According to GlobalData, OA will be the fourth leading cause of disability by the year 2020. GlobalData estimates that diagnosed cases will grow to approximately 131 million cases by 2024.

In normal joints, a firm, rubbery material called cartilage covers the end of each bone. Cartilage provides a smooth, gliding surface for joint motion and acts as a cushion between the bones. In OA, the cartilage breaks down, causing pain, swelling and problems moving the joint. As OA worsens over time, bones may break down and develop growths called spurs. Bits of bone or cartilage may chip off and float around in the joint. In the body, an inflammatory process occurs and cytokines (proteins) and enzymes develop that further damage the cartilage. In the final stages of OA, the cartilage wears away and bone rubs against bone leading to joint damage and more pain.

Although OA occurs in people of all ages, it is most common in people older than 65. Common risk factors include obesity, previous joint injury, over-use of the joint, and weak thigh muscles. One in two adults will develop symptoms of knee OA during their lives. One in four adults will develop symptoms of hip OA by age 85. Current treatments for OA include weight loss, physical therapy, pain and anti-inflammatory medicines, and surgery, all of which address only the symptoms of the disease. There are currently no disease-modifying therapies available for OA, with drug sales for OA patients amounting to approximately $4 billion in generic painkillers in 2016.

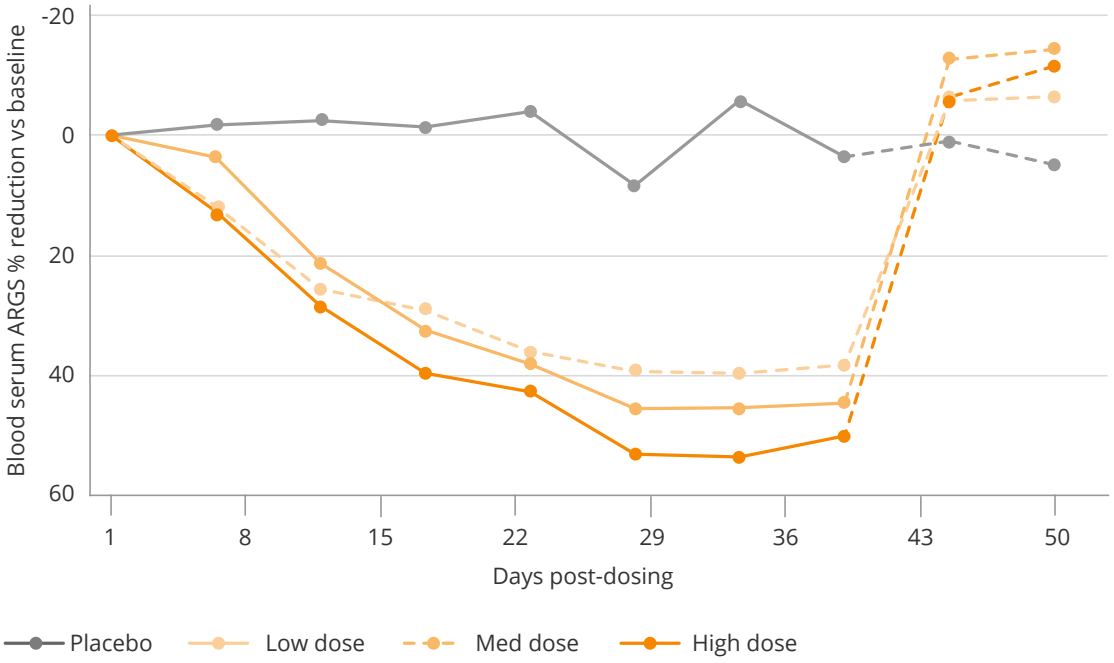
GLPG1972 is a candidate drug developed by us under our collaboration agreement with Servier. GLPG1972 acts on ADAMTS-5, a key aggrecanase involved in the breakdown of aggrecan in joint cartilage. ADAMTS-5 has been validated in the literature in both animal models and human explants, and AGRS, a byproduct of the cartilage breakdown action of ADAMTS-5, has been shown to be elevated in the joints of human OA patients.

In June 2016, we announced that GLPG1972 was shown to be safe and well tolerated in healthy human volunteers in a Phase 1 first-in-human trial. In this trial, dosing with GLPG1972 reduced ARGS neoepitope, a biomarker for cartilage breakdown via the ADAMTS-5 pathway, by up to 60% in these volunteers within two weeks.

We evaluated GLPG1972 in a randomized, placebo-controlled, double-blind Phase 1b trial in 30 patients aged 50 to 75 years with diagnosis of knee and/or hip osteoarthritis, in the United States. Patients were given one of three doses of GLPG1972 or placebo for a total of 4 weeks, with a 3 week follow-up period.

In this Phase 1b trial, GLPG1972 was well tolerated. There was one treatment discontinuation with reversible abnormal liver function test on Day 15 in the highest dose cohort. Patients on treatment achieved a dose-dependent, reduction of ARGS neoepitope versus placebo:

Strong reduction of ARGS
'1972 Ph1b study in OA patients



We work with Servier to develop GLPG1972. We are eligible to receive milestones and single-digit royalties on potential commercial sales for GLPG1972, while we retain full commercial rights in the United States. In July 2017, Servier licensed GLPG1972 for further development into OA patient trials outside the United States. Both companies are preparing a global Phase 2 program to evaluate the risk/benefit profile of GLPG1972 in OA patients, expected to start in 2018.

Our AtD program

Atopic dermatitis (AtD), the most severe and common type of eczema, is a chronic relapsing inflammatory skin disease that causes severe itch, dry skin and rashes, predominantly on the face, inner side of the elbows and knees, and on hands and feet. Scratching of the afflicted skin leads to a vicious cycle causing redness, swelling, cracking, scaling of the skin and an increased risk of bacterial infections. Lichenification, thickening of the skin, is characteristic in older children and adults. The National Eczema Association estimates that AtD affects over 30 million Americans or up to 25% of children and 2-3% of adults. Sixty percent of AtD patients are diagnosed in the first year of life, and 90% of patients have a disease onset before age five. Symptoms commonly fade during childhood, however, approximately 10-30% of the patients will suffer from atopic dermatitis for life. A smaller percentage first develop symptoms as adults.

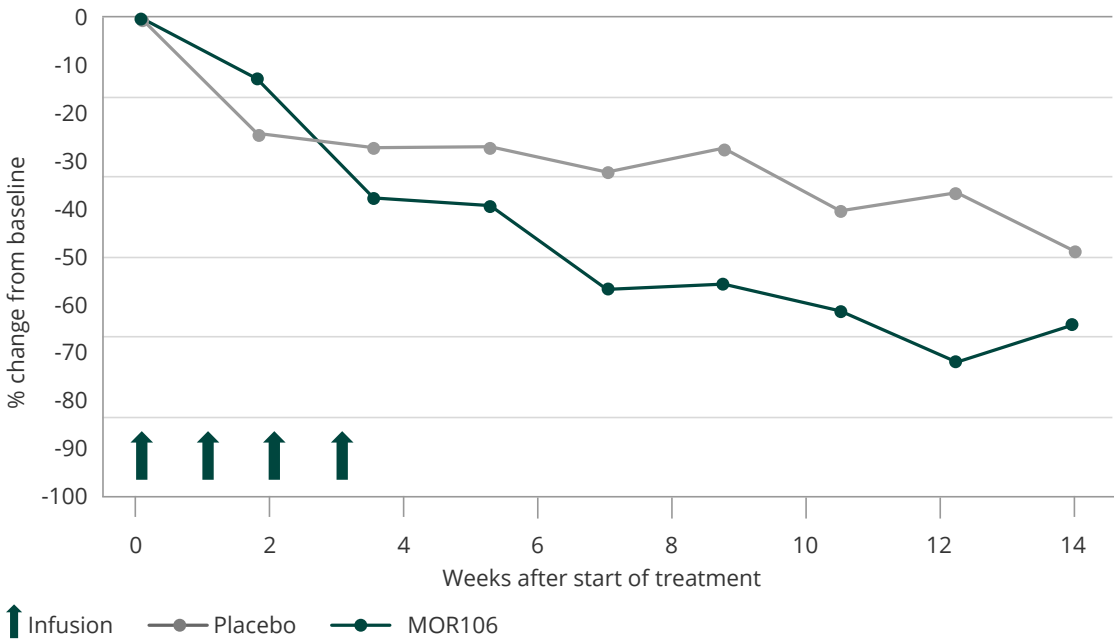
Generic drugs are the approved standard of care, including immunomodulators cyclosporine and mycophenolate mofetil and topical treatments. There are disease-modifying biologics and small molecules currently in development, with dupilimab (IL-4Rα) most recently approved.

MOR106 is a human monoclonal antibody designed to selectively target IL-17C in clinical development worldwide. IL-17C is a target discovered by us and has been shown to be distinct from other members of the IL-17 cytokine family, playing an important and pro-inflammatory role in certain skin disorders. MOR106 potently inhibits the binding of IL-17C to its receptor and thus inhibits its biological activity.

MOR106 arises from an alliance between us and MorphoSys, in which both companies contribute their core technologies and expertise and equally share costs and benefits.

We evaluated MOR106 in a randomized, double-blind, placebo-controlled Phase 1 trial. MOR106 showed favorable safety and PK results when administered to healthy volunteers in the ongoing trial. In the second portion of the trial with MOR106 in 24 AtD patients, all adverse drug reactions observed were mild-to-moderate and transient in nature and did not lead to clinically relevant safety signals. No serious adverse events and no infusion-related reactions were recorded. Even though the trial was not statistically powered to show differences in efficacy between treatment groups, at the highest dose level of MOR106, in 83% of patients (5 out of 6) an improvement of at least 50% in signs and symptoms of atopic dermatitis measured by the Eczema Area and Severity Index (EASI-50) was recorded at week 4. The onset of activity was rapid and occurred within few weeks and was maintained for over 2 months after the last treatment. Among patients receiving placebo, in 17% of patients (1 out of 6) an EASI-50 improvement was seen at week 4. As reported at AAD 2018, the pooled, mean EASI scores over time versus placebo show a sustained effect for weeks after completion of dosing:

MOR106 Ph1b
EASI, % change from baseline, pooled data, median



We and MorphoSys are preparing for a Phase 2 trial with MOR106, expected to initiate in the first half of 2018.