Portfolio

Our programs in immunology and oncology

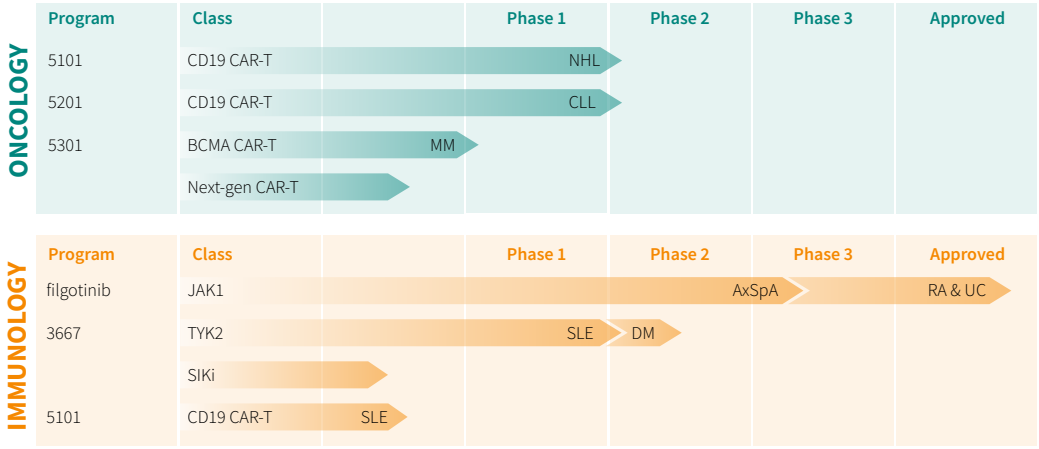
Outlook for 2023

Forward with Purpose

Portfolio and outlook 2023

Portfolio

The following chart provides an overview of our lead product and product candidates currently in development as of the date of the publication of this report.



Note: filgotinib is approved for RA and UC in Europe and Japan.
AxSpA, axial spondyloarthritis; RA, rheumatoid arthritis; UC, ulcerative colitis; rSLE, refractory systemic lupus erythematosus; DM, dermatomyositis; NHL, non-Hodgkin lymphoma; CLL, chronic lymphocytic leukemia; MM, multiple myeloma

Outlook 2023

Topline results

- Filgotinib: FILOSOPHY Phase 4 in RA
- GLPG5101: CD19 CAR-T Phase 1 part of Phase 1/2 in NHL
- GLPG5201: CD19 CAR-T Phase 1 part of Phase 1/2 in CLL

Regulatory progress

- CD19 CAR-T IND submission in the US

Trial initations

- Filgotinib: Phase 3 in AxSpA
- CD19 CAR-T Phase 2 in rSLE
- GLPG5101/ GLPG5201: CD19 CAR-T NHL/CLL expansion cohorts
- GLPG5301: BCMA CAR-T Phase 1/2 in MM
- GLPG3667: TYK2i Phase 2 in DM & SLE

Immunology

Small Molecules pipeline

Jyseleca® franchise

Jyseleca® in rheumatoid arthritis (RA)

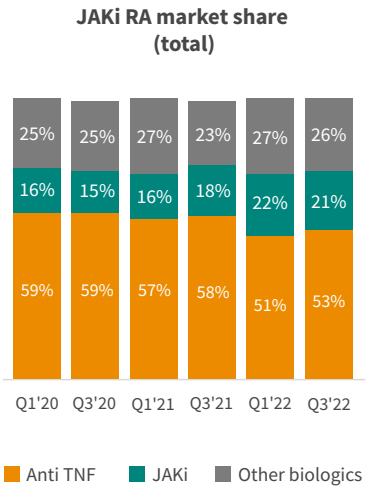
RA is a chronic autoimmune disease that affects more than three million patients in the United States and Europe. RA is characterized by inflammation and degeneration of the joints. Patients suffer from pain, stiffness, and restricted mobility due to a persistent inflammation of multiple joints, ultimately resulting in irreversible damage of the joint cartilage and bone. The current market for RA treatments in the five major European markets (EU5) is approximately €3.3 billion. Despite progress in the treatment of RA, there remains a considerable unmet need as sustained remission remains rare.[7]

In 2003, we discovered JAK1 as a novel, differentiated target in an inflammation target discovery assay and subsequently developed filgotinib as a novel small molecule inhibitor with preferential selectivity for JAK1.

To date there are 4 JAK inhibitors approved for the treatment of RA in the EU5, including Jyseleca® (filgotinib) an orally administered preferential JAK1 inhibitor.

Below we present the RA market in the EU5.

[7] Chen Y, et al. Clin Rheumatol. 2019 Mar;38(3):727-738. doi: 10.1007/s10067-018-4340-7. Epub 2018 Oct 19.



Source: Market research from Therapy Watch, Q3 2022 (6 month average)

Regulatory progress of Jyseleca® in RA

In 2020, Jyseleca® (filgotinib 200mg and 100mg) obtained regulatory approval in Europe, Great-Britain, and Japan for the treatment of adult patients with moderate to severe active RA.

The European Summary of Product Characteristics for filgotinib, which includes contraindications and special warnings and precautions, is available at **www.ema.europa.eu**. The Great Britain Summary of Product Characteristics for filgotinib can be found at **www.medicines.org.uk/emc** and the Northern Ireland Summary of Product Characteristics for filgotinib can be found at **www.emcmedicines.com/en-GB/northernireland**, respectively. The interview form from the Japanese Ministry of Health, Labour and Welfare is available at **www.info.pmda.go.jp**.

Also in 2020, Gilead Sciences, Inc (Gilead) received a Complete Response Letter (CRL) from the US Food and Drug Administration (FDA) for the New Drug Application (NDA) for filgotinib. Consequently, Gilead decided not to advance with resubmission in the US for approval of filgotinib as a treatment for RA in the U.S.

In 2022, the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) concluded its Article 20 safety review of all JAK inhibitors approved in the EU for the treatment of inflammatory diseases and recommended the harmonization of all labels. PRAC concluded that JAK inhibitors should maintain their indication for the treatment of patients with RA who have responded inadequately to or who cannot tolerate disease modifying anti-rheumatic drugs (DMARDs) therapy, and for patients with UC who have responded inadequately to or who cannot tolerate conventional therapy or biologics. PRAC also recommended all JAK inhibitor product labels be updated to include a precautionary approach for use of JAK inhibitors in patients with identified risk factors only if no suitable treatment alternative is available

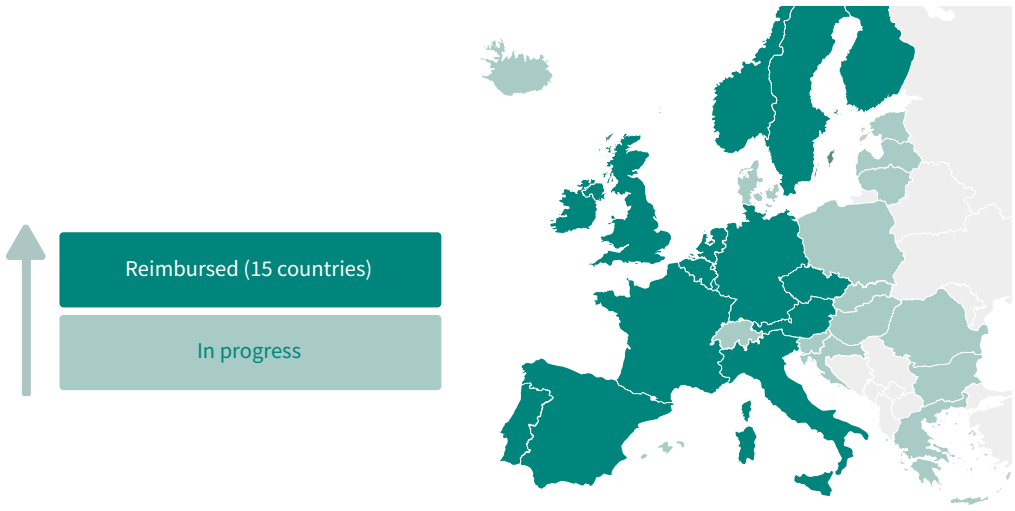
(Section 4.4 of the product label – Warning and Precautions). On 11 November 2022, the Committee for Medicinal Products for Human Use (CHMP), the scientific committee of the EMA, adopted PRAC's recommendation and on 10 March 2023, this decision was approved by the European Commission.

Commercialization of Jyseleca® in RA

In 2021, we took full ownership of the manufacturing and commercialization of Jyseleca® in Europe and became the Marketing Authorization Holder (MAH) in 27 countries in Europe. Jyseleca® is now reimbursed in 15 countries for RA, including the major markets Germany, France, Spain, Italy, and Great Britain.

In Central and Eastern Europe, Portugal, Greece and the Baltic countries, our partner Swedish Orphan Biovitrum AB (Sobi) is responsible for the distribution and commercialization of Jyseleca®. The graphic below represents the reimbursement progress of Jyseleca® throughout Europe since its approval for RA in September 2020.

Jyseleca® reimbursement in RA in Europe



Eastern and Central Europe, Portugal, Greece, Baltic countries partnered with Sobi

Under our amended collaboration agreement with Gilead, Gilead remains responsible for the commercialization and distribution of Jyseleca® outside of Europe, including in Japan where Jyseleca® is approved in RA and is co-marketed with Eisai.

See further details regarding the revised Gilead collaboration agreement for filgotinib in our **Notes to the consolidated financial statements**.

Safety and efficacy in the filgotinib RA development program

Filgotinib has shown favorable results in terms of onset of action, efficacy, safety, and tolerability from the FINCH Phase 3 and DARWIN Phase 2 clinical programs.

As part of the filgotinib development program, we initiated FINCH 4 in RA. The FINCH 4 study is a multi-center, open-label, long-term extension study to assess the safety and efficacy of filgotinib in patients with RA, which enrolled subjects who completed either the FINCH 1, FINCH 2, or FINCH 3 studies.

We and Gilead published integrated safety data from 7 RA studies in *Annals of the Rheumatic Diseases* (Winthrop *et al.* 2021). Data were integrated from 3 Phase 3 studies (FINCH 1 – 3), 2 Phase 2 studies (DARWIN 1, 2), and 2 long-term extension studies (DARWIN 3, FINCH 4) including up to 5.6 years of filgotinib exposure, and over a median of 1.6 years. In this pooled analysis, filgotinib was well-tolerated, and no new safety concerns were identified. Adverse events of MACE and DVT/PE were rare and occurred in similar numbers among all treatment groups, and with a similar incidence rate across all dose groups. The data underscore the acceptable safety and tolerability profile of filgotinib as monotherapy and in conjunction with MTX/csDMARDs[8] in RA.

In preclinical animal toxicology studies, when administered at doses beyond its approved dose in humans, filgotinib induced adverse effects on semen parameters. Consequently, we and Gilead conducted dedicated male patient semen analysis studies in UC and CD patients called MANTA, and RA, ankylosing spondylitis (AS), and psoriatic arthritis (PsA) patients, called MANTA-RAy, concurrent to all Phase 3 programs.

In March 2021, we reported on the primary endpoint with the MANTA and MANTA-RAy studies investigating the effect on semen parameters, which indicated that 8.3% of patients on placebo and 6.7% of patients on 200mg filgotinib had a 50% or more decline in sperm concentration at Week 13. Subsequently, a Type II variation application was submitted to the EMA in June 2022, supported by interim data on the primary, secondary and exploratory endpoints at Week 13 and 26 for subjects who met a prespecified sperm decrease at these timepoints (up to Week 52) from the MANTA and MANTA-RAy studies. Following assessment of the interim data by the CHMP, it was concluded in the opinion that the data did not reveal a difference between treatment groups in the proportion of patients who had a 50% or more decrease from baseline in semen parameters at Week 13 (pooled primary endpoint: filgotinib 6.7%, placebo 8.3%) and at Week 26. Further, CHMP concluded that the data did not show any relevant changes in sex hormone levels or change from baseline in semen parameters across treatment groups. The CHMP concluded that these clinical data were not suggestive of filgotinib-related effects on testicular function. In October 2022, we received a positive CHMP opinion to update the European label whereby the language in the section of the Special Warnings and Precautions about the potential effect of filgotinib on sperm production and male fertility was removed from the Summary of Product Characteristics (SmPC). In addition, the MANTA/RAy studies were removed from the Risk Management Plan (RMP).

In 2022, we presented preliminary results from our first international, real-world arthritis study, FILOSOPHY, *FILgotinib Observational Study Of Patient Health-related outcomes*, at the American College of Rheumatology (ACR) Convergence 2022 meeting. The data showed that filgotinib induced rapid relief in pain and fatigue as early as Week 1 as well as improvements in disease activity[9] at Month 1. These interim results were based

[8] Conventional synthetic DMARDs
[9] Galloway J, Bevers K, Vershueren P, et al. Presented at: ACR Convergence 2022; November 10-14, 2022; Philadelphia, Pennsylvania.

on data from 200 real-world patients with moderate to severe active RA enrolled in Germany, the United Kingdom, the Netherlands, Belgium and Italy.

Jyseleca® in ulcerative colitis (UC)

UC is an inflammatory bowel disease (IBD) resulting in ulcerations and inflammation of the inner layer of the colon and rectum. The current market for UC treatments is estimated at ~€1.0 billion in the EU5.

Current treatment landscape in UC in Europe

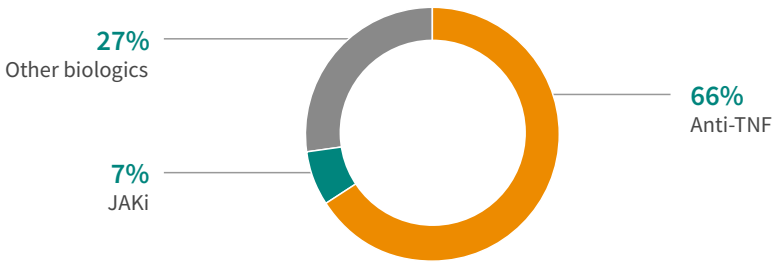
Biologic therapies for UC were dominated by tumor necrosis factor (TNF) antagonists for nearly 20 years, but anti-integrin and anti-interleukin IL-12/IL-23 antibodies have recently become available.

Although the introduction of advanced therapies has improved the treatment of UC for some patients, 30% of patients do not respond to treatment,[10] and 19% to 59% of initial responders do not have a sustainable treatment response.[11]

Therefore, the medical need for improved treatment efficacy with additional treatment options remains high.

The current market in Europe for UC is approximately €1.0 billion and is expected to grow at a CAGR of 10% between 2020 and 2029.[12]

Current European treatment landscape in UC



Source: UC Therapy Watch (Research Partnership) Q3 2021. Share of prescriptions of advanced therapies

[10] Allez M et al. Report of the ECCO pathogenesis workshop on anti-TNF therapy failures in inflammatory bowel diseases: definitions, frequency and pharmacological aspects. J Crohns Colitis. 2010 Oct;4(4):355-66.
[11] Ma C et al. Outpatient Ulcerative Colitis Primary Anti-TNF Responders Receiving Adalimumab or Infliximab Maintenance Therapy Have Similar Rates of Secondary Loss of Response. J Clin Gastroenterol. 2015 Sep;49(8):675-82.
[12] CAGR: compounded annual growth rate. Source: UC Therapy Watch

Regulatory progress and commercialization of Jyseleca® in UC

Filgotinib obtained regulatory approval for the treatment of adults with moderate to severe UC in the European Union in 2021, and in Great Britain and Japan in January and March 2022, respectively.

Filgotinib is marketed as Jyseleca® in Europe and Japan for the treatment of adult patients with moderate to severe active UC who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic agent. Jyseleca (filgotinib) 100mg and 200mg are registered in the above-mentioned territories.

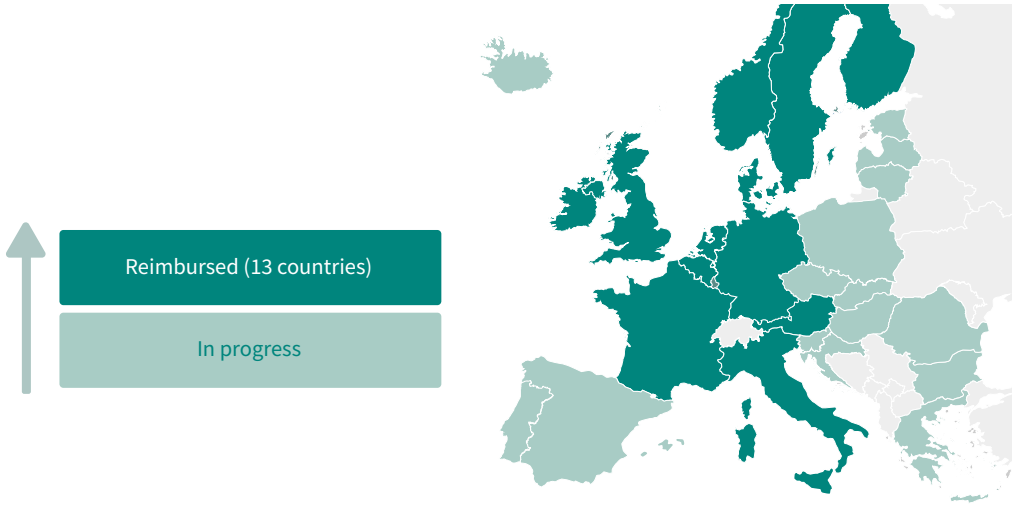
The European Summary of Product Characteristics for filgotinib, which includes contraindications and special warnings and precautions, is available at **www.ema.europa.eu**. The Great Britain Summary of Product Characteristics for filgotinib can be found at **www.medicines.org.uk/emc** and the Northern Ireland Summary of Product Characteristics for filgotinib can be found at **www.emcmedicines.com/en-GB/northernireland**, respectively. The interview form from the Japanese Ministry of Health, Labour and Welfare is available at **www.info.pmda.go.jp**.

Jyseleca® reimbursement in UC in Europe

Jyseleca® is marketed by Galapagos in Europe and is now reimbursed in 13 countries in Europe (see graph below), including the major markets Great Britain, France and Germany. In Central and Eastern Europe, Portugal, Greece and the Baltic countries, our partner Sobi is responsible for the distribution and commercialization of Jyseleca®.

Gilead is responsible for the distribution and commercialization of Jyseleca® outside of Europe, including in Japan where Jyseleca® is approved in UC and is co-marketed with Eisai.

Jyseleca® reimbursements in UC



Eastern and Central Europe, Portugal, Greece, Baltic countries partnered with Sobi

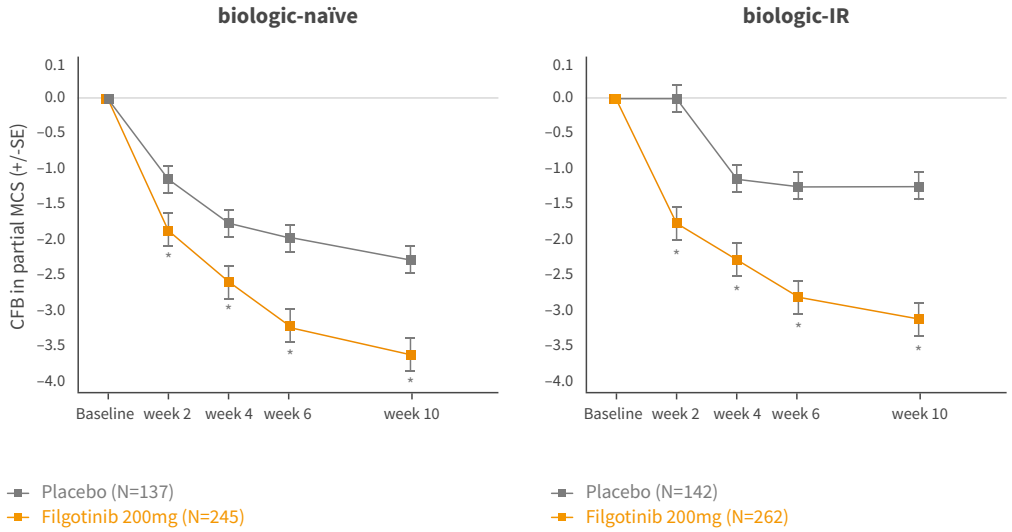
Safety and efficacy in the filgotinib UC development program

Filgotinib 200mg has shown favorable results in terms of rapid onset of action, efficacy, safety, and tolerability from the SELECTION Phase 3 program in patients with moderate to severe UC. The SELECTION Phase 3 data (Feagan *et al.* 2021) were published in *The Lancet*.

Both in biologic-naïve and in biologic-experienced patients, a rapid onset of action for filgotinib 200mg at Week 2, with a sustained effect up to 10 weeks, was observed in a pre-specified exploratory analysis of the SELECTION study. The graph below shows the rapid onset in both cohorts using the partial Mayo Clinic Score.

Rapid response with symptom relief from Week 2

Induction (SELECTION)

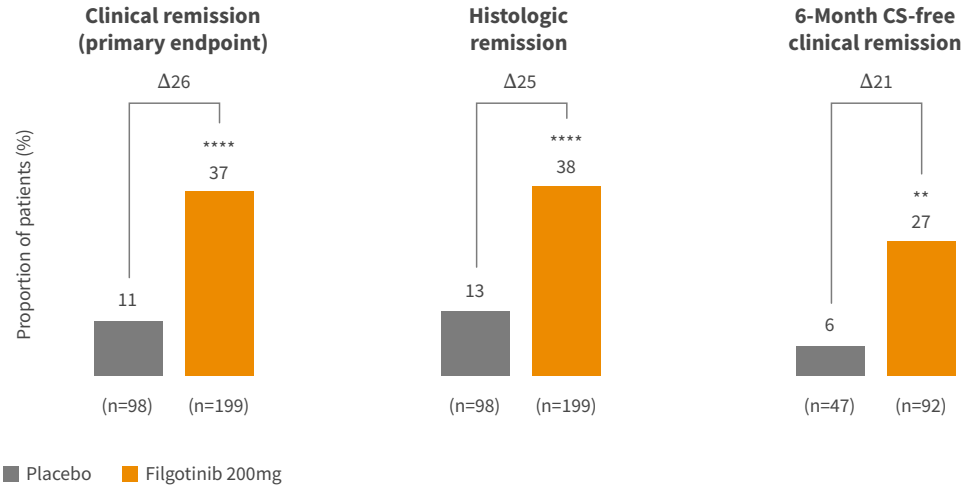


Results from a pre-specified exploratory analysis
* P < .05 filgotinib vs placebo (nominal p-values)
Biologic-IR: biologic-inadequate response, CFB: change from baseline, partial MCS: partial Mayo Clinic Score
Partial Mayo Clinic Score is based on all MCS subscores except for the endoscopy score

Additionally, data from a post-hoc analysis of the maintenance study showed that a greater proportion of biologic-naïve and biologic-experienced patients receiving filgotinib 200mg maintained clinical remission up to 58 weeks versus those receiving placebo (37% versus 11%; p<0.001) and had histologic remission (38% versus 13%; p<0.001) and 6-month corticosteroid-free clinical remission (27% versus 6%; p<0.01) as shown in the graph below, and published in *The Lancet* (Feagan *et al.* 2021).

Sustained remission at Week 58

Maintenance (SELECTION)



** P < .01; **** P < .0001 filgotinib vs placebo
CS: corticosteroid
Clinical remission as measured by EBS (endoscopy subscore of 0 or 1, rectal bleeding subscore of 0, stool frequency subscore of 0 or 1)

Furthermore in 2021, additional safety data from the SELECTION studies were presented at the 16th European Crohn's and Colitis Organisation (ECCO) 2021 virtual congress (Schreiber *et al.* 2021). Data were analyzed from the SELECTION induction, maintenance, and long-term extension study with a cumulative treatment exposure of 1,207 patient years for filgotinib 200mg versus 318 patient years for placebo, showing results consistent with the original induction and maintenance studies, where filgotinib was well tolerated in patients with moderate to severe active UC.

In 2022, we presented a set of new data from the SELECTION study and SELECTION long-term extension study in UC at the ECCO 2022 annual conference. The key findings were:

1. Continued treatment with filgotinib for up to an additional 96 weeks in the long-term extension study was effective in maintaining long-term improvements in UC symptoms;
2. Retreatment with filgotinib upon interruption resulted in recovery of efficacy in most patients and filgotinib was well tolerated with no new safety concerns;
3. Filgotinib's efficacy profile was consistent and the safety profile acceptable regardless of the age group, analysing patients up to 75 years of age; and
4. Filgotinib was able to achieve the high bar of efficacy as defined by a combined endpoint of clinical and quality of life (QoL) remission, endoscopic and biomarker improvement.

In 2023, we presented additional new analyses from the SELECTION program with filgotinib at the annual ECCO congress. These include new analysis from the long-term extension (LTE) study evaluating the safety and efficacy of filgotinib in UC for nearly four years; an analysis of the prolonged benefit of filgotinib in UC; an analysis exploring factors associated with the partial Mayo Clinic Score (pMCS) over time; and analysis of the effect of filgotinib on anaemia in UC patients. Additionally, we presented pooled data from five Phase 2/3 trials, and two long-term extension trials of filgotinib designed to further understand the safety profile of filgotinib in UC and RA. Data from the SELECTIONLTE study showed that filgotinib 200mg maintained symptomatic remission and health-related quality of life (HRQoL) for up to approximately four years. Amongst subjects who completed the study, the reduction in mean pMCS in SELECTION was maintained up to LTE Week 144. In non-responders, mean pMCS decreased from LTE baseline to Week 192. The results also showed that a high proportion of completers (>80% of patients) and non-responders (>70% of patients) achieved remission according to the Inflammatory Bowel Disease Questionnaire[13]. The safety profile of filgotinib 200mg in the SELECTIONLTE study was generally consistent with the safety profile observed in previous SELECTION studies, with no new safety signals observed.

Filgotinib in Crohn's disease (CD)

CD is an IBD of unknown cause, which results in chronic inflammation of the gastrointestinal (GI) tract with a relapsing and remitting course.

FITZROY Phase 2 program in CD

The FITZROY Phase 2 trial evaluated the efficacy and safety of filgotinib 200mg once-daily in 174 patients with moderate to severe active CD and mucosal ulceration, who were either anti-TNF naive or anti-TNF failures. As reported in *The Lancet* (Vermeire *et al.* 2016), the FITZROY Phase 2 trial achieved the primary endpoint of clinical remission at Week 10, and filgotinib demonstrated a favorable tolerability profile consistent with the DARWIN trials in RA.

DIVERSITY Phase 3 program in CD

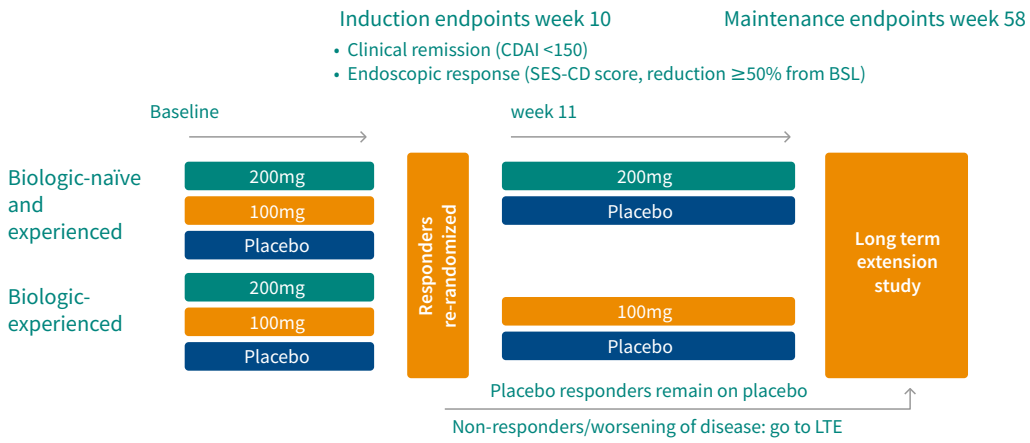
Gilead initiated the Phase 3 DIVERSITY trial with filgotinib in CD in November 2016, and following our amended collaboration agreement with Gilead, Galapagos became the sole sponsor of DIVERSITY (including all development costs) and the long-term extension study, and the parties completed the transfer of all data to Galapagos in March 2023. Under the terms of the amended agreement, Gilead made a one-time payment of $15 million to Galapagos.

DIVERSITY consisted of a combined (induction and maintenance), double-blind, placebo-controlled Phase 3 trial, enrolling 1,374 biologic-naive and biologic-experienced patients with moderate to severe active CD in 384 centers worldwide. The primary objectives of the trial were to evaluate the safety and efficacy of filgotinib 100mg or 200mg, once-daily oral treatments, versus placebo.

[13] The Inflammatory Bowel Disease Questionnaire is a widely used questionnaire for HRQoL assessment in patients with inflammatory bowel diseases.

The co-primary endpoints at Week 10 and Week 58 were clinical remission per Patient Reported Outcome (PRO-2) and endoscopic response per Simple Endoscopic Score for Crohn's Disease (SES-CD). Clinical remission measured by the Crohn's Disease Activity Index (CDAI) was a key secondary endpoint in the induction and maintenance phase of the study. Additional secondary endpoints were clinical remission and endoscopic response (combined into a single endpoint on a patient level) at Week 10, clinical remission and endoscopic response (combined into a single endpoint on a patient level) at Weeks 10 and 58, sustained clinical remission and endoscopic response at Weeks 10 and 58, and 6-month corticosteroid-free clinical remission at Week 58 (see graphic below).

Induction Cohort A included biologic-naïve (54%) and biologic-experienced (46%) patients; induction Cohort B included biologic-experienced patients. In total, 33% of patients in Cohort A and 52% of patients in Cohort B had failed treatment with 3 or more biologic drugs.



Filgotinib is not approved in CD by any regulatory authority

On 8 February 2023, Galapagos announced topline results from the DIVERSITY study.

Both induction cohorts of the study failed to meet the co-primary endpoints of clinical remission and endoscopic response for filgotinib, 100mg and 200mg once-daily. In the maintenance phase of the study, a statistically significant higher proportion of patients receiving filgotinib 200mg once-daily achieved the co-primary endpoints of clinical remission (43.8% vs. 26.4%; p=0.0382) and endoscopic response (30.4% vs. 9.4%; p=0.0038) compared to placebo at Week 58.

The safety observations of the study were in line with the underlying disease and were consistent with the safety profile of filgotinib observed in previous studies across indications.

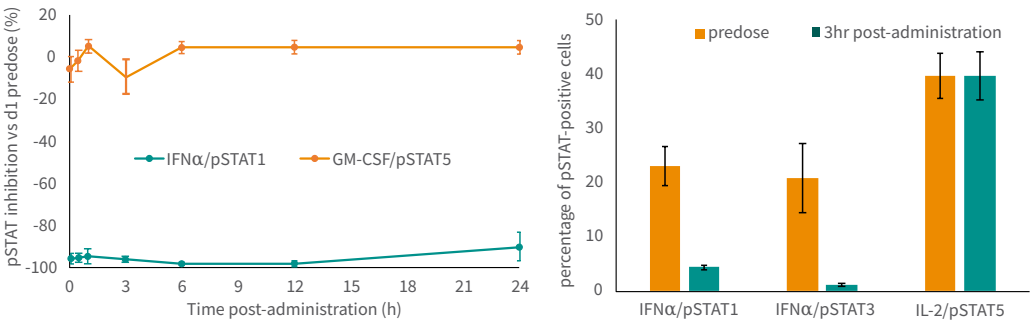
Based on these topline data, Galapagos decided not to submit a Marketing Authorization Application in Europe for filgotinib in CD. The full results will be further analyzed to gain valuable insights to guide future research efforts.

Our TYK2 program: GLPG3667

GLPG3667 is an investigational reversible and selective TYK2 kinase domain inhibitor that was discovered by us and evaluated in a Phase 1 healthy volunteer study in 2020. The Phase 1 study was a randomized, double-blind, placebo-controlled dose escalation study evaluating safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of single and multiple ascending oral doses of GLPG3667 for 13 days.

Blood was drawn at multiple time points on Day 1 and on Day 10 and stimulated *ex vivo* with several cytokines, including IFNα, to analyze the level of inhibition of inflammation, including the effect on phosphorylated signal transducer and activator of transcription (pSTAT) signaling as well as hematological parameters, lipids and creatine-phosphokinase (CPK) (see graphs below).

'3667 is a potent, selective TYK2 inhibitor

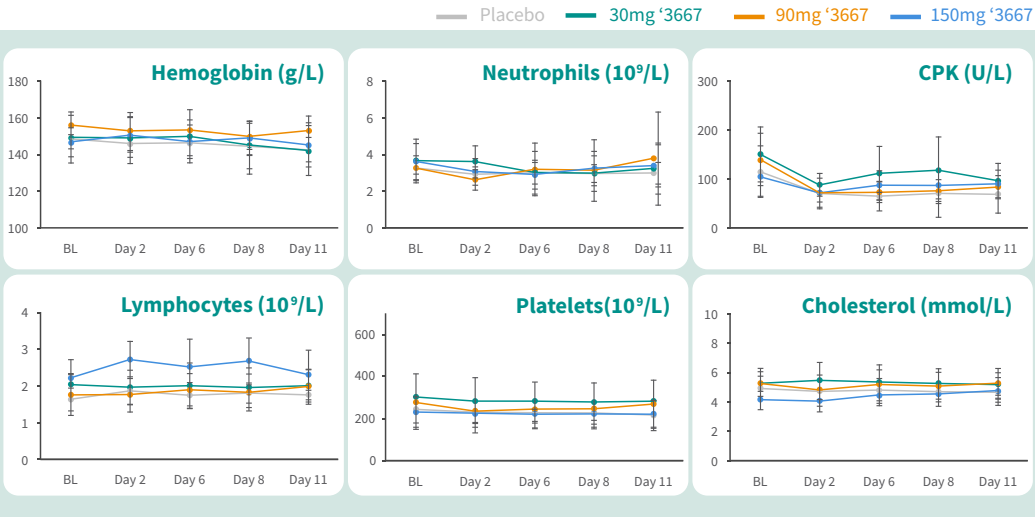


- '3667 high dose (150mg QD) in HV for 14 days (n=6)
- Collected blood (day 10) triggered ex vivo with IFNα or GM-CSF

- '3667 high dose (150mg QD) in HV for 4 days (n=14)
- Blood collected at T_{max} (3h post-administration) triggered ex vivo with IFNα, IL-2

HV, healthy volunteer. Source: company data

No effect on hematological parameters, lipids and CPK



Mean values. Source: company data. CPK: creatine phosphokinase

Following these results, we initiated a randomized, placebo-controlled, double-blind Phase 1b study in 31 patients with moderate to severe plaque psoriasis. Patients were randomized in a 1:1:1 ratio to a daily oral dose of GLPG3667 (low dose or high dose) or placebo, for a total of 4 weeks.

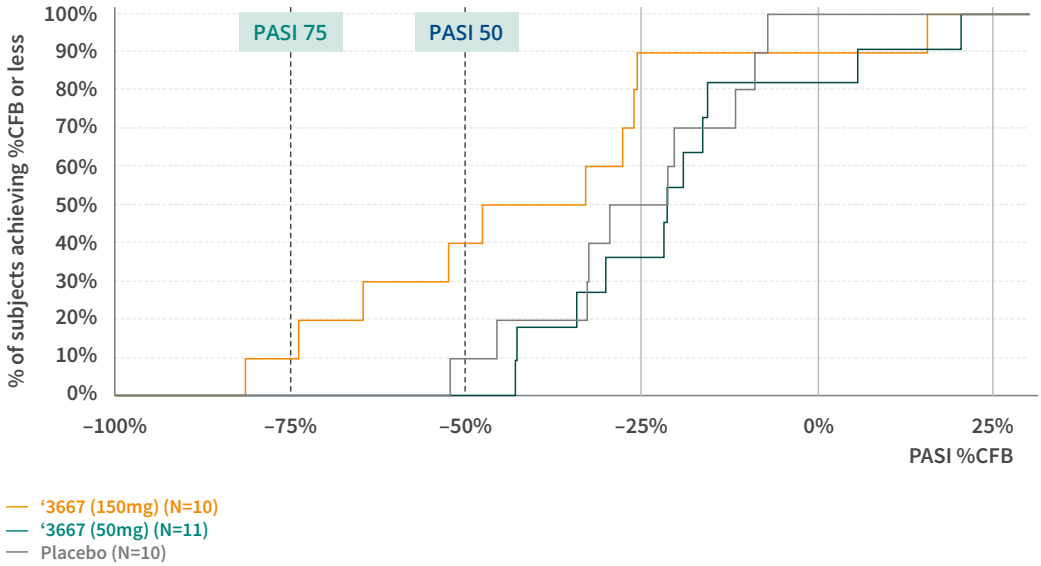
In July 2021, we announced positive topline results demonstrating that GLPG3667 was generally well tolerated with a positive response signal at Week 4 (see graph below):

- At Week 4, four out of 10 patients in the high dose group had a Psoriasis Area and Severity Index (PASI)50 response, defined as at least a 50% improvement in PASI from baseline, compared to one out of 10 subjects on placebo. There were no subjects with a PASI 50 response on the low dose of GLPG3667. The 4 responders in the high dose group of GLPG3667 achieved a 52%, 65%, 74% and 81% improvement respectively in their PASI scores from baseline, while the subject randomized to placebo improved by 52%. Positive efficacy signals were also observed with the high dose for other endpoints, including affected Body Surface Area and physician and patient global assessment, versus placebo at Week 4.

GLPG3667: clinical activity in Psoriasis at Week 4

Phase 1b psoriasis study with '3667

Clinical activity at 4 weeks with once daily dosing



CFB, change from baseline. Source: company data
*Papp et al, NEJM, 2018

- One subject in the low dose group interrupted participation in the study for one day due to exacerbation of psoriasis. The majority of treatment related adverse events (AEs) were mild in nature and transient. There were no deaths or serious adverse events (SAEs) in this 4-week study.

Following these results, in 2022, we initiated the preparations for the Phase 2 studies with GLPG3667 in dermatomyositis (DM) and systemic lupus erythematosus (SLE).

DM is the most common form of idiopathic inflammatory myopathies (IIM) and is characterized by inflammatory and degenerative changes of the muscles and skin. IIMs are a heterogenous group of rare autoimmune disorders primarily affecting the proximal muscles. They are characterized by severe muscle weakness, muscle enzyme elevations, inflammation on muscle biopsy, and extra-muscular manifestations. The quality of life of patients with DM is impaired due to muscle weakness and pain, and skin disease activity. [14] The overall mortality ratio in DM patients also remains three times higher compared to the general population, with cancer, lung, and cardiac complications and infections being the most common causes of death.

The Phase 2 studies in DM and SLE are expected to start later in 2023.

[14] Goreshi R, et al. Quality of life in dermatomyositis. *J Am Acad Dermatol.* 2011 Dec;65(6):1107-16.

Our SIK program

The Salt-Inducible Kinases (SIK) belong to a novel class of targets with immune-modulatory function discovered in an inflammation phenotypic cell assay with our proprietary target discovery platform. The search, identification, and validation for this novel class of targets started with the ambition to find novel druggable targets with a differentiating mechanism-of-action to develop new therapeutic candidates demonstrating an improved efficacy and safety profile relative to existing therapies. Although significant progress has been made with novel therapies in recent years, for instance in psoriasis, the unmet need to manage chronic inflammatory diseases related to joints, the bowel, and other organs remains an important objective in public health.

The SIK family, which includes 3 members SIK1, SIK2, and SIK3, has been shown to contribute to biologic pathways across multiple immune cells. SIK inhibition has the potential to reduce the production of pro-inflammatory cytokines coupled with enhanced production of immunoregulatory mediators. This unique mechanism-of-action offers the potential to restore the immune balance that is typically out of balance in autoimmune diseases, and differentiate product candidates from existing therapies that predominantly act by suppressing the immune system.

We have been focusing our medicinal chemistry efforts on these targets, delivering over 5,000 synthesized molecules, and more than 11 different chemical series with different SIK-isoform selectivity profiles. The first lead molecule from this program, GLPG3970, a selective SIK2/SIK3 inhibitor, has demonstrated a response across several disease models that has led to the investigation of a series of early-stage clinical trials in psoriasis (CALOSOMA), UC (SEA TURTLE), and RA (LADYBUG). The topline results for GLPG3970 were announced in July 2021.

Thorough analysis of clinical endpoints and exploratory biomarker research has confirmed meaningful signals of biological activity in psoriasis and UC patients despite short treatment duration and suboptimal PK properties. A second candidate, GLPG4399, selective for SIK3, was tested in a Phase 1 healthy volunteer study but will not be further pursued for clinical development.

SIK portfolio outlook

From the clinical studies described above we learned that the SIK pathway has the potential to play an important role in inflammation and confirms the therapeutic potential of SIK inhibitors in inflammatory diseases. Although we will not progress GLPG3970 and GLPG4399 further into clinical development, the study results are an essential part of the broad evidence package that we are assembling on our SIK program. This strengthens our understanding of the best approach going forward. We are currently performing medicinal chemistry activities with the goal to start preclinical development with a selective SIK inhibitor later in 2023.

CAR-T pipeline

GLPG5101 in refractory SLE

SLE is a female predominant, relapsing and remitting autoimmune disease, characterized by the formation of autoantibodies and immune complex–mediated inflammation. This results in systemic progressive multiple organ damage, which is associated with high morbidity and mortality.

Recently published data from a pilot study indicate that CAR-T cell therapy may have the potential to achieve long-term drug-free SLE remission.[15,16]

Given our deep disease knowledge and expertise in the field of immunology and our novel approach in the manufacturing of CAR-T therapies at the point-of care (**see ONCOLOGY section**), we plan to initiate a Phase 1b patient study with our CD19 CAR-T candidate, GLPG5101, later in 2023.

Oncology

Our differentiating approach

In 2022, we entered the field of oncology, CAR-T, and antibody-therapy research and development through the acquisitions of CellPoint and AboundBio. The transactions provide us with end-to-end capabilities in CAR-T therapy development and offer the potential for a paradigm shift in the space through the implementation of a breakthrough, decentralized point-of-care manufacturing model, and cutting-edge fully human antibody-based capabilities to design next-generation CAR-Ts and biologicals.

Point-of-care manufacturing

Despite continued progress with current CAR-T cancer therapies, long lead times, costly central manufacturing and complex logistics continue to be limiting factors for large-scale capacity and broad patient access.

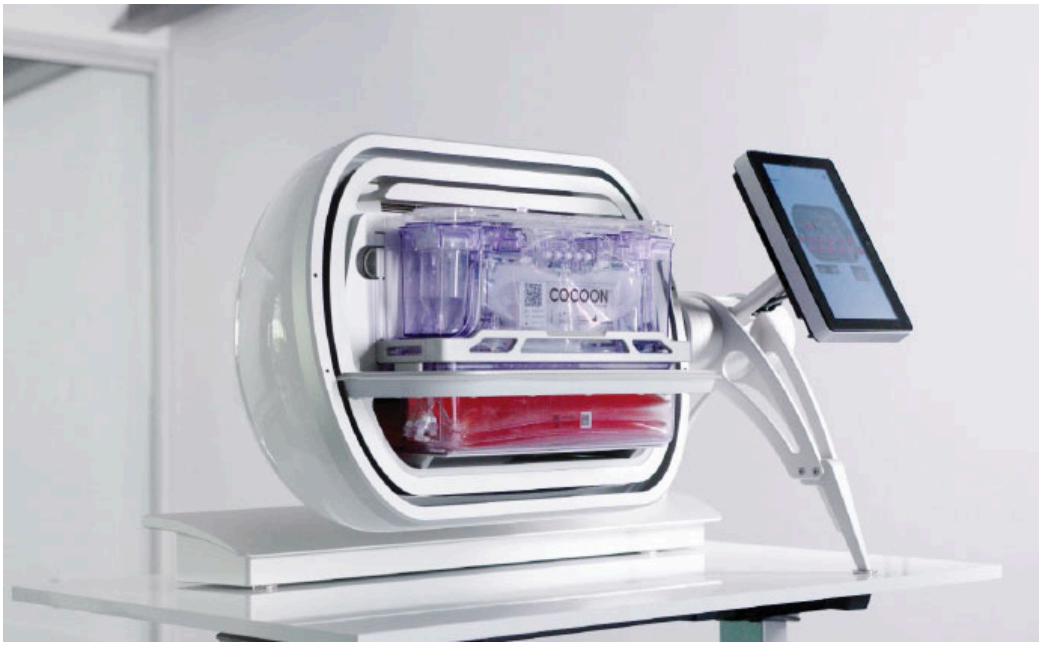
To address important limitations of current CAR-T treatments, CellPoint (a Galapagos company) has developed, in a strategic collaboration with Lonza, a novel decentralized delivery model designed to manufacture non-frozen CAR-T therapies at the point-of-care.

Through decentralized manufacturing, complex logistics and cryopreservation of the cells can be avoided, and the average vein-to-vein time can be drastically reduced from up to months for currently approved CAR-T therapies to 7 days with our CAR-T candidates currently observed in our clinical trials.

[15] Anti-CD19 CAR-T cell therapy for refractory systemic lupus erythematosus. Mackensen A, Müller F, Mougiakakos D, et al. Nat Med. 2022 Sep 15.
[16] CD19-targeted CAR-T cells in refractory systemic lupus erythematosus. Mougiakako Ds , Krönke G Völkl S, et al. N Engl J Med. 2021 Aug 5;385(6):567-569.

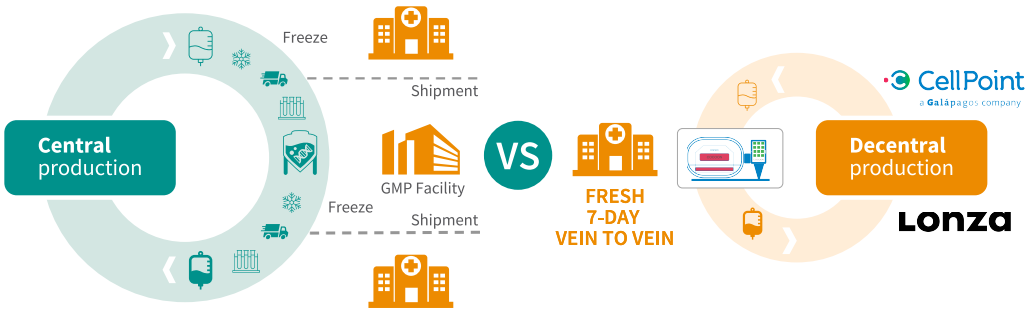
The proprietary platform consists of CellPoint's end-to-end xCellit workflow management and monitoring software and Lonza's Cocoon®, a functionally closed, automated manufacturing platform for cell therapies.

The novel point-of-care model is compliant with the EMA and FDA guidance for clinical trials.



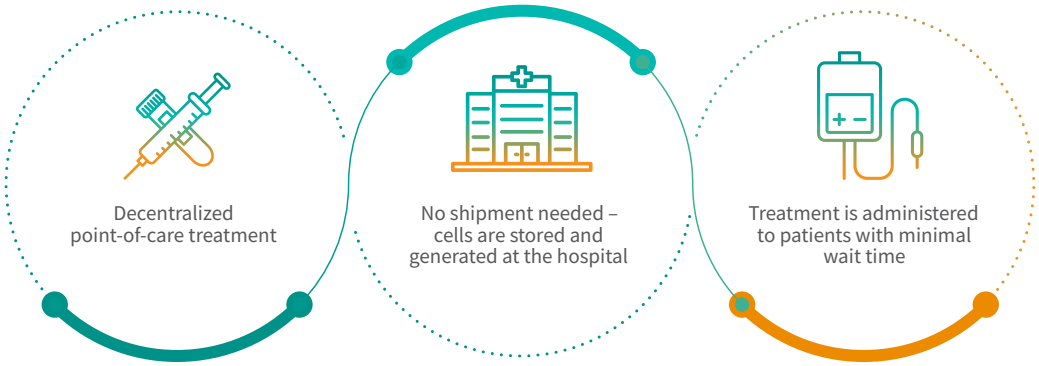
The Cocoon® Platform - Picture curtosy of Lonza

Increase patient access with point-of-care manufacturing



*vein to vein time: time between leukapheresis and infusion delivery at the hospital

Streamlining CAR-T Therapy



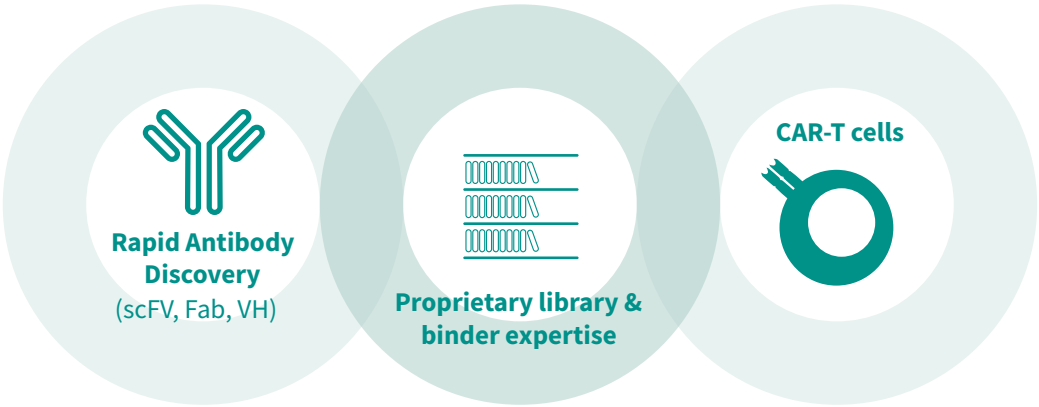
Antibody engineering capabilities

AboundBio (a Galapagos company) has developed several very large, diverse human antibody libraries in standard fragments of antigen binding (Fab), single-chain variable fragments (scFv), and unique variable (VH) domain formats. The team can rapidly (days to weeks) discover novel, high affinity, binders in multiple formats, engineer them if needed to improve their developability properties, and convert them for multiple uses including multi-specific, CARs, fusion proteins and antibody drug conjugates (ADCs). The proprietary methodologies to build large fully-human antibody-based libraries offer the potential to increase binder diversity, affinity and specificity; coverage of potential antigens; screening capacity; and probability of identifying a lead therapeutic antibody candidate.

In the field of oncology, AboundBio provides unique research capabilities for next generation CAR-T therapies that have the potential to deliver deeper and durable clinical responses, as well as additional drug modalities beyond small molecules.

Our new generation of fully human, multi-specific CAR-T constructs have the potential to transform patient outcomes through potentially more effective and longer-lasting care options, even in the event of relapse after previous CAR-T-cell therapy. Together with the decentralized CAR-T point-of-care manufacturing model, we aim to broaden patient access and ultimately hope to change their lives.

Scientific capabilities



scFV, single-chain fragment variable; Fab, fragment antigen-binding; VH, heavy chain variable domain

Pipeline CAR-T manufactured at point-of-care

GLPG5101: CD19 CAR-T in relapsed/refractory non-Hodgkin's lymphoma

Non-Hodgkin's lymphoma (NHL) is a cancer originating from lymphocytes, a type of white blood cell which is part of the body's immune system. NHL can occur at any age although it is more common in adults over 50 years old. Initial symptoms usually are enlarged lymph nodes, fever, and weight loss. There are many different types of NHL. These types can be divided into aggressive (fast-growing) and indolent (slow-growing) types, and they can be formed from either B lymphocytes (B cells) or in lesser extent from T lymphocytes (T cells) or Natural Killer cells (NK cells). B cell lymphoma makes up about 85% of NHL cases diagnosed in the US. Prognosis and treatment of NHL depend on the stage and type of disease.

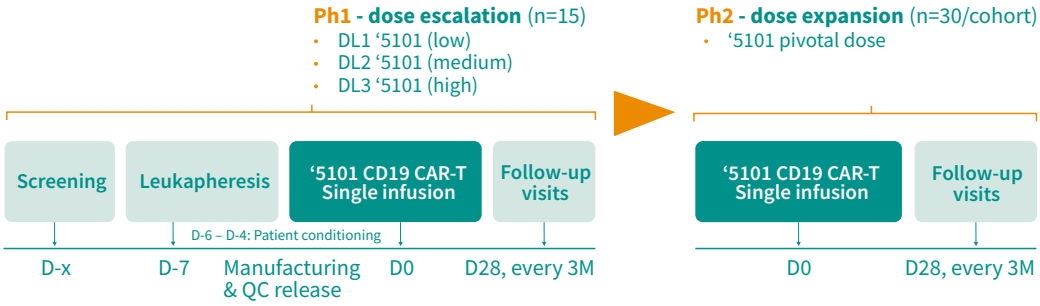
GLPG5101 is our second generation anti-CD19/4-1BB CAR-T product candidate, administered as an intravenous infusion of a fresh product candidate in a single fixed dose. Its feasibility, safety, and efficacy of point-of-care manufacturing are currently being evaluated in the ATALANTA-1 Phase 1/2, open-label, multicenter study in patients with relapsed/refractory non-Hodgkin lymphoma (rrNHL).

The primary objective of the Phase 1 part of the ATALANTA-1 study is to evaluate safety and to determine the recommended dose for the Phase 2 part of the study. Secondary

objectives include assessment of efficacy and feasibility of point-of-care manufacturing of GLPG5101. The dose levels that are evaluated in the Phase 1 part are $50x10^6$ (DL1), $110x10^6$ (DL2) and $250x10^6$ (DL3) CAR-T cells. The primary objective of the Phase 2 part is to evaluate the objective response rate (ORR) while the secondary objectives include complete response rate (CRR), duration of response, progression free survival, overall survival, safety, pharmacokinetic profile, and feasibility of point-of-care manufacturing. Each enrolled patient will be followed for 24 months.

ATALANTA CD19 CAR-T Phase 1/2a in rrNHL

Evaluating feasibility, safety and efficacy of point-of-care CD19 CAR-T



DL, dose level; rrNHL, refractory/relapsed non-Hodgkin lymphoma. Start of dose expansion in 2023 pending regulatory approval

In December 2022, we presented initial data from the ATALANTA-1 Phase 1 study during a poster session at the 64th Annual American Society of Hematology (ASH) Congress in New Orleans, Louisiana. The initial results from 7 patients that were eligible for efficacy evaluation (ATALANTA-1 Phase 1 study cut-off date: 8 November 2022) indicated that a 7-day vein-to-vein time was feasible and demonstrated strong and consistent *in vivo* CAR-T expansion levels. Moreover, the initial efficacy results were encouraging with an observed ORR of 86% and a complete response (CR) observed in all responding patients. A duration of response of up to 7 months has been reported and follow-up is ongoing. Two patients who received DL1 that progressed, after initial stable disease or CR respectively, had a CD19-negative escape. No CD19-positive relapses have been observed.

In the initial safety analysis of these 7 patients, adverse events were consistent with the known toxicities of CD19 CAR-T treatment. No grade 3 or higher cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS) was observed in any of the patients. At DL2, CRS grade 1 or 2 was reported in 4 patients and ICANS grade 1 was reported in 3 patients. Patients at DL1 did not experience any grade of CRS or ICANS. Dose-limiting toxicity (neutropenia grade 4 for >21 days) was observed in 1 patient (DL2) and the majority of grade ≥3 adverse events were hematological toxicities.

The study is currently enrolling rrNHL patients in Europe and the first expansion cohort for Mantle Cell Lymphoma, a form of NHL, is currently open for recruitment. We aim to provide Phase 1 topline results around mid-2023.

GLPG5201: CD19 CAR-T in relapsed and refractory chronic lymphocytic leukemia

Chronic lymphocytic leukemia (CLL) is one of the chronic lymphoproliferative disorders (lymphoid neoplasms). It is characterized by the excessive and uncontrolled proliferation of functionally incompetent B lymphocytes from monoclonal origin. CLL and small cell lymphocyte leukemia (SLL) are essentially the same type of B-cell non-Hodgkin lymphoma (NHL), with the only difference the location where the primary cancer occurs. CLL affects B-cells in the blood and bone marrow and SLL cancer cells are located in lymph nodes and/or the spleen. Richter's Transformation (RT) is an uncommon clinicopathological condition observed in patients with CLL. It is characterized by the sudden transformation of the CLL into a significantly more aggressive form of large cell lymphoma, and occurs in approximately 2 – 10%[16] of all CLL patients. CLL/SLL usually follows an indolent course and is an incurable disease. Patients who develop relapsed and refractory disease and become resistant to new agents have a dismal prognosis and a high unmet medical need for new therapeutic options such as CAR-T cells. With an estimated incidence rate of 4.7 new cases per 100,000 individuals, CLL/SLL are the most prevalent lymphoid malignancies and the most common forms of adult leukemia in the US and in Europe[17].

EUPLAGIA-1 is an ongoing Phase 1/2 study in heavily pre-treated patients with rrCLL and rrSLL, with or without RT, to evaluate the safety, efficacy, and feasibility of GLPG5201, a non-frozen CD19 CAR-T product candidate manufactured at point-of-care.

GLPG5201 is our second generation anti-CD19/4-1BB CAR-T product candidate, administered as an intravenous infusion of a fresh product candidate in a single fixed dose.

Patients with CD19 rrCLL or rrSLL with >2 lines of therapy are eligible to participate, and patients with RT are eligible regardless of prior therapy. The primary objective of the Phase 1 part of the study is to evaluate safety and determine the recommended dose for the Phase 2 part of the study. The dose levels that are evaluated in the Phase 1 part of the study are $35x10^6$ (DL1), $100x10^6$ (DL2) and $300x10^6$ (DL3) CAR+ viable T cells. The primary objective of the Phase 2 part of the study is to assess the ORR and the secondary objectives include the analysis of the CRR, duration of response, progression free survival, overall survival, safety pharmacokinetic profile, and feasibility of point-of-care manufacturing.

[16] CD19-targeted CAR-T cells in refractory systemic lupus erythematosus. Mougiakako Ds , Krönke G Völkl S, et al. N Engl J Med. 2021 Aug 5;385(6):567-569.
[17] Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA: A Cancer Journal for Clinicians. 2021;71(1):7-33. **https://www.ncbi.nlm.nih.gov/books/NBK493173**

We presented initial encouraging safety and efficacy data from the EUPLAGIA -1 Phase 1 study during a poster session at the EBMT-EHA 5th European CAR-T-cell Meeting in Rotterdam in February 2023 (EUPLAGIA-1 Phase 1 study data cut-off date: 9 January 2023). At the moment of analysis on 9 January 2023, 7 patients diagnosed with rrCLL (4 patients of which have RT) were enrolled in the study (n=4 at dose level 1 (DL1); n=3 at dose level 2 (DL2). All patients received GLPG5201 as a fresh infusion with a median vein-to-vein time of 7 days.[19]

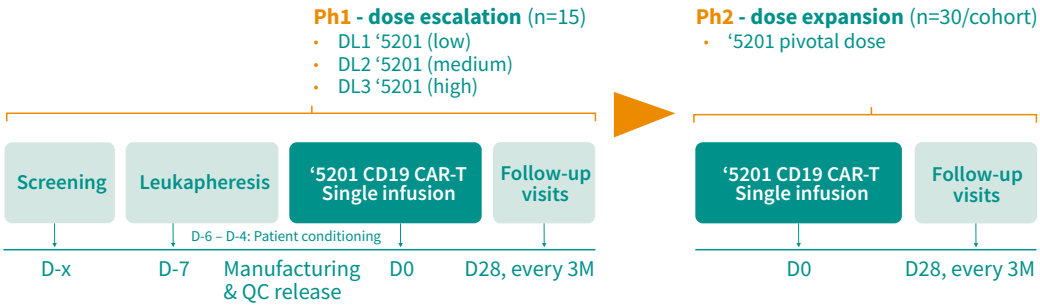
The initial results from these 7 patients that were eligible for efficacy analysis (EUPLAGIA -1 Phase 1 cut-off date: 9 January 2023) indicated that a 7 day vein-to-vein time was feasible and that the 'fresh' CAR-T product candidate demonstrated strong and consistent *in vivo* CAR-T expansion levels. Moreover, the initial efficacy results were encouraging with an observed ORR of 100%. A CR was observed in 6 out of 7 patients (86%) and in all 4 patients with RT. A duration of response of up to 7.9 months has been reported and follow-up is ongoing. Only 1 patient (DL1) progressed (progressive disease after partial response, (PR)) and had a CD19-negative relapse with confirmed Richter's transformation.

In the safety analysis of these 7 patients, adverse events were consistent with the known toxicities of CD19 CAR-T treatment. None of the patients experienced a cytokine release syndrome (CRS) higher than grade 2 at both dose levels and no immune effector cell associated neurotoxicity syndrome (ICANS) was reported. No dose limiting toxicities (DLTs) were reported and the majority of grade ≥3 adverse events were hematological. Only one serious adverse event was reported at DL2 with a patient experiencing a CRS grade 2, but the event was resolved after 7 days.

The EUPLAGIA-1 study is continuing to enrol rrCLL and rrSLL patients in Europe, including patients with RT, and we aim to provide Phase 1 topline results around mid-2023.

EUPLAGIA CD19 CAR-T Ph1/2a in r/rCLL

Evaluating feasibility, safety and efficacy of point-of-care CD19 CAR-T



DL, dose level; r/rCLL, relapsed/refractory chronic lymphocytic leukemia

[19] N. Martinez-Cibrian , S. Betriu , V. Ortiz-Maldonado , D. Esteban , L. Alserawan , M. Montoro , A.D. Van Muyden , M. Spoon , M.J Pont , C. Jacques , J.Delgado (2023, February 9-11) *Initial clinical results of Euplagia-1, a Phase I/II Trial of Point-of-Care Manufactured GLPG5201 in R/R CLL/SLL with or without Richter's transformation* [Poster presentation]. EBMT-EHA 5th European CAR T-cell Meeting, Rotterdam, the Netherlands

GLPG5301: BCMA CAR-T in relapsed and refractory multiple myeloma

Multiple myeloma (MM) is typically characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and may result in extensive skeletal destruction with osteopenia, and osteolytic lesions with or without pathologic fractures. The diagnosis of MM is made when one (or more) of the following clinical presentations are present: bone pain with lytic lesions discovered on routine skeletal films or other imaging modalities, an increased total serum protein concentration with the presence of a monoclonal protein in the urine or serum, and anemia, hypercalcemia or renal failure. The patient may be either symptomatic or their disease may be discovered incidentally.

PAPILIO-1 is a Phase 1/2, open-label, multicenter study to evaluate the feasibility, safety, and efficacy of point-of-care manufactured GLPG5301, our BCMA CAR-T product candidate, in patients with relapsed/refractory multiple myeloma (rrMM).

GLPG5301 is a second generation anti-BMCA/4-1BB CAR-T product candidate, administered as an intravenous infusion of a fresh product candidate in a single fixed dose. Each enrolled patient will be followed for 24 months.

The primary objective of the Phase 1 part of the PAPILIO-1 study is to evaluate safety and determine the recommended dose for the Phase 2 part of the study. Secondary objectives of the Phase 1 part of the study include assessment of efficacy and feasibility of point-of-care manufacturing of GLPG5301.

The primary objective of Phase 2 of the study is to evaluate the ORR while the secondary objectives include assessment of CRR, duration of response, progression free survival, overall survival, safety, pharmacokinetic profile, and feasibility of point-of-care manufacturing.

We expect to start enrolling patients with rrMM in Europe in the second quarter of 2023.