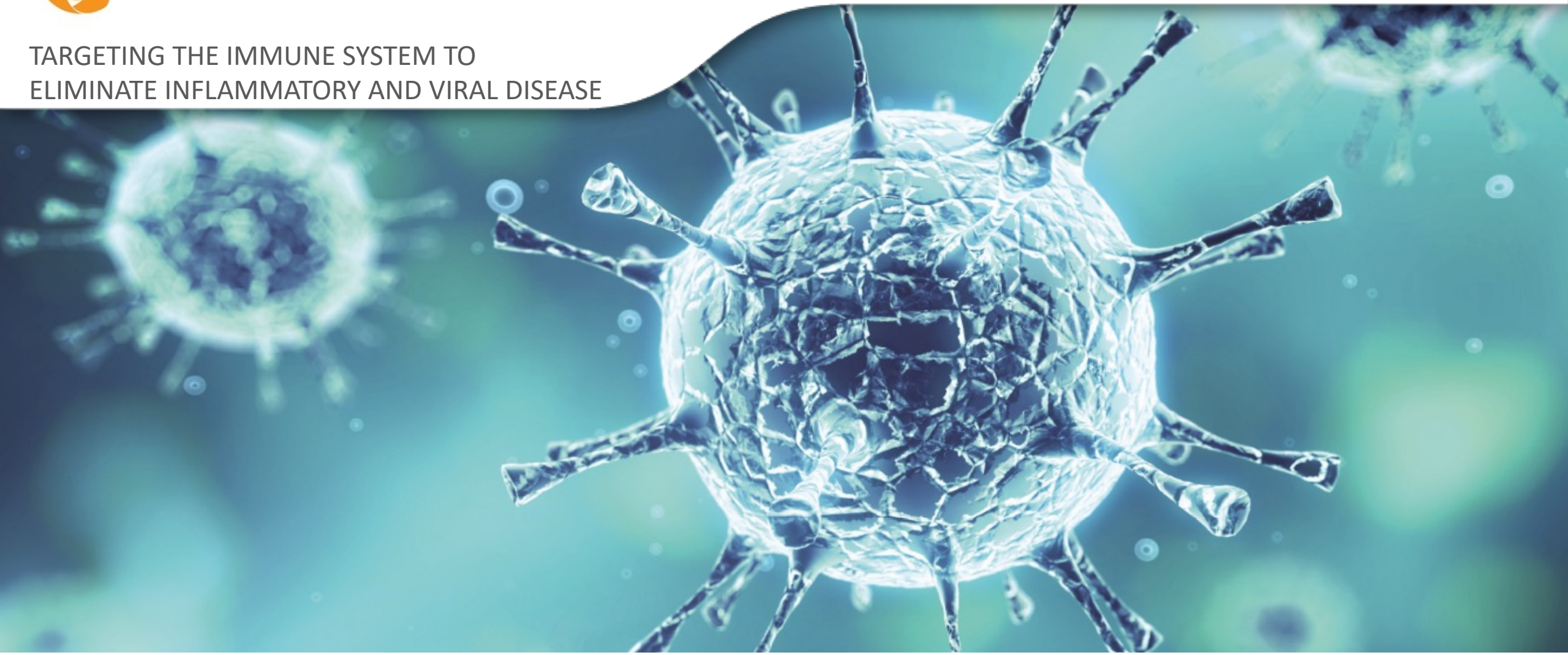
abivax

TARGETING THE IMMUNE SYSTEM TO
ELIMINATE INFLAMMATORY AND VIRAL DISEASE



Reprioritizing towards Inflammatory Diseases

February 2019

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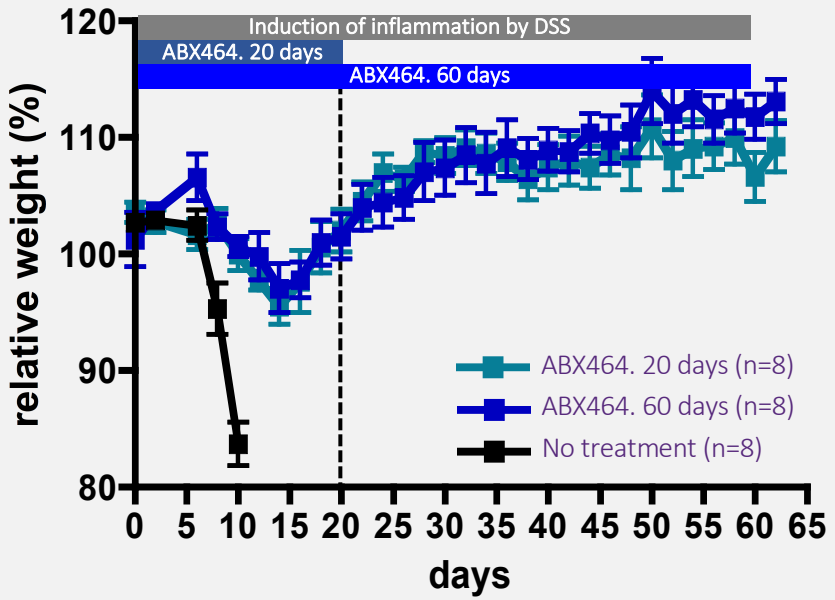
ABX464: The path towards inflammatory disease

Robust preclinical data from the IBD animal model

Invention ABX464

- **2015:** Recognition of ABX464 having strong anti-inflammatory properties through an increase of miRNA124 expression

ABX464 protects mice from death in the DSS mouse model



Preclinical validation in Ulcerative Colitis (UC) mouse model

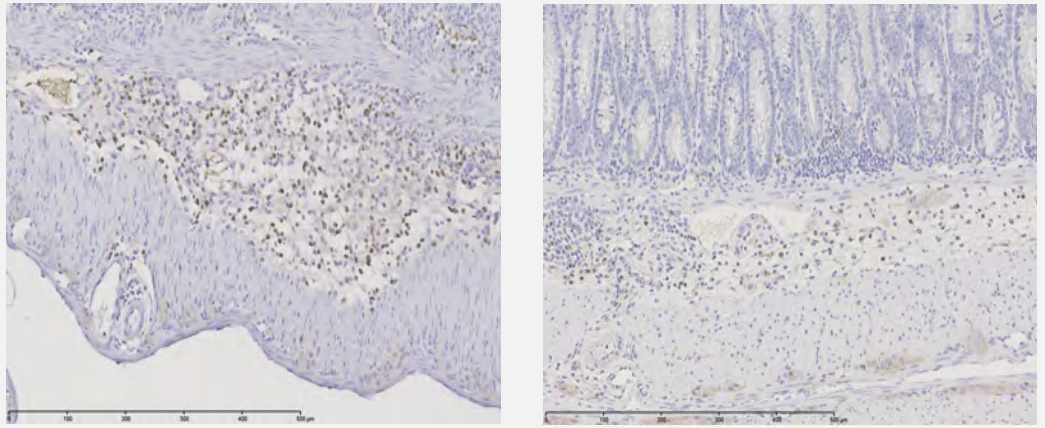
- **July 2017**: Nature scientific reports publication of compelling anti-inflammatory efficacy in a DSS[1] mouse model

SCIENTIFIC REPORTS

The Anti-Hiv Candidate Abx464 Dampens Intestinal Inflammation by Triggering Il-22 Production in Activated Macrophages

DSS without treatment leads to intestinal damage

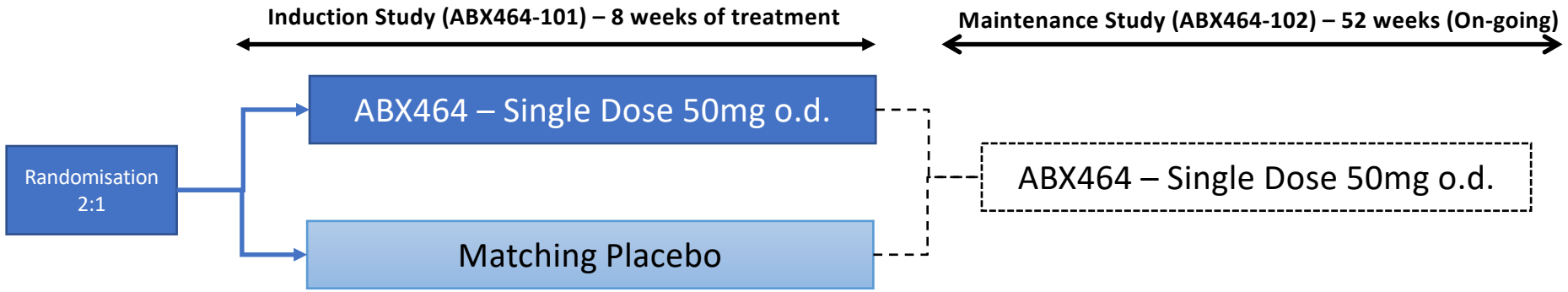
ABX464 protects intestinal Structure



In the DSS model, ABX464 leads to reduced expression of pro-inflammatory cytokines: IL-6 (2x), TNF (7.5x) and MCP-1 (6x) and increased expression of the anti-inflammatory IL-22

Phase IIa Study Design (ABX464-101)

Randomized, double-blind, placebo controlled, multi-national study



- Study Population = Patients with Moderate to Severe Active UC who have failed or are intolerant to immunomodulators, Anti-TNFα, vedolizumab and/or corticosteroids
  - Confirmed diagnosis of UC for at least 3 months with a Total Mayo Score (TMS) of 6 to 12 with endoscopic sub-score of 2 or 3
  - Previous Treatment Failure to : Salicylates, corticoids, immunomodulators or biologics
- Key Study Endpoints
  - Safety - Adverse Events
  - Mayo Score and Endoscopy (Central reading)
  - Fecal Calprotectin level, Geboes Score (histopathology), miRNA-124 expression, Microbiome
  - Quality of Life (SF-36)
  - Pharmacokinetics (Optional procedure; N=4)

- Coordinator : Prof Séverine Vermeire (Univ. Leuven)
- Countries involved : Belgium, France, Germany, Austria, Poland, Hungary, Czech Republic and Spain *
- Robust study methodology using central reading of the endoscopies & Central lab for all biological endpoints

** Underlined = Inactive countries*

Patient demographics and baseline disease characteristics

Groups well-balanced

		ABX-464 N = 23	Placebo N = 9	Total N = 32
Age (years)	*Mean (Min-Max)*	42.96 (*20.0 – 73.0*)	44.11 (*20.0 – 64.0*)	43.28 (*20.0 -73.0*)
Sex	*Male*	12 (52.2%)	8 (88.9%)	20 (62.5%)
BMI (kg/m^2) at Screening	*Mean*	25.63 (*17.6 - 38.6*)	25.96 (*20.3 - 32.9*)	25.72 (*17.6 – 38.6*)
CRP (mg/L)	*Mean / Median*	7.4 / 2.5	4.5 / 1.8	6.6 / 2.3
	Min-Max	*0.4- 66.8*	*0.4-19.2*	*0.4- 66.8*
Fecal Calprotectin (µg/g)	*Geometric Mean (N)*	958.9 (23)	786,01 (8)	910,9 (31)
	Min-Max	*78.7 – 19109.0*	*39.2 – 5150.3*	*39.2 – 5150.3*
Disease Duration (years)	*Mean / Median*	7.60 / 5.76	6.47 / 5.17	7.28
	Min-Max	*0.3- 26.0*	*2.9- 13.0*	*0.3- 26.0*
Previous Biologics Exposure		10/23 (43.5%)	6/9 (66.6%)	16/32 (50%)
Refractory to anti-TNF & Vedo		*5/10 (50%)*	*4/6 (67%)*	*9/16 (56%)*
Refractory to anti-TNF		*5/10 (50%)*	*2/6 (33%)*	*7/16 (44%)*
Total Mayo Score	*Mean (Min-Max)*	8.65 (*6 – 11*)	7.89 (*4 – 11*)	8.44 (*4 – 11*)
Partial Mayo Score	*Mean (Min-Max)*	6.17 (*4 – 8*)	5.56 (*2 – 8*)	6,0 (*2 – 8*)

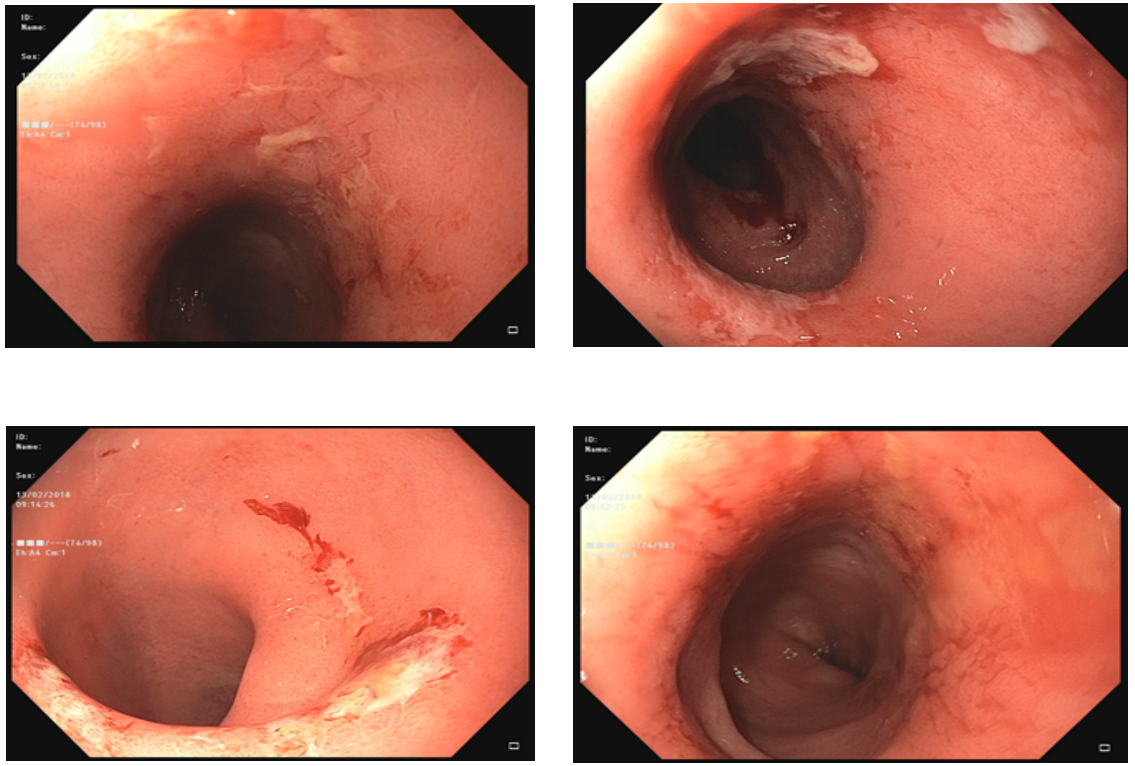
Strong efficacy signal observed

- Clinical Remission rate
  - **35.0 %** of ABX464 patients in Clinical Remission (Placebo = 11.1%, consistent with literature in UC studies) defined as Total Mayo Score being less than or equal to two, with no individual sub-score greater than one.
  - **35.0 %** of ABX464 patients in Clinical Remission (Placebo = 11.1%, consistent with literature in UC studies) defined as a rectal bleeding sub-score = 0 with an endoscopy sub-score ≤1 and at least one-point decrease in stool frequency sub-score from baseline to achieve a stool frequency sub-score ≤1 (as per 2016 FDA Guideline).
- Mucosal Healing rate
  - **50.0 %*** (p=0.03) of ABX464 patients with Mucosal Healing (Placebo = 11.1%)
- Clinical Response rate
  - **70.0 %** of ABX464 patients with a Clinical Response (Placebo = 33.3%)

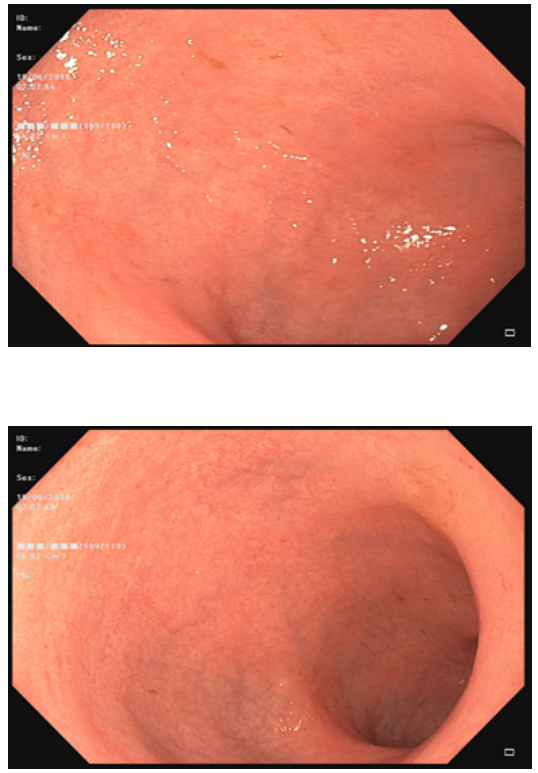
Mucosal healing in an ABX464 treated patient

Courtesy of Prof. Severine Vermeire

Before ABX464



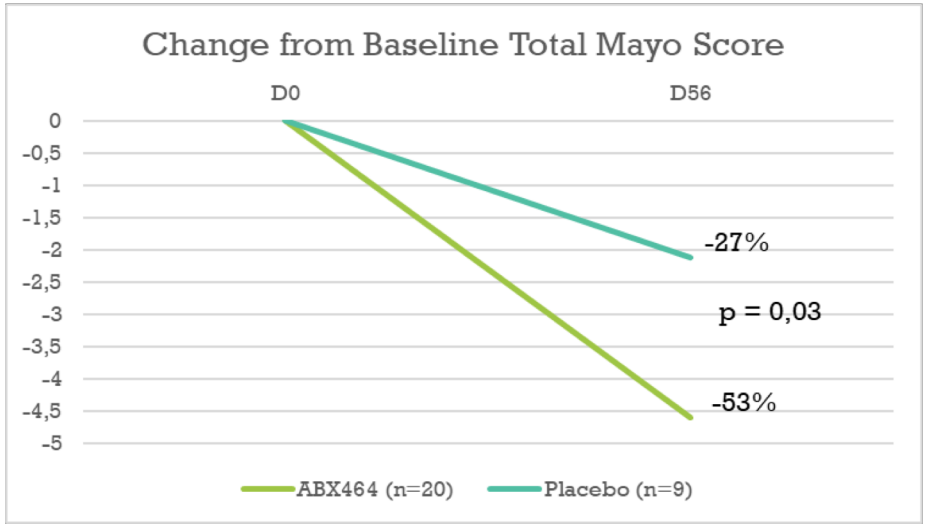
After ABX464

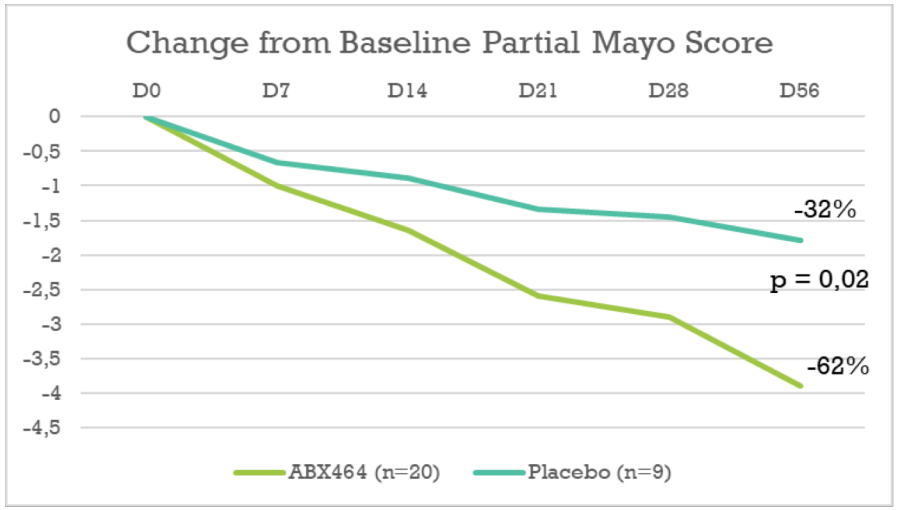


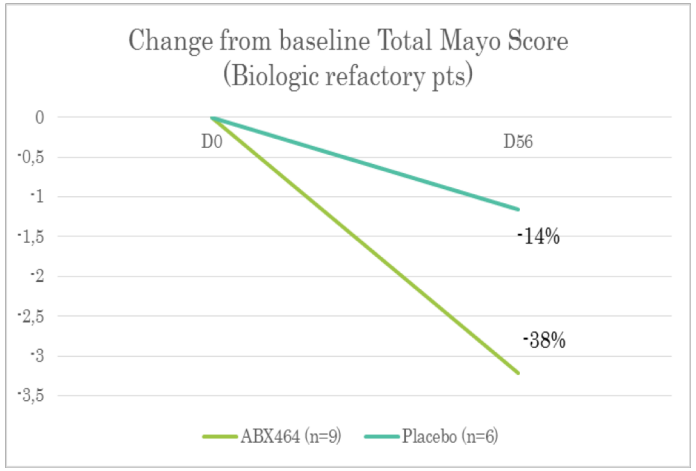
Mayo Score Results

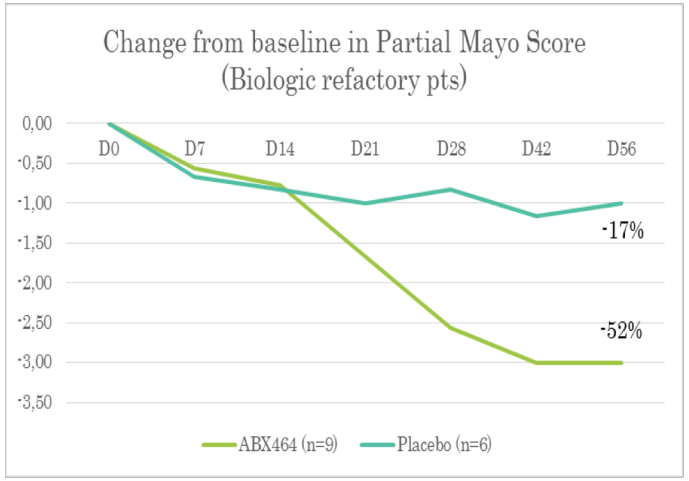
Statistically significant signal observed in TMS and PMS

ABX464: Fast onset of action and clinical responses in patients who failed on biologics



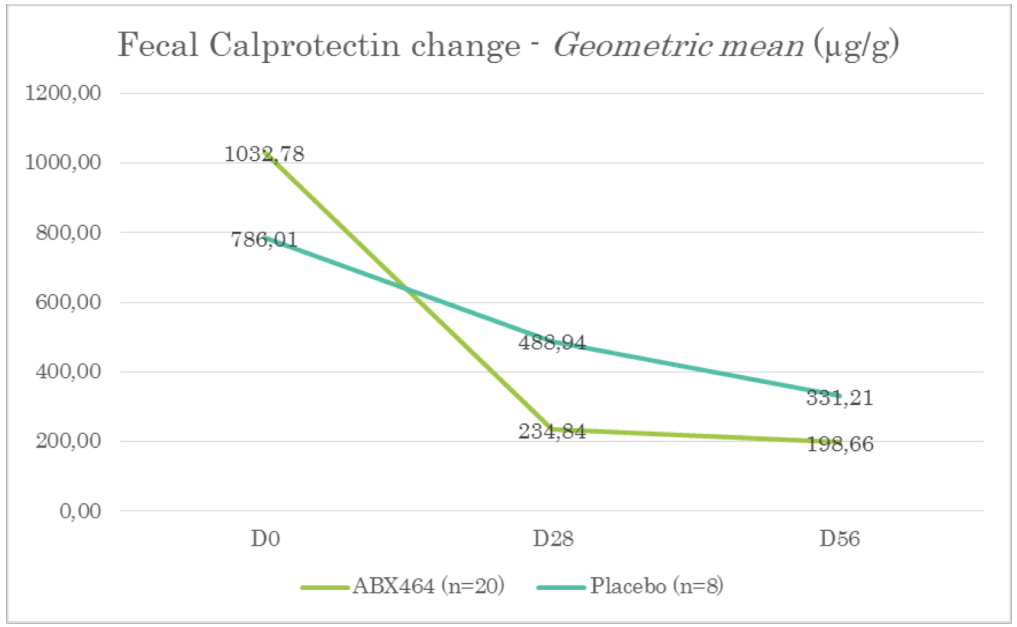






Calprotectin level

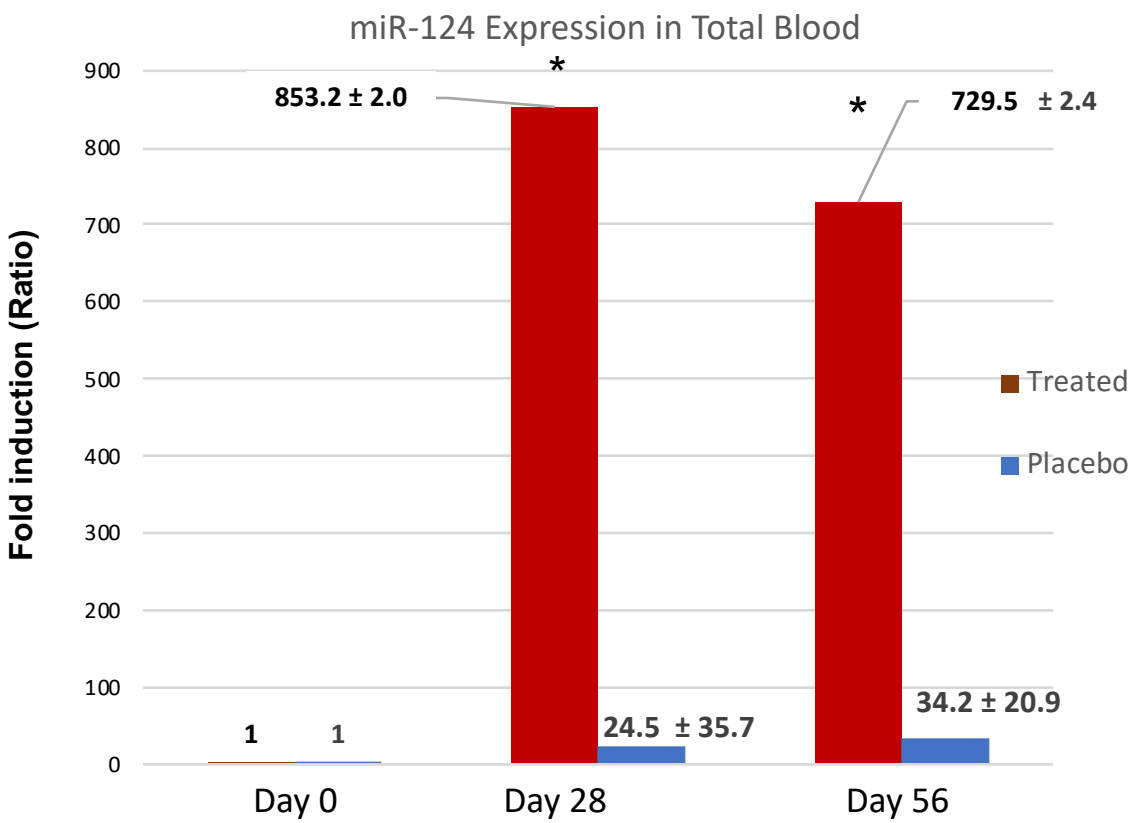
Trend of greater reduction despite high placebo response – Consistent with TMS results

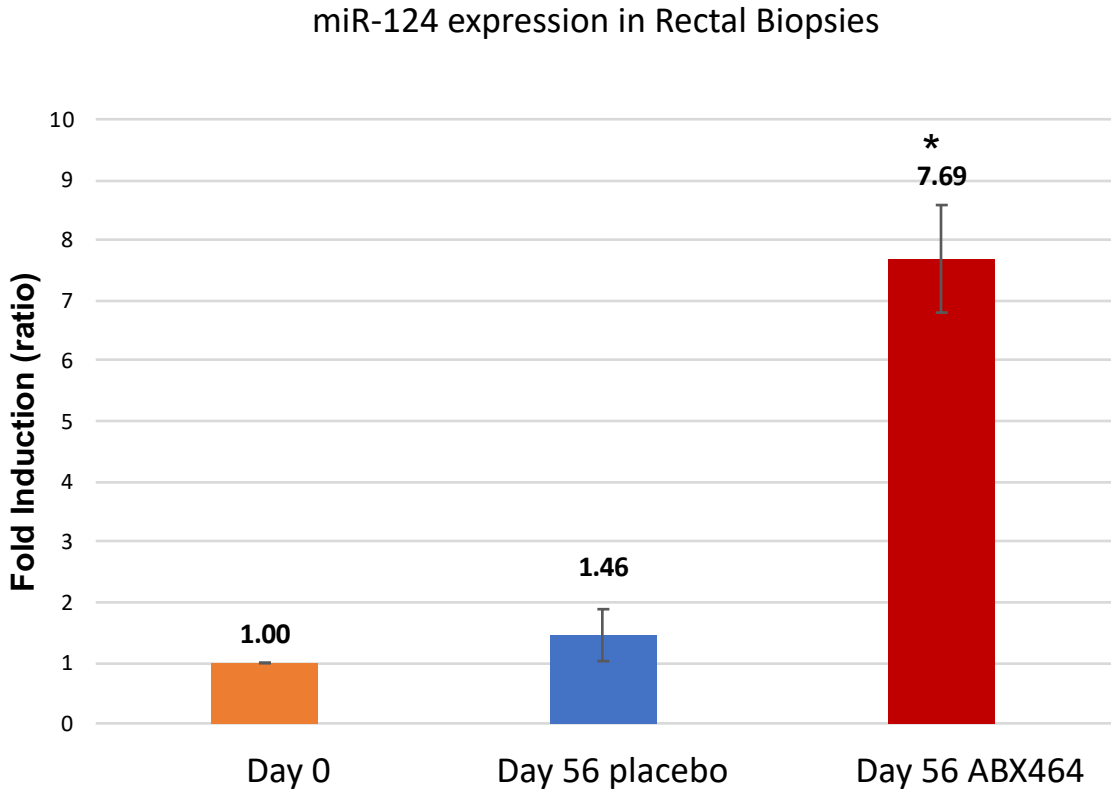


% of patients with at least a 50% reduction from Baseline in Fecal Calprotectin	
ABX464 (n=20)	75.0%
Placebo (n=8)	50.0%

Statistically significant increase in miR-124 expression during ABX464 treatment

Total blood and Rectal tissue





** p value < 0.05 (Treatment and time point)*

Safety Profile

Good safety profile – Consistent with previous studies

Patients experiencing at least one TEAEs (Treatment Emergent Adverse Events) by SOC and PT (>5%) regardless of causality		ABX-464 (N=23)	Placebo (N=9)
		N (%)	N (%)
Any Treatment-Emergent Adverse Events		**18 (78.3%)**	**5 (55.6%)**
Gastrointestinal disorders		8 (34.8%)	2 (22.2%)
	Abdominal pain	4 (17.4%)	1 (11.1%)
	Abdominal pain upper	3 (13.0%)	0 (0.0%)
	Diarrhoea	0 (0.0%)	1 (11.1%)
	Nausea	2 (8.7%)	0 (0.0%)
General disorders and administration site conditions		3 (13.0%)	0 (0.0%)
	Chest pain	2 (8.7%)	0 (0.0%)
	Influenza like illness	2 (8.7%)	0 (0.0%)
Hepatobiliary disorders		0 (0.0%)	1 (11.1%)
	Cholestasis	0 (0.0%)	1 (11.1%)
Infections and infestations		4 (17.4%)	1 (11.1%)
	Nasopharyngitis	1 (4.3%)	1 (11.1%)
Investigations		1 (4.3%)	1 (11.1%)
	Glutamate dehydrogenase increased	0 (0.0%)	1 (11.1%)
Metabolism and nutrition disorders		2 (8.7%)	2 (22.2%)
	Hypophosphataemia	1 (4.3%)	2 (22.2%)
Nervous system disorders		5 (21.7%)	0 (0.0%)
	Headache	4 (17.4%)	0 (0.0%)
Renal and urinary disorders		0 (0.0%)	1 (11.1%)
	Nephrolithiasis	0 (0.0%)	1 (11.1%)
	Renal colic	0 (0.0%)	1 (11.1%)

ABX464 – 102: one year open-label extension study

Second year of open label extension already approved in Belgium

- 22 patients enrolled in the 52-week maintenance phase (including 7 previously placebo treated patients), dosed with ABX464 50mg once daily.
- Safety profile is good with no severe adverse reactions. One myocardial infraction (SAE) reported, but not related to ABX464. Patient is doing well and continues on treatment.
- Based on the safety of ABX464, DSMB approved amendment to expand the open label treatment duration by one more year (investigators' request) approved in Belgium and submitted in Poland and Hungary (approval pending).
- First patient entered the extension of the maintenance study on Jan 24, 2019 (i.e. now more than 14 months on ABX464).
- Soft-lock of the clinical database (min. 6 months data for all patients) planned in March. 2019.
- 6 months interim data to be presented during plenary session at ECCO (March 8, Copenhagen, Denmark)

Phase 2a results support continuation of ABX464 in UC as well as clinical exploration in other inflammatory indications

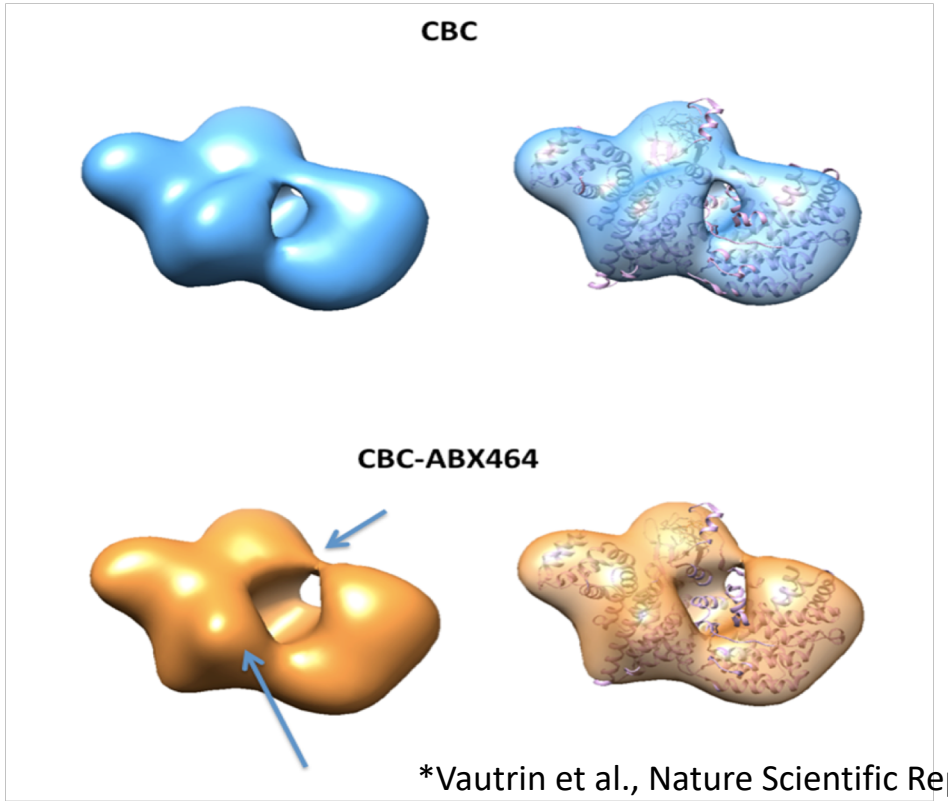
- Clinical results warrant the conduct of Phase 2b Study – clinical study ABX464-103
  - Patients with moderate to severe Ulcerative Colitis refractory to conventional and/or biological therapies
  - 25mg, 50mg, 100mg or placebo – daily dosing
  - Induction phase of treatment with Clinical Remission evaluated at Week 8
  - 232 patients (100-120 centres) – Coordinator: Prof. Severine Vermeire
  - First Clinical Trial Application Feb 2019
  - Results of induction phase expected prior to EoP 2 meeting with FDA in H2 2020

- Abstract with study results (including 6 months data from the ongoing one year open label maintenance study) accepted for oral plenary presentation at the ECCO 2019 Conference (March 8, Copenhagen)

- Phase 2a Proof of Concept studies in additional inflammatory diseases (Rheumatoid Arthritis and Crohn's disease) will be submitted in Q1 2019, as well as in other inflammatory indications based on animal models and cash resources

ABX464: Mechanism of Action*

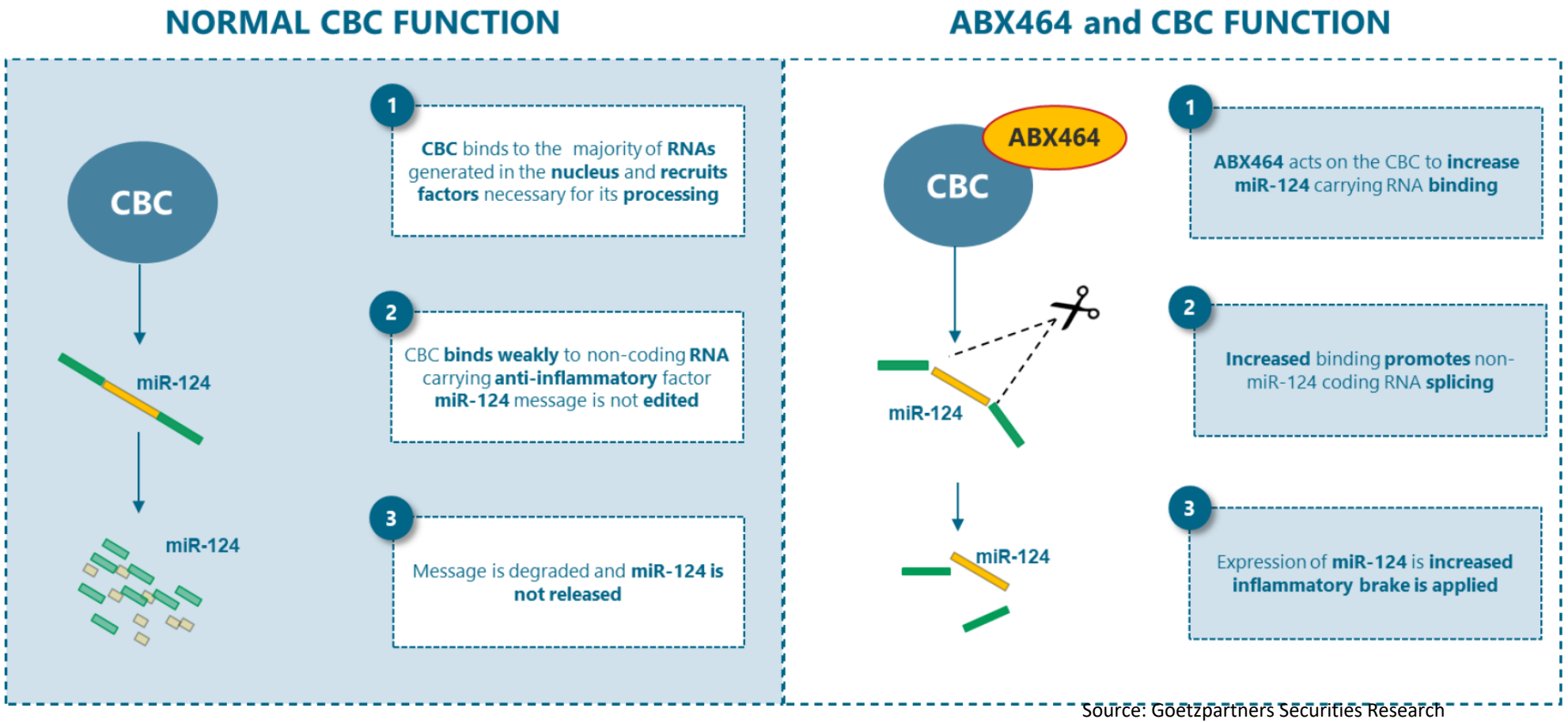
Cryo-EM of the CBC and the ABX464-CBC complex structure



1. **ABX464 binds to its molecular target, the cap binding complex (CBC) that is present on the 5’ end of every human RNA**
2. **This binding induces a conformational change of the CBC that leads to enhanced RNA splicing**

*Vautrin et al., Nature Scientific Reports 9 (2019)

CBC-mediated effects of ABX464 on inflammation*



Source: Goetzpartners Securities Research

*Vautrin et al., Nature Scientific Reports 9 (2019)

ABX464 in Inflammatory Diseases: Summary

- ABX464 is a small molecule from ABIVAX's proprietary RNA biogenesis platform with a novel mode of action through its binding to a nuclear cellular protein complex (Cap Binding Complex) involved in the biogenesis of RNAs.
- Binding of ABX464/N-Glu ABX464 to CBC enhances the splicing of a Long Non Coding RNA to up-regulate a single endogenous anti-inflammatory microRNA (miR-124) without interfering with splicing of endogenous genes.
- This up-regulation of miR-124 was demonstrated in-vitro and in patients (blood and tissue).
- Anti-inflammatory properties of ABX464/N-Glu ABX464 were demonstrated in pre-clinical models (DSS for IBD, collagen induced arthritis for RA).
- 198 subjects have been dosed with ABX464; good safety profile, suitable for long-term use.
- Convenient oral once-a-day regimen.
- Phase 2a POC induction study (n=32) in patients with moderate to severe ulcerative colitis showed statistically significant efficacy based on both clinical and endoscopic endpoints.
- Next steps: Initiation of phase 2b in Ulcerative Colitis and phase 2a POC studies in Crohn's disease and rheumatoid arthritis. All protocols to be submitted for regulatory approval during Q1, 2019.
- Additional inflammatory indications currently being assessed in pre-clinical models for add'l clinical development (e.g. MS, Parkinson's, psoriasis).

Abivax has three key core pillars of value

ABX464

Targets CBC 80/20 complex, thereby inducing enhanced RNA splicing

ABX196

Targets and activates **invariant natural killer T immune cells**

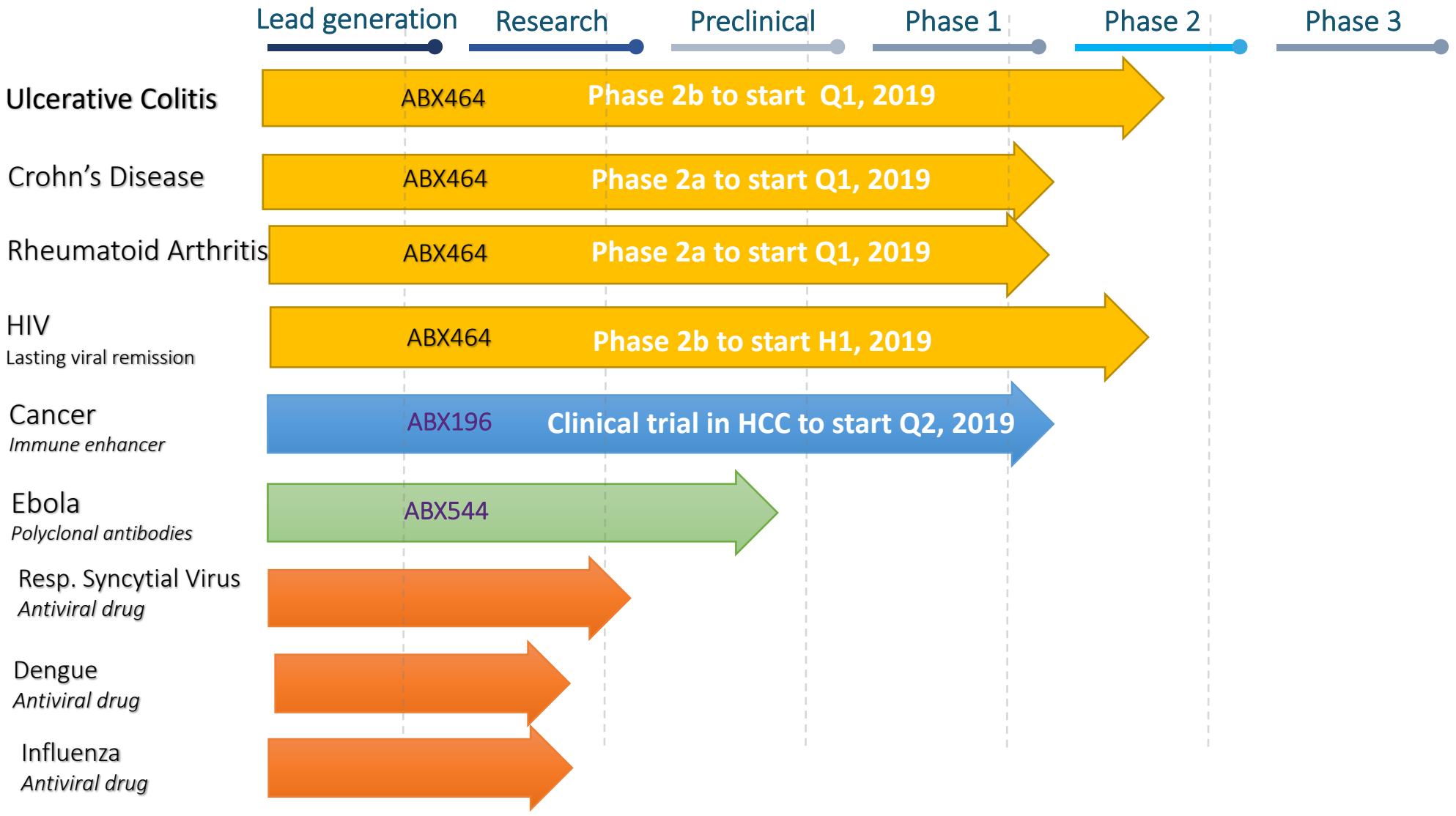
	1 Ulcerative Colitis	2 HIV	3 Hepatocellular Carcinoma
What:	• Upregulation of miRNA124 resulting in reduced inflammation in colon tissue	• Long-lasting HIV viral suppression, as shown in humanized mice • Decrease in HIV DNA in reservoir containing cells, as shown in patients	• Specific enhancer of cellular immune responses in cancer
Promise:	• Strong therapeutic potential in UC as demonstrated in phase 2a clinical trial, as well as Crohn's disease and RA as demonstrated in preclinical models	• A potential functional cure to HIV, having already shown an up to **50% viral reservoir reduction in the blood of patients**[1]	• Strong therapeutic potential in Hepatocellular Carcinoma (HCC) and other cancers in combination with checkpoint inhibitor
Next:	• Today: Results from phase 2a study in 30 UC patients in Europe • Q1 2019: Start phase 2B in UC • Q2 2019: Start ph 2a in Crohn's and RA	• Today: Three months results of ongoing phase IIa study • H1 2019: Start phase IIb study	• Q1 2019: Start of US phase 1/2 study in HCC patients

Multiple drug discovery platforms to drive drug candidate pipeline

- Antiviral platform: novel antiviral drugs for Respiratory Syncytial Virus, Influenza, Dengue
- Immune Enhancer platform: novel anti-cancer drugs
- Polyclonal Antibodies platform: novel polyclonal antibodies for Ebola

1: As demonstrated in phase IIa clinical studies after 28 days of ABX464 treatment

Abivax: A strong and diversified pipeline



Key company facts

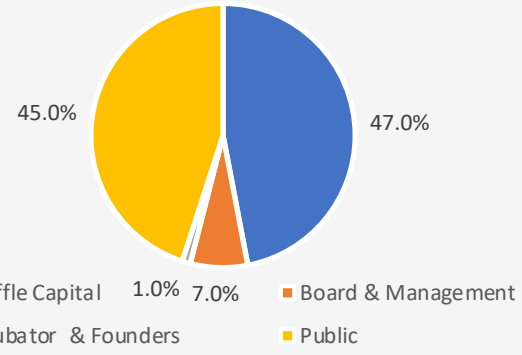
Overview

Founded in 2013 by Truffle Capital

Abivax went public in June 2015, raising EUR 57.7m

Primary listing: Euronext (Paris)
ABVX : FR0012333284
Liquidity: 30K shares/day in 2018[1]

Shareholder Structure 3 (undiluted)



Location

Operations

25 Employees 3

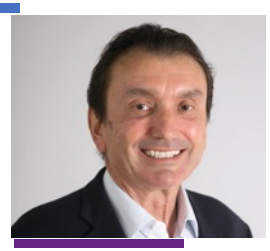
19 in R&D

6 in Support

Cash[2] € 17.6m

1: Boursorama
2: Actual June 30th, 2018 + Kreos Capital Tranche1 €10m paid in July 2018 - last public information available -
3: Actual Dec. 31st, 2018

Highly experienced Executive Committee

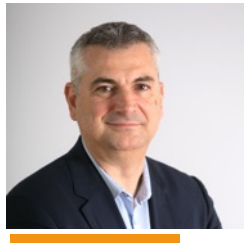


Prof. Hartmut Ehrlich, M.D.
Chief Executive Officer

Ex-Head of Global R&D, Baxter BioScience
Baxter · SANDOZ · Lilly

Didier Blondel
Chief Financial Officer & Board Secretary

SANOFI · sanofi pasteur MSD vaccines for life



Pierre Courteille Pharmacist, MBA
Chief Commercial Officer & VP, BD

sanofi pasteur · Guerbet Contrast for Life

Jérôme Denis, Ph.D.
VP, Process Dev. & & Manufacturing

imaXio · LYONBIOPOLE

Alexandra Pearce Ph.D.
VP, Regulatory Affairs, Quality, PV

AMGEN · Pfizer

Paul Gineste Pharm.D.
VP, Clinical Operations

Boehringer Ingelheim · ALTANA

Didier Scherrer, Ph.D.
VP, R&D

AstraZeneca

Jean-Marc Steens, M.D.
Chief Medical Officer

ViiV Healthcare · gsk GlaxoSmithKline

Prof. Jamal Tazi Ph.D.
CNRS Director & Founder of antiviral platform

cnrs

Competencies from discovery to global commercialization

Abivax Investment Opportunity

- ABX464's mode of action represents a potential first-in-class approach to treating inflammatory diseases as well as HIV infection
- ABX464 has potent anti-inflammatory effects
  - Already confirmed in multiple Phase 2a trials in UC and HIV patients
  - Mechanism and preclinical data support its broad potential for treatment of inflammatory disease.
  - There is a substantial unmet need and market opportunity in ulcerative colitis, Crohn's disease, rheumatoid arthritis, multiple sclerosis and other inflammatory diseases.
- In our opinion, an effective novel clinical-stage anti-inflammatory therapeutic candidate, like ABX464, is attractive for potential partners as well as investors