



# ABX464 – A future game changer for the treatment of chronic inflammatory diseases

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Abivax, a late-stage clinical biotech company

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Future clinical development including phase 3 design and initiation is subject to assessment of the overall preclinical, CMC, toxicology, clinical efficacy and safety data of ABX464 by EMA, FDA and other regulatory authorities. These top-line results have not yet been reviewed by regulatory authorities.

# Abivax and ABX464 for chronic inflammatory diseases: Main take-home messages

1

ABX464 is a potent anti-inflammatory oral drug candidate with a novel first-in-class mechanism of action: Upregulation of the physiological anti-inflammatory microRNA, miR-124

2

Safety and efficacy demonstrated in phase 2a and 2b induction and maintenance studies in moderate to severe ulcerative colitis (UC): ABX464 clinically differentiated from competitors, especially through impressive clinical remission rates during maintenance

3

FDA EoP2 feedback and EMA scientific advice feedback allow the finalization of the design of the ABX464 UC phase 3 global pivotal study program; FPI planned for Q2 2022

4

Abivax plans to go straight into a phase 2b in Crohn's disease (CD) - based on similar mechanisms of disease propagation - and in rheumatoid arthritis (RA) - based on encouraging phase 2a proof-of-concept data: ABX464 has the potential to treat a variety of chronic inflammatory diseases

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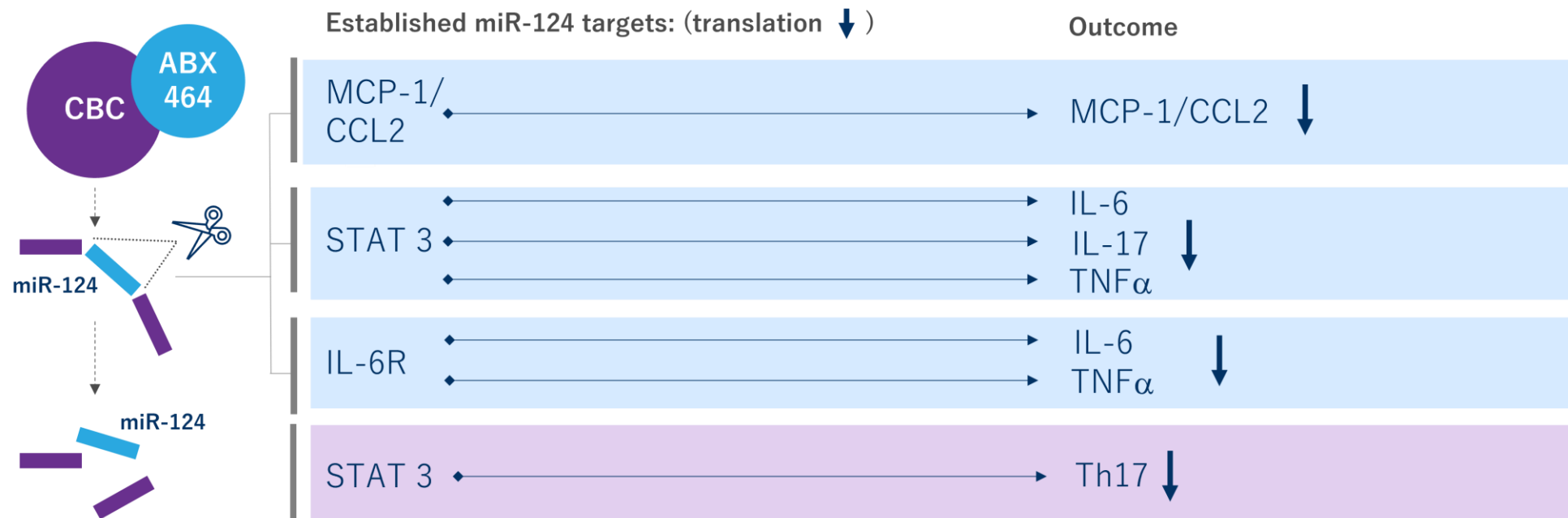
Manufacturing ready for phase 3

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2021 total pharmaceutical sales in UC, CD and RA were USD 42B – ABX464 has the potential to take a significant market share and become a potential mega-blockbuster in IBD and RA

# ABX464 novel mechanism of action: Potent and specific upregulation of miR-124, activating a “physiological brake” by reducing the expression of inflammatory cytokines and cells to normal levels

- First-in-class mechanism of action related to intracellular upregulation of miR-124.
- microRNAs work by down-regulating the translation of their respective target genes.
- Out of 1,105 microRNAs, miR-124 was the only microRNA upregulated by ABX464.
- ABX464 has no impact on the splicing of cellular mRNA besides lncRNA00599-205.

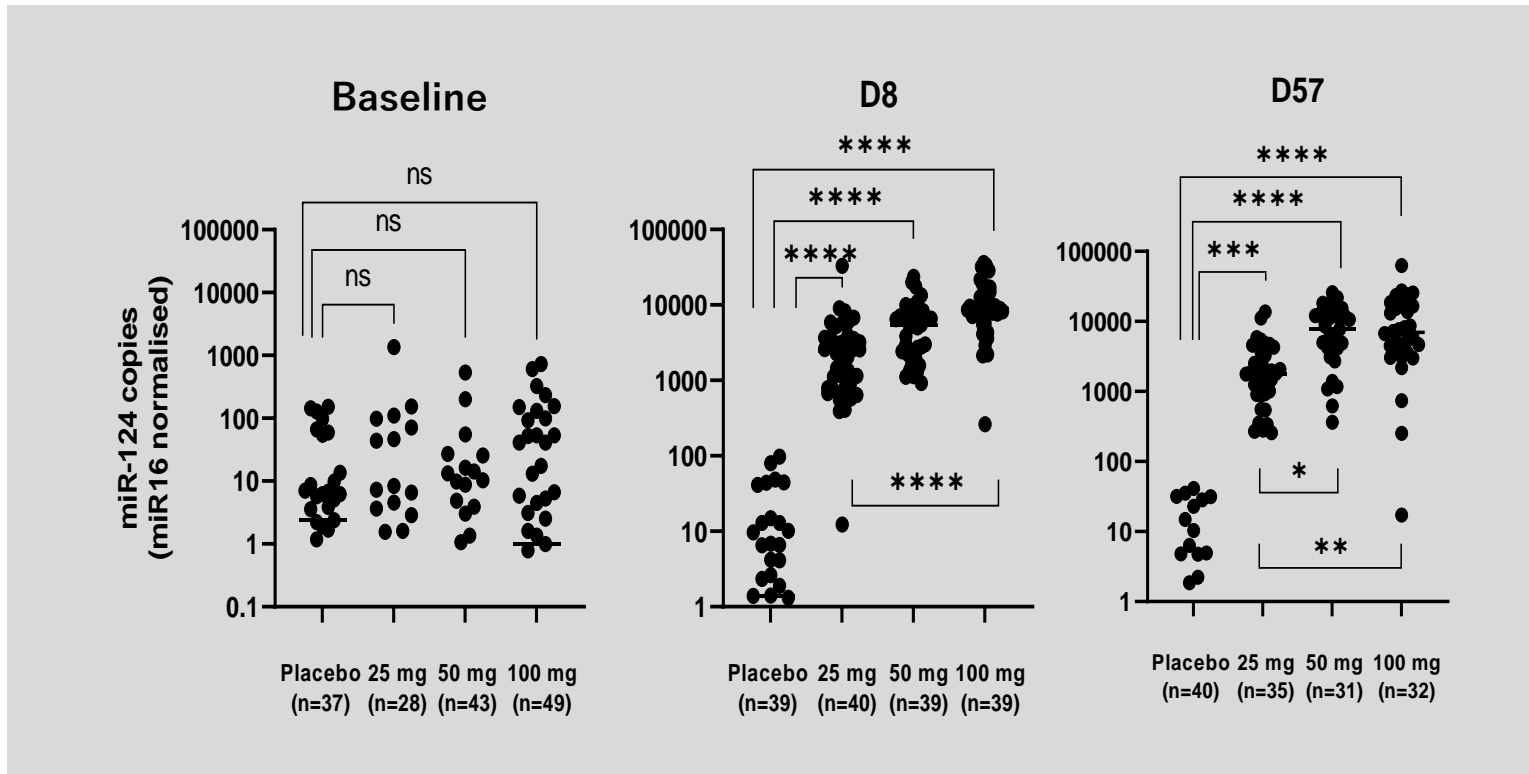


Tazi et al. *Drug Discov. Today* (2021); Poholek et al. *J Exp Med* (2020) 217 (10): e20191761; Lin S, et al. *Frontier in Onc* (2020)

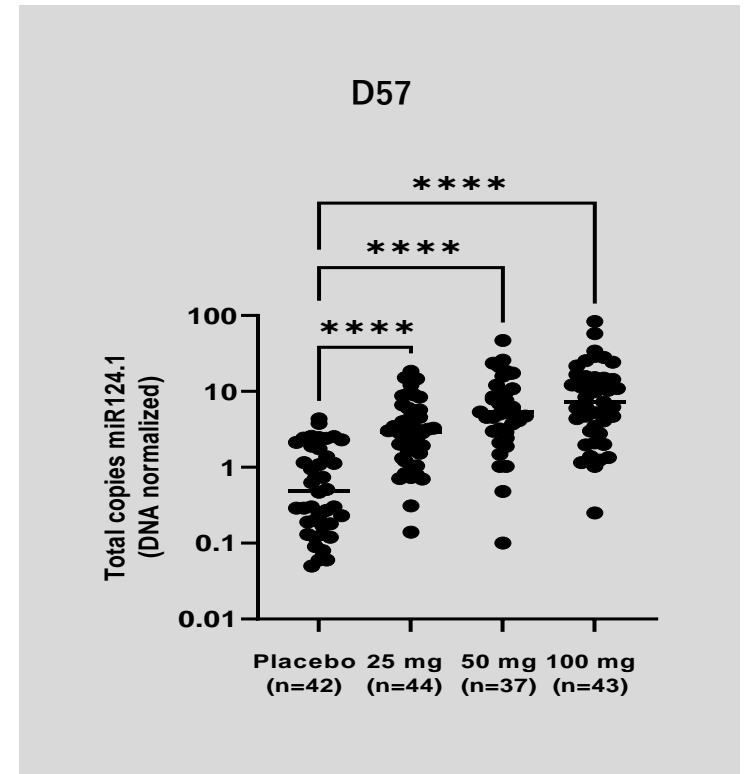
# Significant miR-124 upregulation detected in rectal biopsies and blood (phase 2b UC study)

*Dose relationship observed in rectal tissue and whole blood*

## miR-124 blood levels



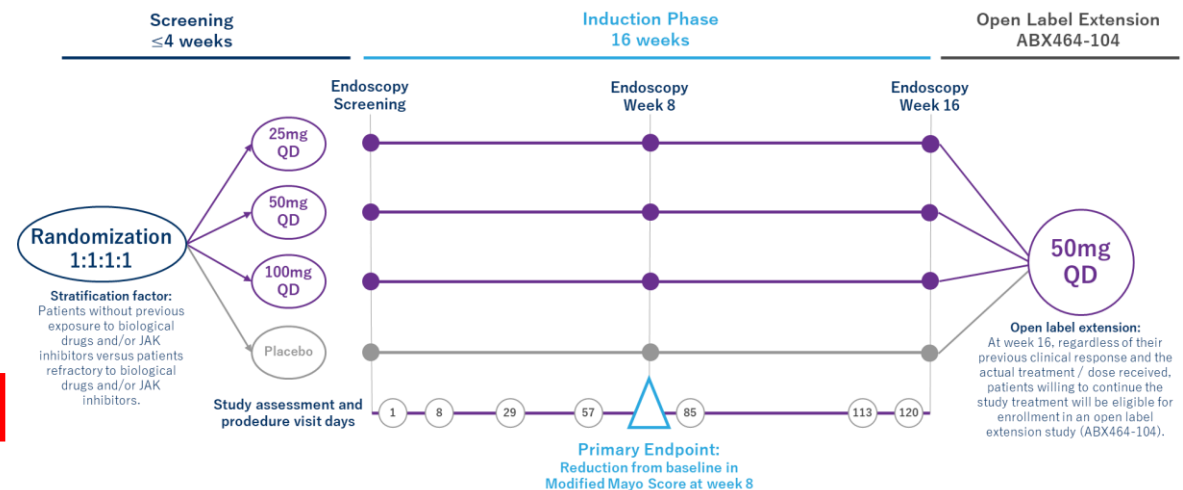
## miR-124 in rectal tissue



# Positive phase 2a study led to the conduct of a large-scale phase 2b study of ABX464 in patients with moderate-to-severe Ulcerative Colitis

- 254 patients in 15 countries in Europe, US and Canada (130 study sites)
- Moderate-to-severe active UC (Modified Mayo Score 5-9)
- Central, independent and blinded reading of endoscopies
- Baseline characteristics well-balanced among the treatment groups, incl. modified mayo sub-score, endoscopic sub-score, fecal calprotectin, majority of patients refractory to several biologics and JAK inhibitor treatments

		100mg (N=64)	50mg (N=63)	25mg (N=61)	Placebo (N=64)
Modified Mayo Score (MMS)	Mean (SD)	7.0 (1.07)	7.1 (0.96)	7.1 (1.09)	7.0 (1.20)
Endoscopic sub-score = 3	%	66%	75%	67%	75%
Fecal Calprotectin (µg/g)	Mean	3778	3441	3022	2452
Previous exposure to biologics/Tofacitinib	n (%)	32 (50.0)	30 (47.6)	30 (49.2)	31 (48.4)
anti-TNF α	n (%)	31 (48.4)	25 (39.7)	25 (41.0)	27 (42.2)
anti-TNF α only	n (%)	1 (1.6)	0	3 (4.9)	1 (1.6)
Vedolizumab	n (%)	20 (31.3)	20 (31.7)	19 (31.1)	22 (34.4)
Tofacitinib	n (%)	13 (20.3)	12 (19.0)	10 (16.4)	12 (18.8)



# Week 8 Efficacy Results (ITT):

Primary Endpoint met - Efficacy confirmed for all patients and also for subset of bio-refractory patients

Week 8 Results (ITT <sup>1</sup> population / n=252)		Placebo	25mg	50mg	100mg
Primary Endpoint					
Modified Mayo Score Mean change from baseline	All patients	-1.9	-3.1 **	-3.2 **	-2.9 *
	Bio-refractory	-1.0	-2.8 **	-2.9 **	-2.8 **

\*p-values of <0.01 versus placebo (ANCOVA)

\*\*p-values of <0.001 versus placebo (ANCOVA)

1) ITT: Intent-to-treat patient population. Drop-out patients were considered as failure for all endpoints. Nearest neighbor imputation, as defined in the SAP. Patient characteristics well balanced between all groups (Modified Mayo Score, ConMeds, Gender, etc.).



# Week 8 Efficacy Results (ITT):

## Secondary endpoints - Efficacy confirmed for all patients and also for subset of bio-refractory patients

Week 8 Results (ITT population / n=252)		Placebo	25mg	50mg	100mg
Key Secondary Endpoints (not powered for statistical significance)					
Endoscopic Improvement <sup>a †</sup>	All patients	8 (13.6%)	20 (34.5%) *	21 (39.6%) *	24 (44.4%) *
	Bio-refractory	1 (3.7%)	8 (28.6%) *	7 (30.4%) *	8 (26.6%) *
*p-values of <0.05 versus placebo using a likelihood ratio chi-square test					
Clinical Remission <sup>b †</sup>	All patients	8 (12.5%)	17 (27.9%) *	11 (17.5%)	16 (25.0%)
	Bio-refractory	1 (3.2%)	6 (20.0%) *	2 (6.7%)	6 (18.8%) *
*p-values of <0.05 versus placebo using a likelihood ratio chi-square test but not according to the predefined Mantel-Haenszel Chi Square test (p=0.06 to 0.08)					
Clinical Response <sup>c †</sup>	All patients	23 (35.9%)	40 (65.6%) *	38 (60.3%) *	35 (54.7%) *
	Bio-refractory	5 (16.1%)	17 (56.6%) *	13 (43.3%) *	15 (46.8%) *
*p-values of <0.05 versus placebo using a likelihood ratio chi-square test					
Fecal Calprotectin (µg/g) Mean change from baseline	All patients	-1027.7	-2192.8 **	-2316.8 **	-2280.9 **

\*\*p-values of <0.01 vs placebo (MMRM)

a Endoscopic improvement is defined as endoscopic subscore ≤1.

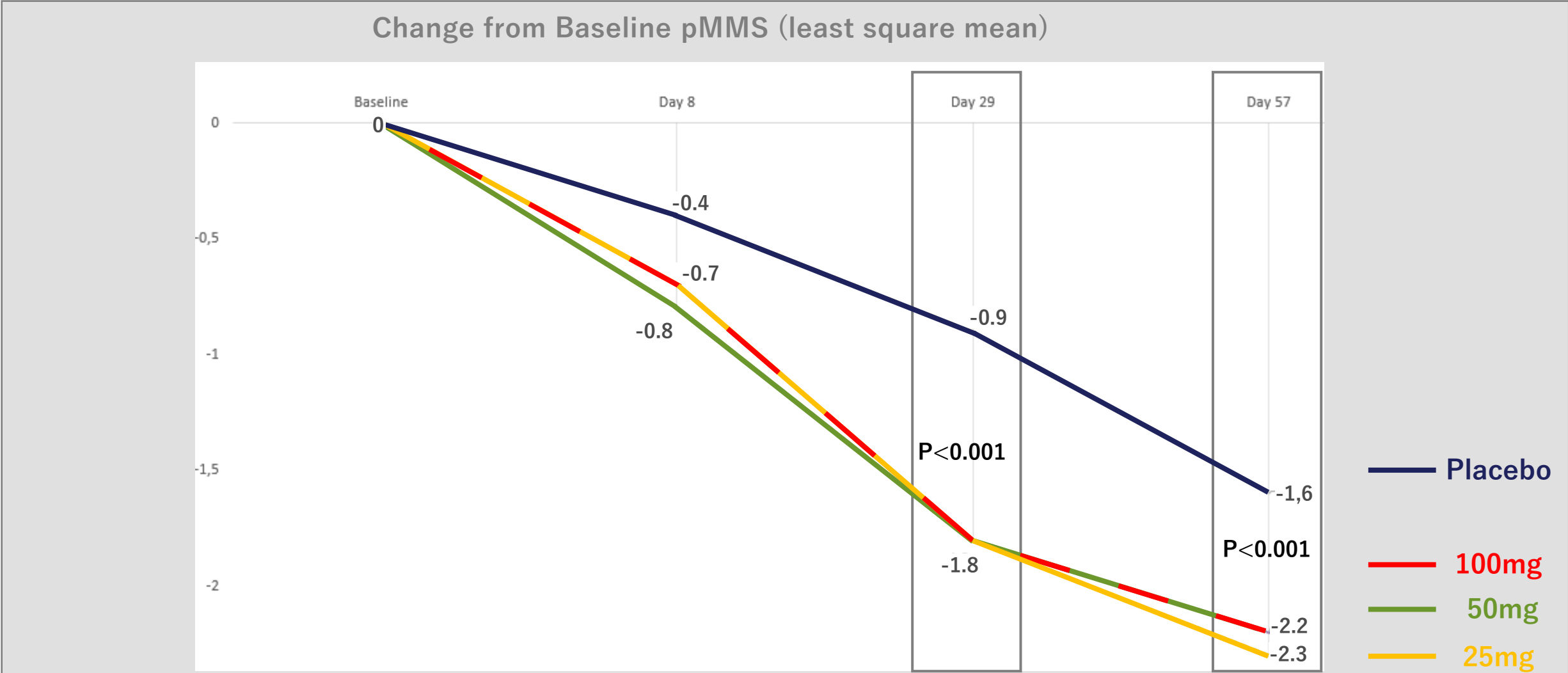
b Clinical remission (per Modified Mayo Score) is defined as stool frequency subscore (SFS) ≤1, rectal bleeding subscore (RBS) of 0 and endoscopic subscore ≤1.

c Clinical response (per Adapted Mayo Score) is defined as a decrease from baseline in the Modified Mayo Score ≥2 points and ≥30 percent from baseline, plus a decrease in RBS ≥1 or an absolute RBS ≤1.

† Evidence of friability during endoscopy confers an endoscopic subscore of 2 or 3



# Week 4 and Week 8 Efficacy Results (ITT): Fast onset of action



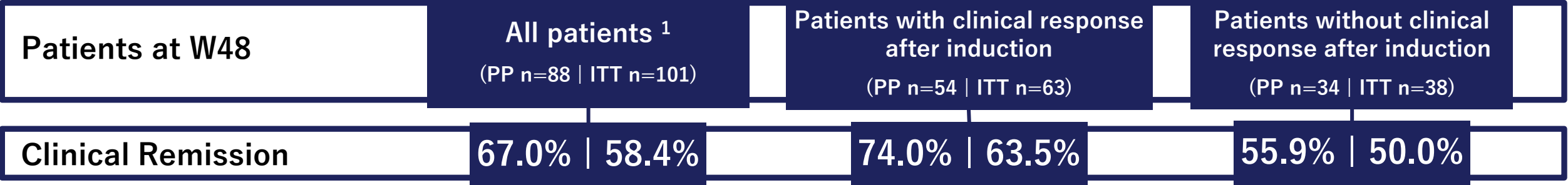
# ABX464 phase 2b maintenance study

## – impressive one-year efficacy confirmed

Phase 2b study: 217/222 eligible patients enrolled into maintenance

The first 101 patients of the 217 were to complete 1<sup>st</sup> year of maintenance by Sept. 15, 2021:

(12 patients were drop-outs, and no data available for 1 patient at W48, these 13 patients were considered treatment failures in ITT )



<sup>1</sup> Irrespective of patient outcome at the end of the induction phase

# ABX464 phase 2a maintenance study

– impressive long-term efficacy (3 years) confirmed

## Phase 2a study <sup>2</sup>

	1 <sup>st</sup> year	2 <sup>nd</sup> year	3 <sup>rd</sup> year
Clinical remission (ITT)	12/22 (54.5%)	11/22 (50.0%)	11/22 (50.0%)

<sup>2</sup> Irrespective of patient outcome at the end of the induction phase

# ABX464 well positioned in the competitive landscape for both induction and maintenance - *Clinical Remission Rates*

Drug	Study	Active	Placebo	Delta	Active	Placebo	Delta
		Results of Induction studies (ITT)*			Results of Maintenance studies (ITT)* (Patients with clinical response at the end of the induction, except for “all comers” in the Etrasimod study)		
Adalimumab	ULTRA I (Ph 3)	18.5%	9.2%	9.3%	17.3%	8.5%	8.8%
	ULTRA II (Ph 3)	16.5%	9.3%	7.2%			
Ustekinumab	Phase 3	15.5%	5.3%	10.3%	43.8%	24%	19.8%
Vedolizumab	GEMINI I (Ph 3)	16.9%	5.4%	11.5%	44.8%	15.9%	28.9%
Tofacitinib	OCTAVE I (Ph 3)	18.5%	8.2%	10.3%	40.6%	11%	29.6%
	OCTAVE II (Ph 3)	16.6%	3.6%	13.0%			
Ozanimod	Truenorth (Ph 3)	18.4%	6.0%	12.4%	37%	18.5%	18.5%
Etrasimod	Phase 2** (12 weeks)	33%	8.1%	24.9%	33%		
Upadacitinib	U-Achieve (Ph 3)	26.0%	5.0%	21.0%	52.0% (30mg)	12.0% (30mg)	40.0% (30mg)
	U-Accomplish (Ph 3)	33.0%	4.0%	29.0%	42.0% (15mg)	12.0% (15mg)	30.0% (15mg)
	Phase 2	19.6%	0.0%	19.6%			
ABX464	Phase 2a (50mg)	30.4%	11.1%	19.3%	66.7% (50mg)	-	-
	Phase 2b (25mg)	27.9%	12.5%	15.4%	63.5% (50mg)	-	-

Marketed drugs in IBD

Drug candidates in late-stage development in IBD

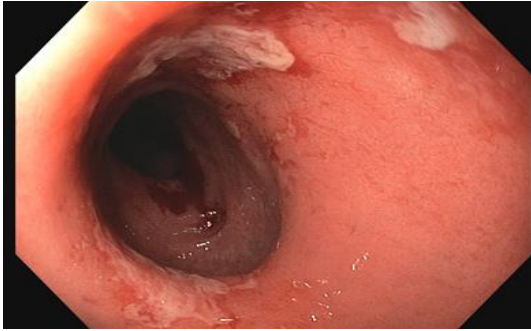
\*non-comparative studies conducted versus placebo

\*\*Sandborn et al, 2020: 12W Induction results

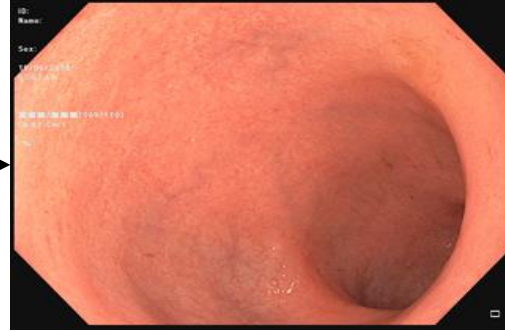


# Complete resolution of UC lesions in an ABX464 treated patient (vedolizumab, infliximab and adalimumab resistant) during 3 years of open-label maintenance treatment

Endoscopy before ABX464



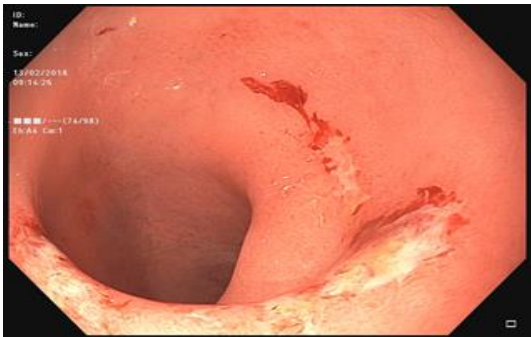
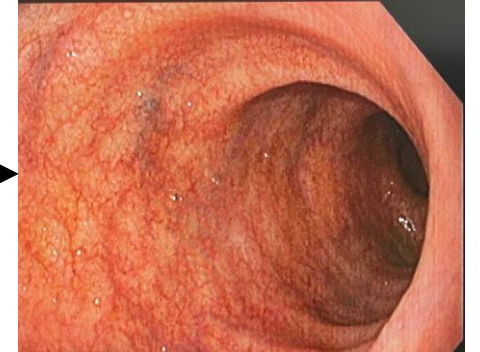
Endoscopy after 1<sup>st</sup> year of ABX464



Endoscopy after 2<sup>nd</sup> year of ABX464



Endoscopy after 3<sup>rd</sup> year of ABX464



Courtesy of Prof. Severine Vermeire, Leuven, Belgium

- 52-year-old patient with severe UC
- Patient had failed on vedolizumab, infliximab and adalimumab
- Fall 2017: Patient was counseled for colectomy
- Nov. 2017: Patient was enrolled in phase 2a induction study with ABX464
- Jan. 2018: Patient was enrolled in open-label maintenance study with ABX464

# Favorable ABX464 safety profile

Safety in phase 2b study in UC patients confirms profile observed in the phase 2a study

- No new safety signal, no death, no malignancy
- Most frequently reported AEs are **headaches** (20% for 25mg and 8% for placebo), **which occur early** (first 10 days of treatment) and are **transient** (few days), **mild or moderate** (grade 1 or 2) and **manageable with or without OTC medications**
- Other AEs  $\geq 5\%$  (related and non-related) are gastrointestinal disorders (nausea, vomiting, upper abdominal pain) and musculoskeletal (arthralgia, myalgia)
- Labs: **No clinically significant changes in laboratory parameters** (liver function tests, Hb, white blood cells)

% Patients with at least one AE	Placebo (N=64)	ABX464 25mg (N=62)	ABX464 50mg (N=63)	ABX464 100mg (N=64)
TEAE leading to Study Discontinuation	6.3%	1.6%	9.5%	9.4%
SAEs <sup>1</sup>	6.3%	1.6%	6.3%	6.3%
Severe Grade 3-4 TEAEs <sup>1</sup>	4.7%	4.8%	7.9%	10.9%
Infections	9.4%	4.8%	12.7%	7.8%

<sup>1</sup> Related and not related to study drug

- **25mg clearly stands out** with a similar safety profile observed in the placebo group (except transient headaches)

## Favorable ABX464 safety profile across all clinical studies

- **More than 1,000 subjects exposed to ABX464** (Cut-off date Nov. 30, 2021)
  - Total subjects exposed: 1,069
  - Subjects exposed at 25mg: 143
  - Subjects exposed at 50mg: 750
  - Subjects exposed at 100mg: 95
- **ABX464 also showed good safety profile in a clinical study conducted in Covid-19 patients**
  - Phase 2b/3, randomized, double blind, 28-days study to evaluate 50mg ABX464 (n=335) compared to placebo (n=170) in SARS-CoV-2-infected high-risk patients
  - No imbalance across the treatment groups in terms of incidence of TEAE, SAE, laboratory results; no new safety signal



# How to bring ABX464 to the market in ulcerative colitis

## Ulcerative colitis phase 3 preparation on track

- **FDA** end of phase 2 meeting feedback and **EMA** scientific advice with guidance and a path forward
- Abivax intends to study **25mg and 50mg** in the induction studies and possibly **one lower dose** during maintenance
- **IQVIA and US and EU KOLs** involved in finalizing study design
- ~ **2 x 700 patients** planned for induction followed by a controlled maintenance study
- FPI planned for **Q2 2022**

## Inclusion of Japan in the global ABX464 phase 3 study program

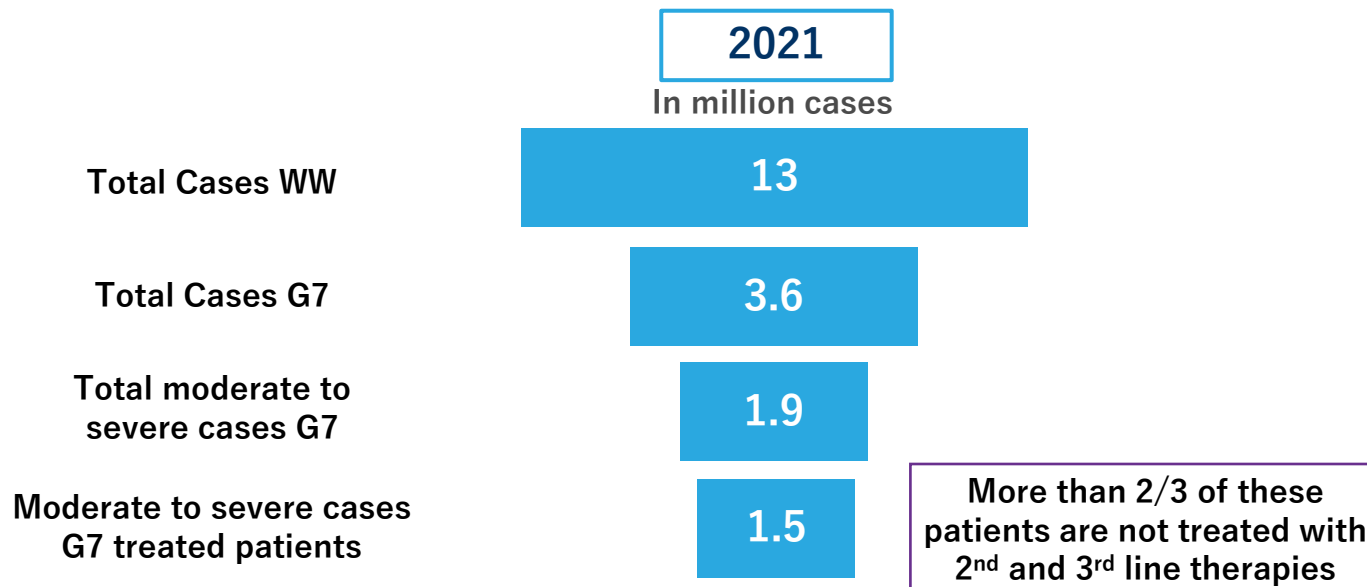
### Required phase 1 study in Japanese healthy volunteers

- Enrollment completed
- Results expected in early Q2 2022

# ABX464: A potential mega-blockbuster in IBD

Size of target market increasing by 70% in UC and by nearly 20% in CD (2021 - 2027)

UC Epidemiology



**Total market size<sup>1</sup>**  
in inflammatory diseases > **USD 90B**

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Market size<sup>1,2</sup>

- UC: USD 6.2B
- CD: USD 13B
- RA: USD 22.3B

ABX464 addresses a market of **USD 42B**

UC & CD Market Potential

	Ulcerative Colitis	Crohn's Disease
ABX464 TPP	Patients with moderate to severe UC and CD who failed on first line therapy, therefore positioned as 2 <sup>nd</sup> and 3 <sup>rd</sup> line treatment	
ABX464 Full Launch	2027 for UC	2028 for CD
G7 Market Size (2 <sup>nd</sup> & 3 <sup>rd</sup> line)	2021: USD 6.2B for UC 2027: USD 10.6B for UC	2021: USD 13B for CD 2027: USD 15.4B for CD
ABX464 Market Share Assumptions	10-20% market share at peak sales for both indications	

1) 2021 data for Europe G5, U.S. and Japan  
2) 2<sup>nd</sup> and 3<sup>rd</sup> line

Source: Global Data & Informa

# ABX464 is a potential drug in IBD and multiple chronic inflammatory diseases

## Phase 2a clinical study in RA - Top-line results allowing to move into phase 2b

3-months induction study in 60 patients (placebo, 50mg and 100mg ABX464): Baseline characteristics well balanced across all groups

Primary endpoint met with ABX464 demonstrating good safety and tolerability profile with 50mg once daily oral administration

A statistically significant difference ( $p < 0.03$ ) was met on key efficacy endpoint ACR20 in the PP population with 60% of ABX464 patients dosed with 50mg reaching that endpoint versus 22% in the placebo group

Other key efficacy endpoints (ACR50, ACR70, DAS28-CRP, CDAI) as well as biological markers (CRP, miR-124, IL-6) showed favorable differences with 50mg ABX464 over placebo

Phase 2a maintenance data in rheumatoid arthritis to be reported in Q1 2022

Abivax intends to start a clinical phase 2b program in rheumatoid arthritis

# ABX464 newsflow through Q2 2022

	Q4 2021	Q1 2022	Q2 2022
UC - Phase 2b (ABX464)		Top-line results (One-year maintenance data)	Publication of full-length phase 2b manuscript
UC - Phase 3 (ABX464)	FDA feedback ✓	EMA feedback ✓	FPI phase 3 study
RA - Phase 2a (ABX464)		Top-line results (One-year maintenance data)	Publication of full-length phase 2a manuscript

# Thank you for your attention!



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