KISSEI

Financial Briefing for the Fiscal Year Ended March 31, 2022 (Fiscal 2021)

Yoshio Furihata
President and COO

May 11, 2022

KISSEI PHARMACEUTICAL CO., LTD.

Summary of Financial Results for Fiscal 2021

Consolidated Results

- Results for fiscal 2021 reached an all-time low
- Kissei aims to recover performance in fiscal 2022, by increasing sales of Beova®, an overactive bladder treatment, launching new products to the market, and acquiring income from overseas out-licensing

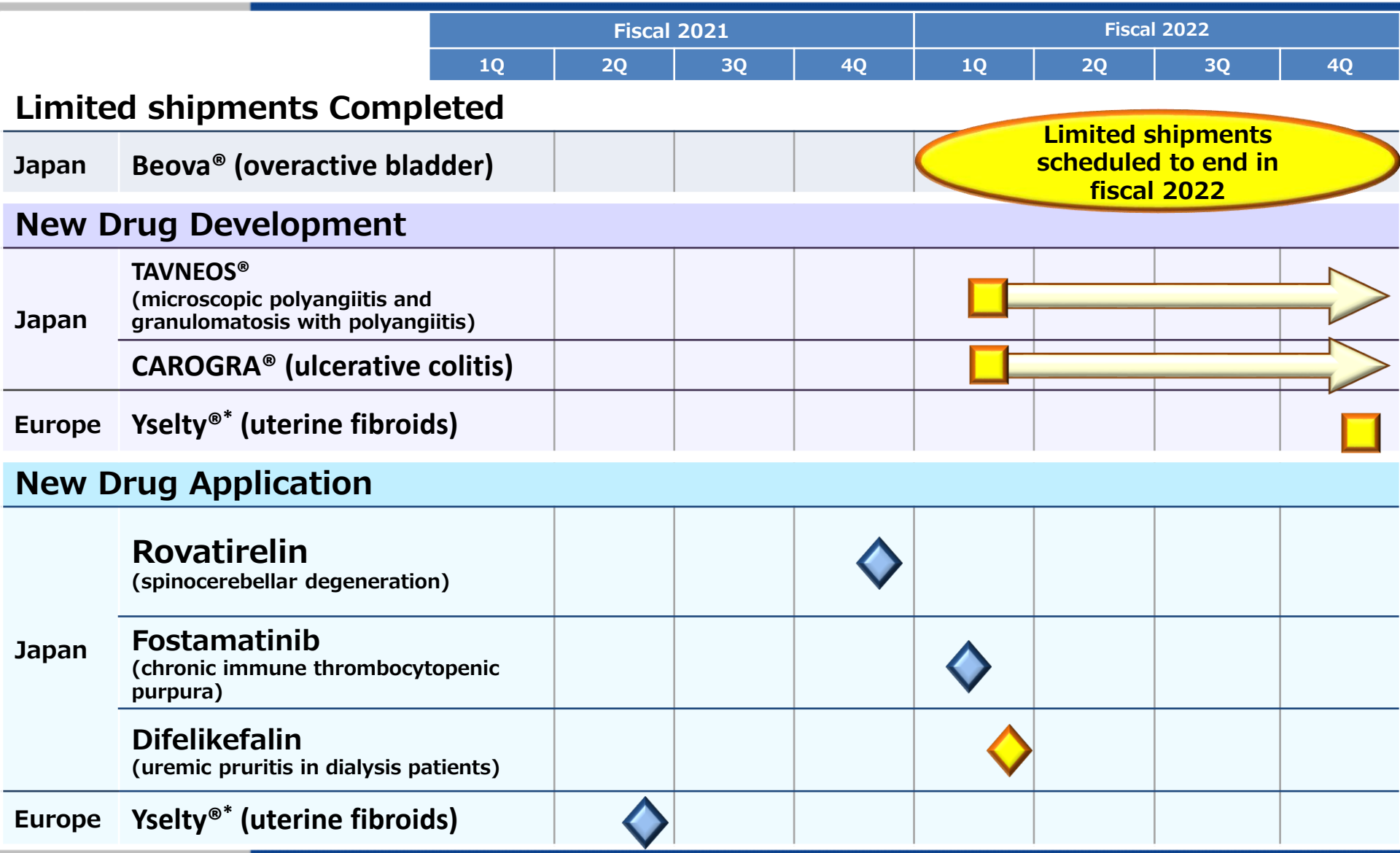
Expand Domestic Development of New Drugs and Enhance Area Strategies

- Received marketing authorization approval for TAVNEOS®, a treatment for microscopic polyangiitis and granulomatosis with polyangiitis, and CAROGRA®,a treatment for ulcerative colitis
- Submitted New Drug Applications for rovatirelin, a treatment for spinocerebellar degeneration, and fostamatinib, a treatment for chronic immune thrombocytopenic purpura
- Achieved the primary endpoint for difelikefalin, a treatment for uremic pruritis in dialysis patients, in a domestic Phase III clinical study
- The Company also began co-promotion of UPASITA®, a treatment for secondary hyperparathyroidism in dialysis patients

Strengthen Our Overseas Earnings Base

- A Marketing Authorisation Application for linzagolix, a treatment for uterine fibroids, was accepted by the Committee for Medicinal Products for Human Use (CHMP) under the European Medicines Agency (EMA). Approval of a New Drug Application is still pending in the United States, while preparations for clinical trials of linzagolix have begun in China
- Development of fostamatinib has begun in China and South Korea

Major Developments in Fiscal 2021–Fiscal 2022



* Product name (generic name: linzagolix)

New Drug Application (submitted) | New Drug Application (forecast) | Launch to market (forecast)

Consolidated Financial Results for Fiscal 2021

	Fiscal 2020		Fiscal 2021			Year on Year
	Result (millions of yen)	Ratio to net sales	Plan*2 (millions of yen)	Result (millions of yen)	Ratio to net sales	
Net sales	69,044	100.0%	65,400	65,381	100.0%	(5.3)%
[Pharmaceutical Business]	[56,407]		[54,600]	[54,147]		[(4.0)%]
Cost of sales	36,322	52.6%	34,500	34,143	52.2%	(6.0)%
Gross profit	32,722	47.4%	30,900	31,238	47.8%	(4.5)%
Selling, general and adminstrative expenses	31,217	45.2%	32,500	32,640	49.9%	4.6%
[R&D expenses]	[9,626]	[13.9%]	[10,000]	[10,363]	[15.9%]	[7.7%]
Operating profit	1,505	2.2%	(1,600)	(1,402)	–	–
Ordinary profit	3,476	5.0%	300	562	0.9%	(83.8)%
Profit*1	5,285	7.7%	11,900	12,921	19.8%	144.5%
[Comprehensive income]	[30,762]			[(13,764)]		

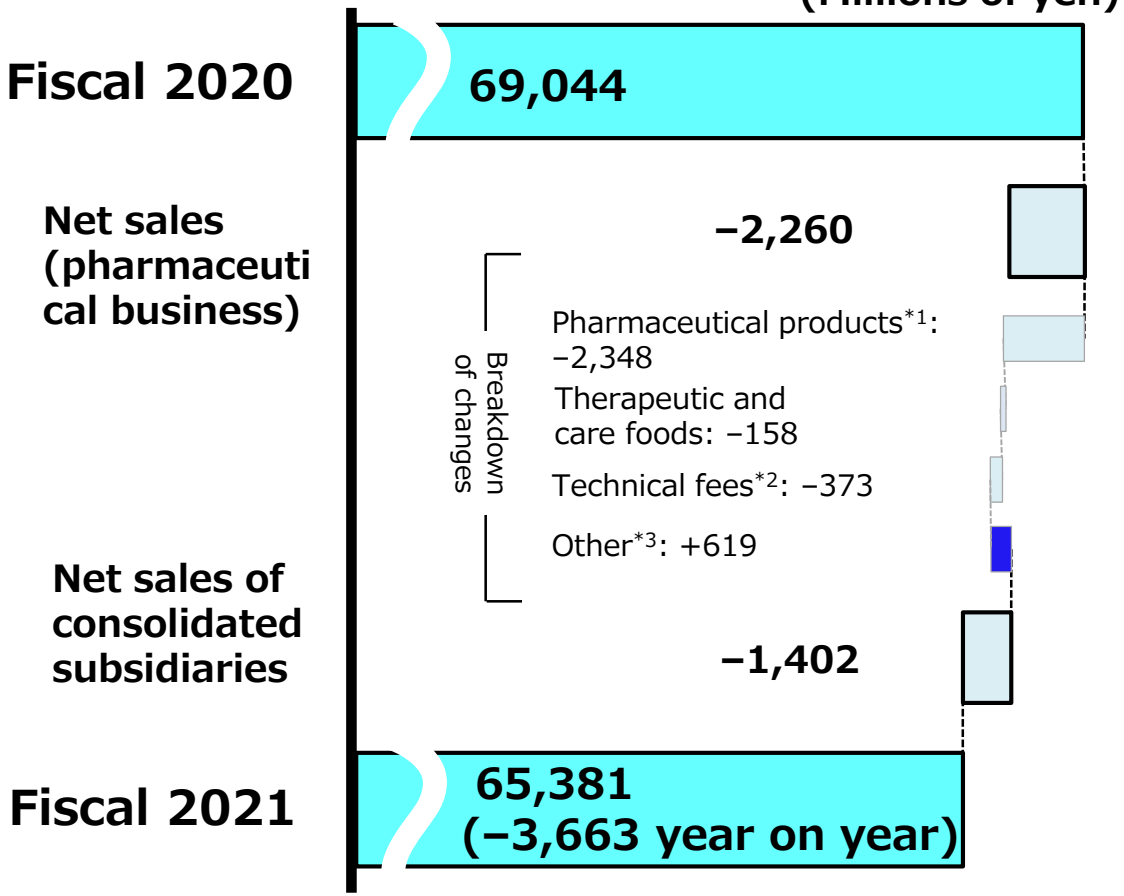
*1 Profit refers to profit attributable to owners of parent
*2 Corresponding to figures from the announcement of financial results from the second quarter of fiscal 2021

Please refer to page 2, 3, and 8 of the Supplementary Explanatory Materials on Financial Results

Consolidated Net Sales Compared with Fiscal 2020

Source of increase | Source of decrease

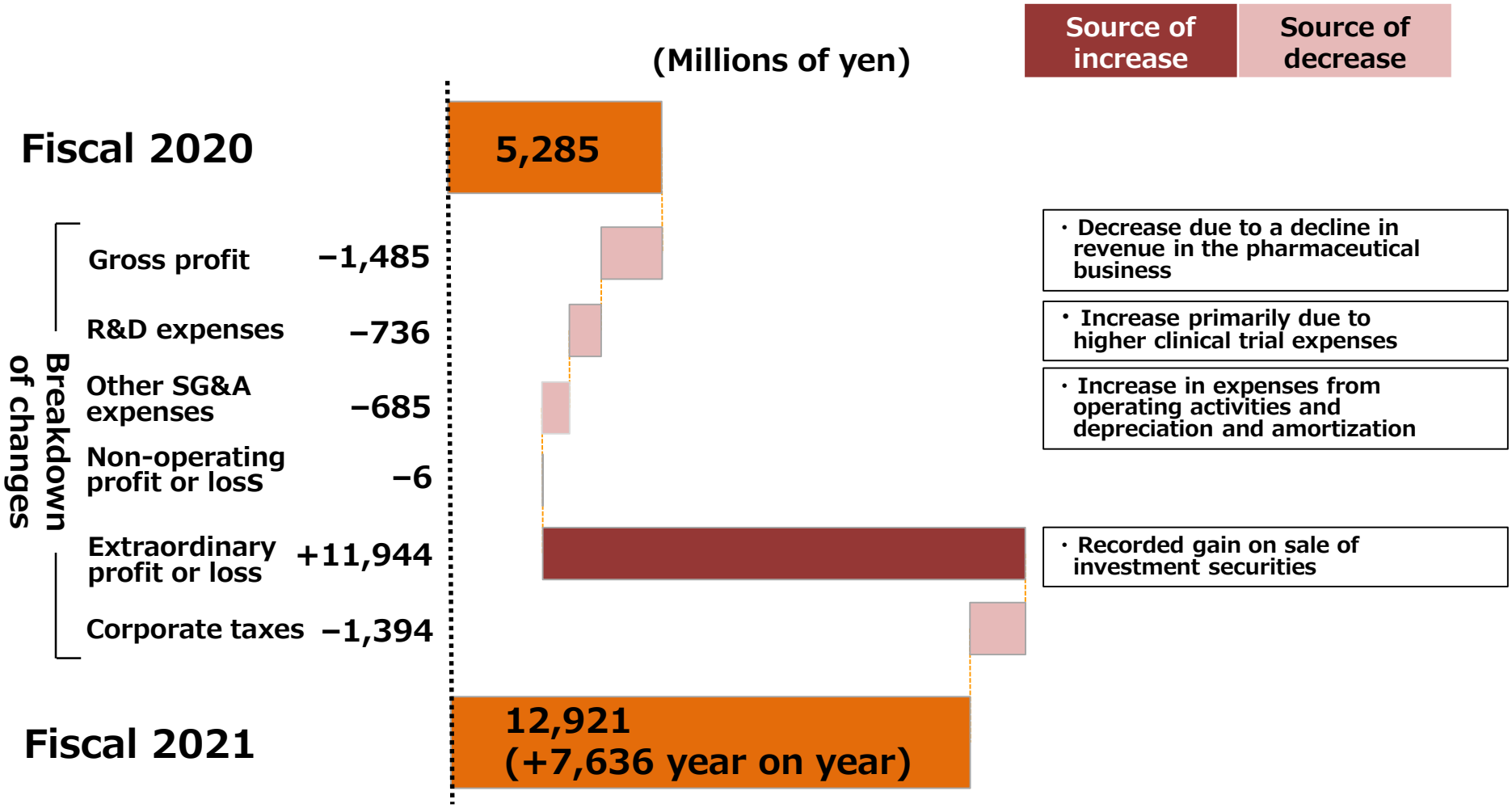
(Millions of yen)



- Decrease in sales for products such as Darbepoetin Alfa BS Injection [JCR], Epoetin Alfa BS Injection [JCR], GLUBES®, and Urief®
- Decrease resulting from a lump-sum payment recorded in fiscal 2020 related to the licensing agreement for KDT-3594
- Increase in revenue from supply to domestic sales partners
- Decrease in revenue from information services and construction and merchandising businesses

*1 Including active pharmaceutical ingredients (API) and bulk exports
*2 Total amount of contracting fees related to out-licensing, milestone payments, and running royalties
*3 Includes amounts from supply to domestic sales partners and co-promotion fees

Consolidated Profit Attributable to Owners of Parent Compared with Fiscal 2020



Plan for Fiscal 2022 (Consolidated)

	Fiscal 2021		Fiscal 2022			
	Result (millions of yen)	Ratio to net sales	Plan (millions of yen)	Ratio to net sales	Year on Year	Result for first half (millions of yen)
Net sales	65,381	100.0%	68,000	100.0%	4.0%	31,000
[Pharmaceutical Business]	[54,147]		[57,000]		[5.3%]	[25,500]
Cost of sales	34,143	52.2%	33,700	49.6%	(1.3)%	16,100
Gross profit	31,238	47.8%	34,300	50.4%	9.8%	14,900
Selling, general and adminstrative expenses	32,640	49.9%	31,500	46.3%	(3.5)%	16,200
[R&D expenses]	[10,363]	[15.9%]	[9,000]	[13.2%]	[(13.2)%]	[5,000]
Operating profit	(1,402)	–	2,800	4.1%	–	(1,300)
Ordinary profit	562	0.9%	4,400	6.5%	682.9%	(500)
Profit*1	12,921	19.8%	10,000	14.7%	(22.6)%	3,000

*1 Profit refers to profit attributable to owners of parent

Please refer to page 2, 3, and 8 of the Supplementary Explanatory Materials on Financial Results

- Utilize financial assets effectively to record extraordinary income in the form of a gain on sale of investment securities

Treatment for overactive bladder **Beova®**

Positioning: Beova® Tablets

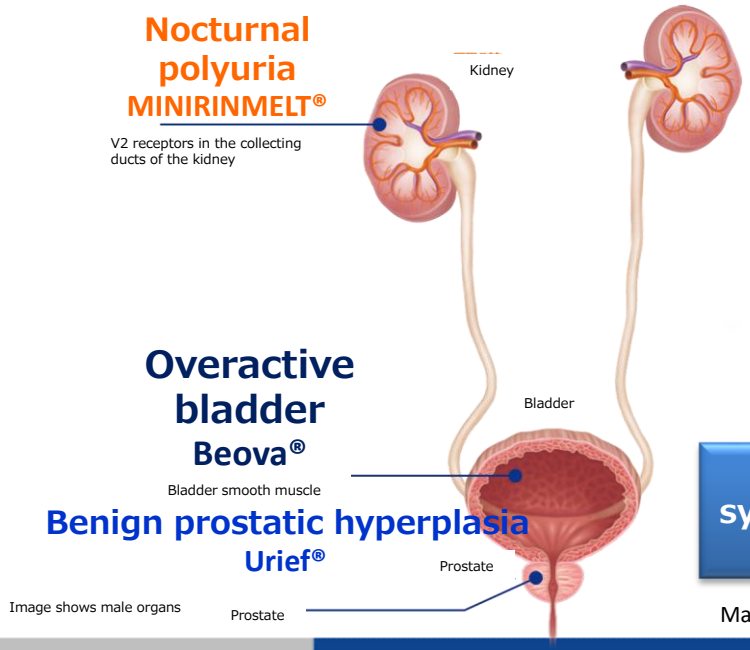
November 2018: Drug launch
Fiscal 2022: Limited shipments scheduled to end

Number of patients diagnosed with overactive bladder: Approx. 3.3 million*1

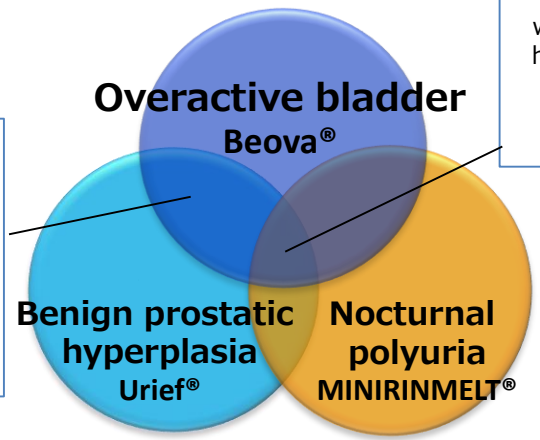
Number of patients taking medication for overactive bladder: Approx. 2.0 million*2

Number of potential patients with overactive bladder (aged 40 and over): Approx. 11.0 million*3

Position Beova® as a beta-3 agonist with high efficacy and safety
Fiscal 2022 plan ¥11,000 million (net sales)



Approx. 50%–75% of patients with benign prostatic hyperplasia also experience overactive bladder*3



Pathological diagram

Approx. 89% of patients who have benign prostatic hyperplasia and/or receive treatment for overactive bladder also experience nocturnal polyuria*4

Help raise the quality of life of patients suffering urinary tract symptoms with treatments for overactive bladder, benign prostatic hyperplasia, and nocturnal polyuria.

Marketing: Kissei Pharmaceutical Co., Ltd. Manufacturing and marketing: KYORIN Pharmaceutical Co., Ltd.

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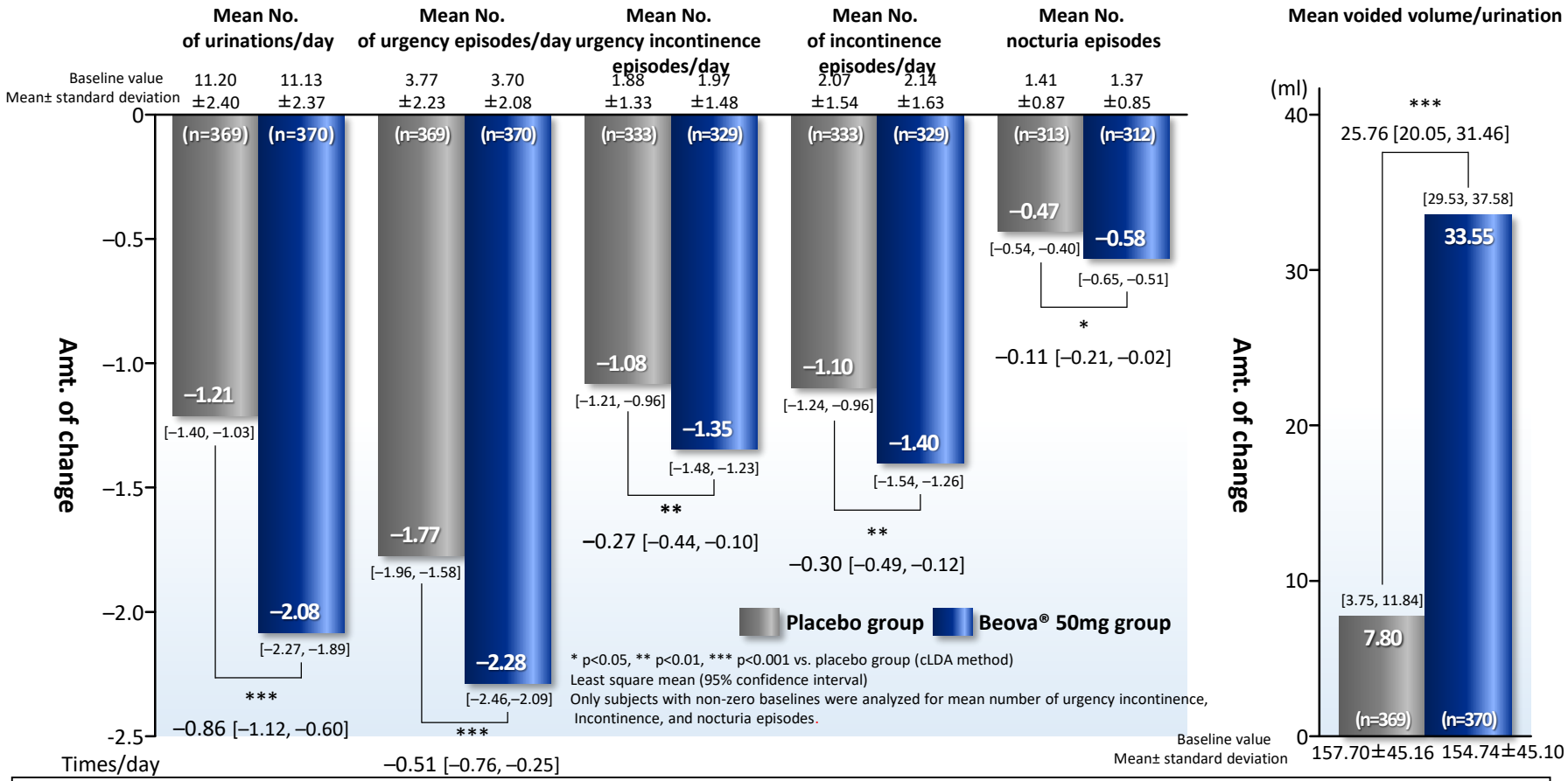
*1 (20) *The Journal of Japanese Continence Society,* 2003: 14(2), 266–277
*2 Calculations based on medical prescriptions received by the health insurance association
*3 *Clinical Guidelines for Overactive Bladder Syndrome* (2nd edition)
*4 Diagram taken from Weiss J.P. et al.: J Urol 2011; 186, 1358–1363. (Clinical trial conducted by Ferring Pharmaceuticals Co., Ltd.)

Changes in Symptoms Over a 12-Week Period (Full Analysis Set)

Primary Endpoint | **Secondary Endpoints**



* p<0.05, ** p<0.01, *** p<0.001 vs. placebo group (cLDA method)
Least square mean (95% confidence interval)
Only subjects with non-zero baselines were analyzed for mean number of urgency incontinence, Incontinence, and nocturia episodes.

Domestic Phase III clinical trial

Objective: Investigate the efficacy (superiority to a placebo) and safety of orally administered Beova® in treating patients with overactive bladder (OAB) over a 12-week period

Target and method: After a two-week observation period, 1,232 OAB patients aged 20 or older were randomly assigned to four groups, receiving Beova® 50mg, Beova® 100mg, a reference drug (imidafenacin 0.2mg), or a placebo, administered orally over the course of 12 weeks

Primary endpoint: The change in the mean number of urinations per day at week 12 from the baseline at 12 weeks

Secondary endpoints: Changes from baselines in each point of evaluation (mean number of urinations, episodes of urgency, urgency incontinence, and incontinence per day, as well as the number of episodes of nocturia, and the mean voided volume/urination), QOL domain score as determined by the King's Health Questionnaire, and a subjective degree of improvement on the Patient Global Impression (PGI) scale

Safety endpoints: Adverse events, laboratory tests, vital signs, 12-lead ECG, and residual urine output

Analysis plan: The superiority of Beova® in 50mg and 100mg doses over a placebo in terms of the primary endpoint was verified through intergroup comparison using constrained longitudinal data analysis (cLDA), with multiplicity control via the closed testing procedure. The secondary endpoints were subject to the cLDA method or the $\chi 2$ test

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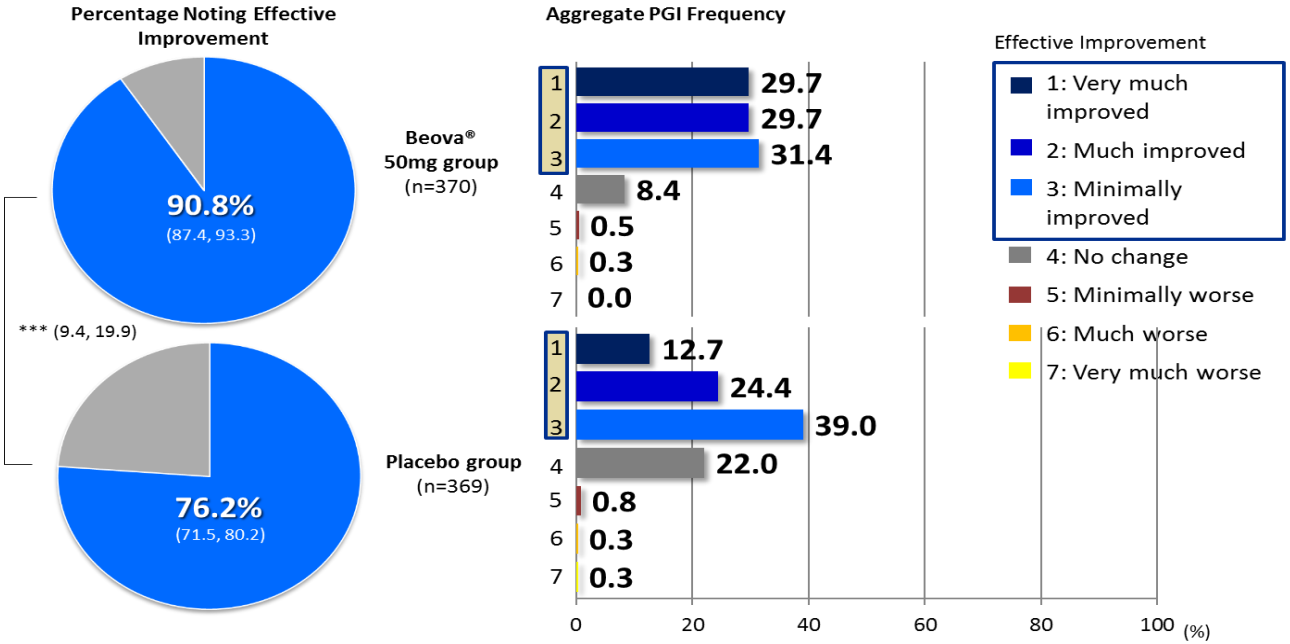
Data from domestic Phase III clinical trials, submitted as part of the application for marketing authorization approval

Percentage of Patients Noting an Effective Improvement of Secondary Endpoints (Determined via Subjective PGI Scores)



*** p<0.001 vs. placebo group (χ^2 test)

() 95% confidence interval

The percentage of patients that noted an effective improvement at the end of the 12-week period (as determined by PGI scores) was significantly higher for Beova® 50mg than that of a placebo.

PGI: Patient Global Impression

Subjects self-evaluate and provide responses on a seven-point scale as to how their OAB-related symptoms have changed since being administered an investigational drug.

Domestic phase III clinical trial

Objective: Investigate the efficacy (superiority to a placebo) and safety of orally-administered Beova® in treating patients with overactive bladder (OAB) over a 12-week period.

Target and method: After a two-week observation period, 1,232 OAB patients aged 20 or older were randomly assigned to four groups, receiving Beova® 50mg, Beova®100mg, a reference drug (imidafenacin 0.2mg) or a placebo, administered orally over the course of 12 weeks.

Primary endpoint: The change in the number of urinations per day at week 12 from the baseline

Secondary endpoints: Changes from baselines in each point of evaluation (daily averages of number of urinations, episodes of urgency, urgency incontinence, incontinence, as well as number episodes of nocturia, and voided volume/urination), QOL domain score as determined by the King's Health Questionnaire, a subjective degree of improvement on the Patient Global Impression (PGI) scale

Safety endpoints: Adverse events, laboratory tests, vital signs, 12-lead ECG, residual urine output

Analysis plan: The superiority of Beova® in 50mg and 100mg doses over a placebo in terms of the primary endpoint was verified through intergroup comparison using constrained longitudinal data analysis (cLDA), with multiplicity control via the closed testing procedure. The secondary endpoint were subject to the cLDA method or the χ2 test.

Data from domestic Phase III clinical trials, submitted as part of the application for marketing authorization approval

TAVNEOS® Capsules (Generic name: avacopan)

Acquired marketing authorization approval in Japan (September 2021)

Indications

Microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA)

Dosage and Administration

Typical adult dosage is 30mg twice daily orally after breakfast and dinner

Overview of TAVNEOS®

- First-in-class, orally administered agent that selectively blocks the complement C5a receptor, which is closely related to MPA and GPA
- Results of the ADVOCATE trial, a global Phase III clinical trial that included participation from Japan, were published in the February 18, 2021, edition of the *New England Journal of Medicine*
- Granted orphan drug designation in Japan (re-assessment period: 10 years)
- There are 10,681 patients suffering from MPA and 3,196 suffering from GPA in Japan as of December 31, 2020, for a total of approximately 14,000 patients[*1]
- In October 2021, ChemoCentryx, Inc., originator of the drug, acquired approval for a New Drug Application in the U.S.
- In January 2022, Vifor Fresenius Medical Care Renal Pharma Ltd. acquired approval for a New Drug Application in the E.U.

Microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA)

- Onset of MPA and GPA is related to antineutrophil cytoplasmic antibodies (ANCAs), and they are classified as types of ANCA-associated vasculitis (AAV). AAV is a severe and intractable disease characterized by damage to blood vessels caused by inflammation, leading to ischemia, kidney damage due to necrosis, and a variety of other organ disorders.
- Of patients diagnosed with AAV, 11% die after one year.[*2, *3]

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*1 Number of patients receiving medical expense payments for designated intractable diseases (fiscal 2020).
*2 Little M.A., et al. "Early mortality in systemic vasculitis: relative contribution of adverse events and active vasculitis." Ann Rheum Dis. 2010;69:1036-43.
*3 Flossmann O, et al. "Long-term patient survival in ANCA-associated vasculitis." Ann Rheum Dis. 2011;70:488-94.

Positioning: TAVNEOS® Capsules (Generic name: avacopan)

Positioning in accordance with ADVOCATE trial evidence (Initial launch)

Primarily a treatment for MPA/GPA (current)

Remission induction → Remission maintenance

Remission induction upon recurrence

Corticosteroids + immunosuppressive agent

Corticosteroids

Cyclophosphamide or rituximab, etc. → Azathioprine, etc.

Corticosteroids only

Corticosteroids

Assumed positioning (initial launch)

Remission induction → Remission maintenance

Remission induction upon recurrence

TAVNEOS® + immunosuppressive agent + low-dosage, short-term corticosteroids

Corticosteroids

Avacopan

Cyclophosphamide or rituximab, etc. → Azathioprine, etc.

Targets:

- ✓ Initial goal of remission induction treatment through a combination of low-dosage, short-term corticosteroids and an immunosuppressive agent
- ✓ Number of target patients amounts to approx. 3,300 per year (approx. 2,000 new patients + 1,300 patients with recurrences)[*1, *2]

Plan for fiscal 2022
¥700 million
(net sales)

Work with medical experts to build product based on post-launch evidence (Future)

Expected positioning (future)

Remission induction → Remission maintenan

Remission induction upon recurrence

TAVNEOS® + immunosuppressive agent (potentially non-steroid)

Avacopan

Cyclophosphamide or rituximab, etc. → Azathioprine, etc.

TAVNEOS® + low-dosage, short-term corticosteroids (potentially without immunosuppressive agents)

Corticosteroids

Avacopan

Utilize other drugs to maintain remission in patients

Remission induction using other drugs → Avacopan or

Patients undergoing remission maintenance treatment switch to avacopan

Target patients:

- ✓ Almost all patients that require drugs for treatment

Indications: Microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA)

*1 Number of patients receiving medical expense payments for designated intractable diseases (fiscal 2020)
*2 Calculations derived from *Rheumatology* 2011_50_1916-1920, *Arthritis Res Ther.* 2015_17_305, and *J Rheumatol.* 2018_45(4)_521-528

Promoting Proper Usage

Drug indications in Japanese documentation
Microscopic polyangiitis and granulomatosis with polyangiitis

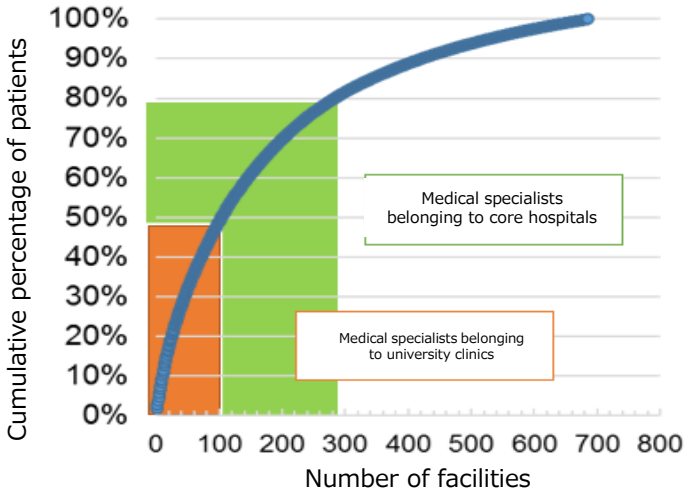
Useable with a wide range of patients, guided by doctors well versed in treatment*

* Description of treatment (usage precautions) included in domestic documentation

Rare Diseases Project
- Sales strategy planning
- Primarily in charge of KOL registered facilities
- Provision of highly specialized drug information in collaboration with medical representatives (MRs)

Provision of drug information

Prescription status, needs



Distribution system
- Unified distribution via Alfresa Group-affiliated companies

Clinical departments for treating patients with AAV
- Approx. 90% of AAV patients are treated in rheumatology and clinical immunology departments and nephrology departments

Promote the proper use of TAVNEOS® and further contribute to patients' treatment through the provision of highly specialized drug information related to disease and treatment

CAROGRA® Tablets (Generic name: carotegrast methyl)

Acquired marketing authorization approval in Japan (March 2022)

Indications

Moderate ulcerative colitis (limited to those patients who had inadequate response to 5-aminosalicylic acid (5-ASA))

Dosage and Administration

Typical adult dosage of carotegrast methyl is 960mg administered orally after a meal three times a day

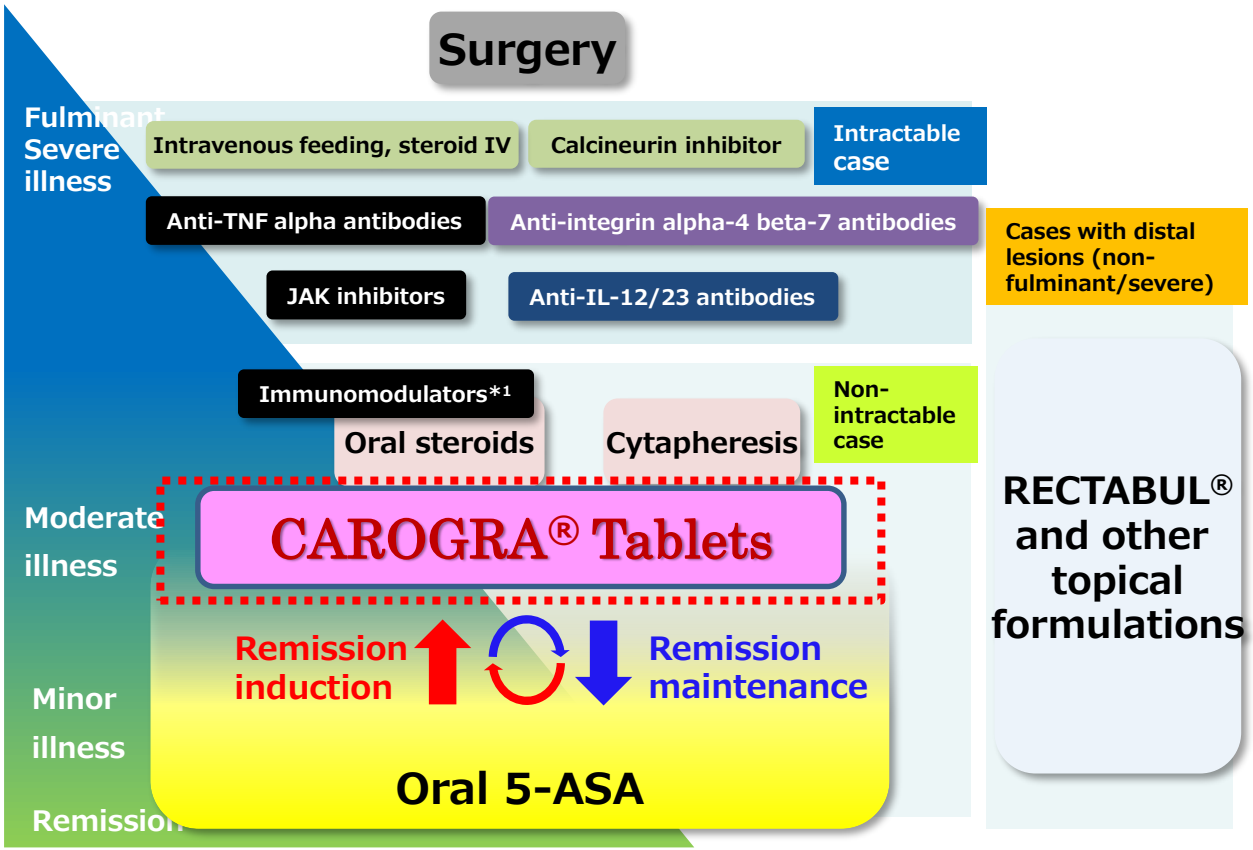
Overview of CAROGRA®

- Small molecule compound originated by EA Pharma Co., Ltd. (formerly Ajinomoto Pharmaceuticals Co., Ltd.), as the world's first alpha-4 integrin antagonist available in an orally administered dosage
- Results of Phase III clinical trial AJM300/CT3 were published in the March 30, 2022, edition of the *Lancet Gastroenterology & Hepatology*
- Approximately 220,000 patients suffer from ulcerative colitis in Japan[*1]
- Provided as a new treatment option for patients with an inadequate response to 5-ASA, the standard form of treatment
- Distribution in Japan by Kissei Pharmaceutical, with co-promotion by EA Pharma

Marketing: Kissei Pharmaceutical Co., Ltd.
Manufacturing and marketing: EA Pharma Co., Ltd.

*1 “Basic Knowledge for the Treatment of Ulcerative Colitis That Everyone Needs to Know,” (revised March 2020) produced by the Research Group for Intractable Inflammatory Bowel Disease as part of the Research Program on Rare and Intractable Diseases, funded by the Ministry of Health, Labour and Welfare's Health Labor and Welfare Sciences Research Grants system

Positioning: CAROGRA® Tablets (Generic name: carotegrast methyl)



*1 Used in cases of steroid dependency or as a remission maintenance drug

Number of patients with ulcerative colitis: Approx. 220,000*2

Number of patients with moderate ulcerative colitis: Approx. 30,000*3

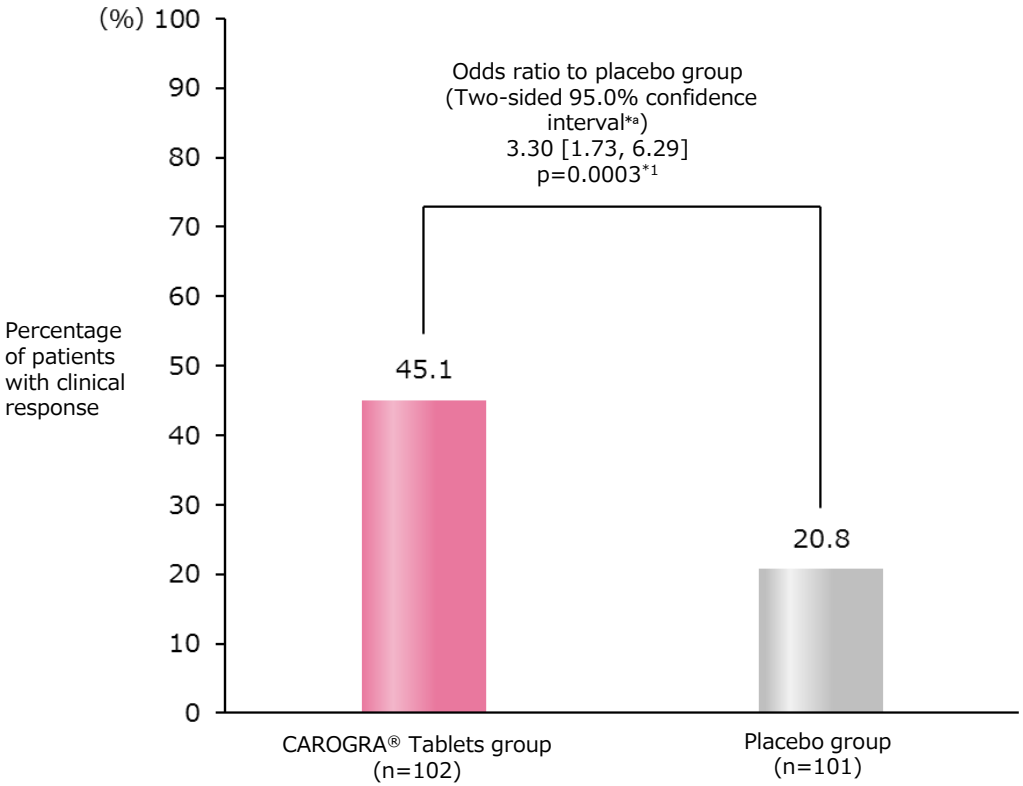
Position CAROGRA® as the first choice for patients with an inadequate response to orally administered 5-ASA

Plan for Fiscal 2022
¥350 million
(net sales)

Utilize the world's first oral alpha-4 integrin antagonist, discovered in Japan to provide a new, non-steroid, non-biologic treatment option for patients with inadequate responses to oral 5-ASA during active periods of moderate ulcerative colitis

*2 "Basic Knowledge for the Treatment of Ulcerative Colitis That Everyone Needs to Know," (revised March 2020) produced by the Research Group for Intractable Inflammatory Bowel Disease as part of the Research Program on Rare and Intractable Diseases, funded by the Ministry of Health, Labour and Welfare's Health Labor and Welfare Sciences Research Grants system
*3 Results of Kissei's market research conducted by an external research organization

Domestic Phase III Clinical Trial (AJM300/CT3) (Confirmatory Trial)
Efficacy of Initial Treatment Phase (Eight Weeks) / Percentage of Patients with a Clinical Response Based on the Mayo Score① (Primary Endpoint) (Verification Analysis of Results)



Percentage of patients with a clinical response based on the Mayo score①:
The percentage of patients meeting the following three conditions:

- A reduction in the Mayo score of 30.0% or more and 3 or more compared with week zero
- A reduction in the rectal bleeding score of 1 or more or rectal bleeding subscore of 1 or less compared with week zero
- An endoscopic subscore of 1 or less

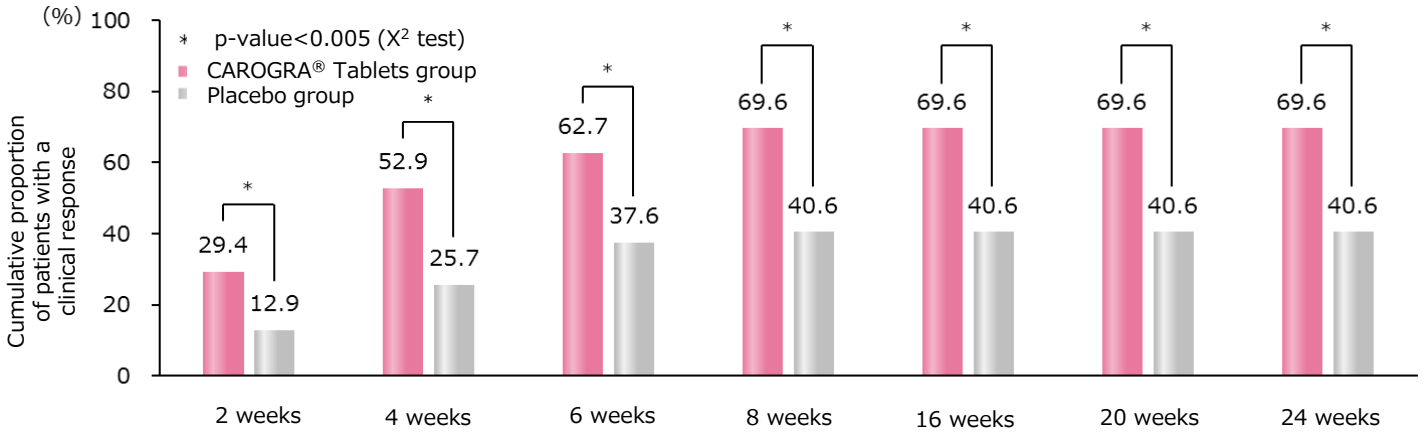
*a Logistic regression analysis, with administration group, Mayo score at the baseline (≥6 to ≤7, ≥8 to ≤10 points), any use of corticosteroid, anti-TNFα antibody, or immunosuppressants during the disease-active period (yes vs. no), and duration of remission induction therapy until randomization (<4 weeks vs. ≥4 weeks) as minimization factors

*1 Wald χ^2

Treatment for ulcerative colitis **CAROGRA®**

Domestic Phase III Clinical Trial (AJM300/CT3) (Confirmatory Trial)

Continued Efficacy from 0–24 Weeks after Initial Treatment Phase and Cumulative Percentage of Patients with a Clinical Response (Secondary Endpoints, Based on Partial Mayo Score)



	2 weeks		4 weeks		8 weeks		12 weeks		16 weeks		20 weeks		24 weeks	
	CAROGRA® Tablets group	Placebo group	CAROGRA® Tablets group	Placebo group	CAROGRA® Tablets group	Placebo group	CAROGRA® Tablets group	Placebo group	CAROGRA® Tablets group	Placebo group	CAROGRA® Tablets group	Placebo group	CAROGRA® Tablets group	Placebo group
Number of analysis targets	102	101	102	101	102	101	102	101	102	101	102	101	102	101
Cumulative number of patients with a clinical response	30	13	54	26	64	38	71	41	71	41	71	41	71	41
Cumulative % of patients with a clinical response	29.4	12.9	52.9	25.7	62.7	37.6	69.6	40.6	69.6	40.6	69.6	40.6	69.6	40.6
p-value (χ^2 test)	0.0039		<0.0001		0.0003		<0.0001		<0.0001		<0.0001		<0.0001	

Percentage of patients with a clinical response refers based on partial Mayo score to the percentage of patients meeting the following two conditions.

- A reduction in the partial Mayo score of 25.0% or more and 2 or more compared with week zero
- A reduction in the rectal bleeding score of 1 or more or rectal bleeding subscore of 1 or less during the administration period

7.Precautions regarding usage and dosage

7.1 If there is no improvement after eight weeks of administration of the drug, reconsider treatment methods, including whether or not to continue taking the drug.

7.2 Expression of progressive multifocal leukoencephalopathy (PML) has been reported in genetic recombinant natalizumab, another integrin antagonist. To reduce the risk of PML onset, the administration period of carotegrast methyl should be limited to six months, and administration should be terminated if remission is achieved within that time. Furthermore, when resuming treatment with the drug, a period of eight weeks should be given after the previous administration period. [See 5.2, 8.2, 9.1.1, 11.1.1]

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In-house documents: Phase III clinical trials results (summary of application materials 2.7.6.14), submitted as part of the application for marketing authorization approval

Strengthen Our Overseas Earnings Base by Out-Licensing Development and Marketing Rights

1. Original product: GnRH antagonist linzagolix (generic name)

- **Worldwide rights, excluding some Asian countries and Japan** ➡ Out-licensing to ObsEva SA (November 2015)
  - ✓ ObsEva entered into a strategic relationship with Syneos Health, Inc. (entered a sales consignment agreement in October 2021)
  - ✓ Entered into a licensing agreement with Theramex SpA to support commercialization (February 2022, excluding the U.S., Canada, and Asia)
- **China** ➡ Out-licensed to China-based Bio Genuine (September 2021)

Partnering has established development and sales routes for linzagolix in the global market, covering the U.S., China, and other countries

2. Original product: non-ergot dopamine agonist KDT-3594 (development code)

- **China, Taiwan, Hong Kong, Macau, and six Southeast Asian countries** ➡ Out-licensed to China-based AffaMed Therapeutics Limited for development and commercialization rights (October 2020)

3. In-licensed product: tyrosine kinase inhibitor fostamatinib (generic name)

- **Korea** ➡ Sub-licensed to Korea-based JW Pharmaceutical Corporation (June 2021)
- **China (including Hong Kong and Macau)** ➡ Sub-licensed to China-based Inmagene Biopharmaceuticals (August 2021)

Development Project Status (In-Licensing)

Product name/ generic name/ development code	Expected indications	Development stage					Remarks
		Phase			NDA in process	NDA acquired, marketing authorization in process	
		1	2	3			
TAVNEOS® /avacopan	Microscopic polyangiitis and granulomatosis with polyangiitis						Acquired marketing authorization approval in Japan (September 2021)
CAROGRA® Tablets /carotegrast methyl	Ulcerative colitis						Acquired marketing authorization approval in Japan (March 2022)
Rovatirelin /KPS-0373	Spinocerebellar degeneration						NDA submitted for Japan (December 2021)
Fostamatinib /R788	Chronic immune thrombocytopenic purpura						NDA submitted for Japan (April 2022)
Difelikefalin /MR13A9	Uremic pruritis in dialysis patients						Primary endpoint achieved
CG0070	Non muscle-invasive bladder cancer						(Conducted jointly with CG Oncology, Inc.) Joint global trials

* Red lettering denotes a designated intractable disease.

Development Project Status (Discovered Products)

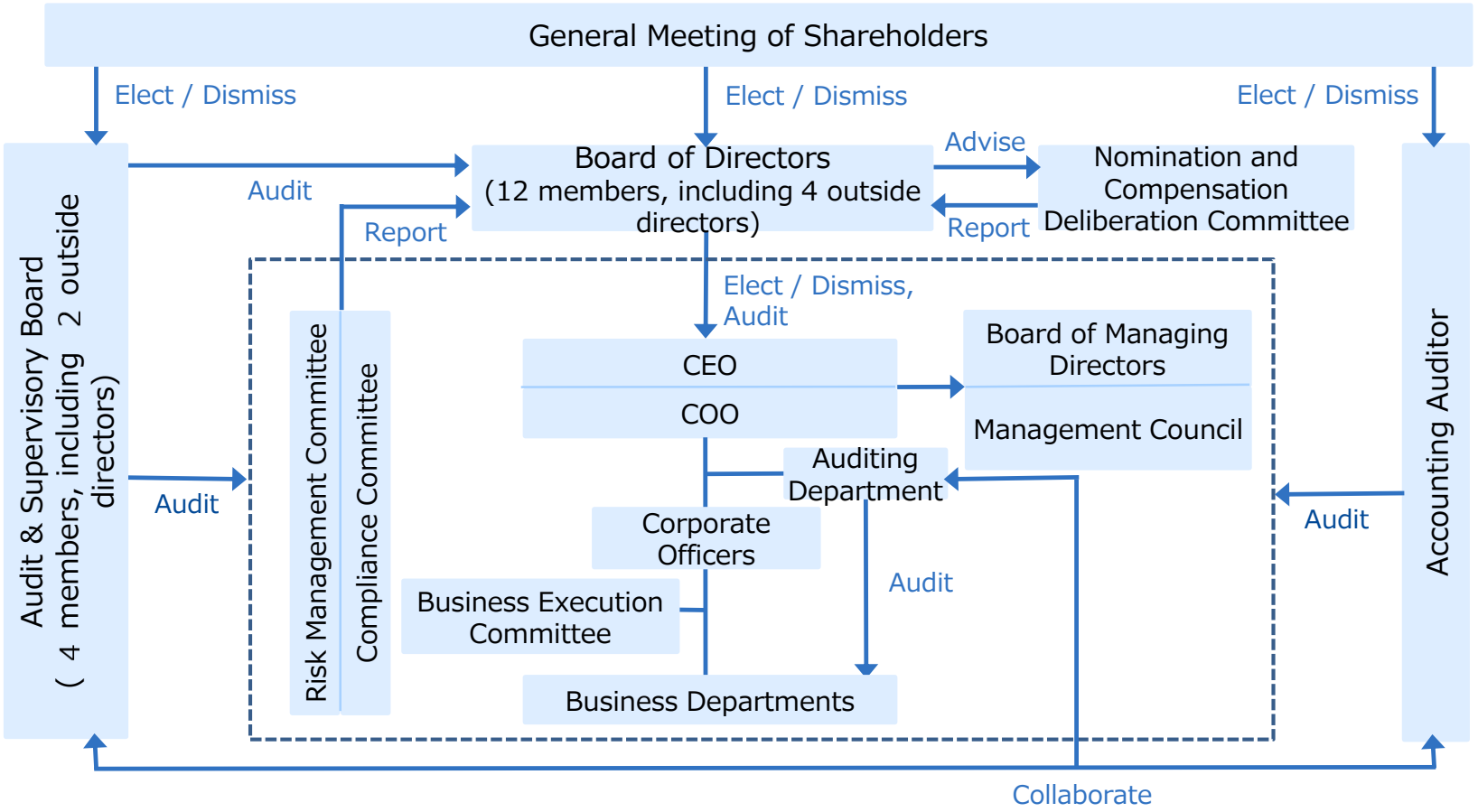
Discovered Products

Generic name/development code	Expected indications	Development stage				Remarks
		Phase			NDA in process	
		1	2	3		
Linzagolix/KLH-2109	Uterine fibroids	(Europe)				(Conducted by ObsEva SA) Marketing Authorisation Application submitted to European Medicines Agency (EMA) in November 2020 New Drug Application submitted to U.S. Food & Drug Administration (FDA) in September 2021
		(U.S.)				
	Endometriosis	(U.S. and Europe)				(Conducted by ObsEva SA)
		(Japan)				
KDT-3594	Parkinson's disease	(China, other countries)				(Conducted by AffaMed Therapeutics Limited)
		(Japan)				
KSP-0243	Inflammatory bowel disease	(Japan)				

Corporate Governance System

Management Philosophy

Contribute to society through high-quality, innovative pharmaceutical products
Serve society through our employees



Scheduled for June 23, 2022

Basic Policy on the Distribution of Profits

◆ Financial Strategy

We will secure net income through the effective use of cross-shareholdings and other financial assets and actively expand and bolster capital investment. This includes investment in R&D (drug discovery research, milestone payments for existing development themes, introduction of new development themes, enhancing R&D facilities), strategic ICT investments (DX), and production facilities.

Regarding profit attributable to owners of parent, our goal is to achieve an ROE of 5.0% or higher.

◆ Basic Policy on the Distribution of Profits

As a company listed on the Prime Market, we aim to secure a solid management base while providing stable, consistent returns to shareholders.

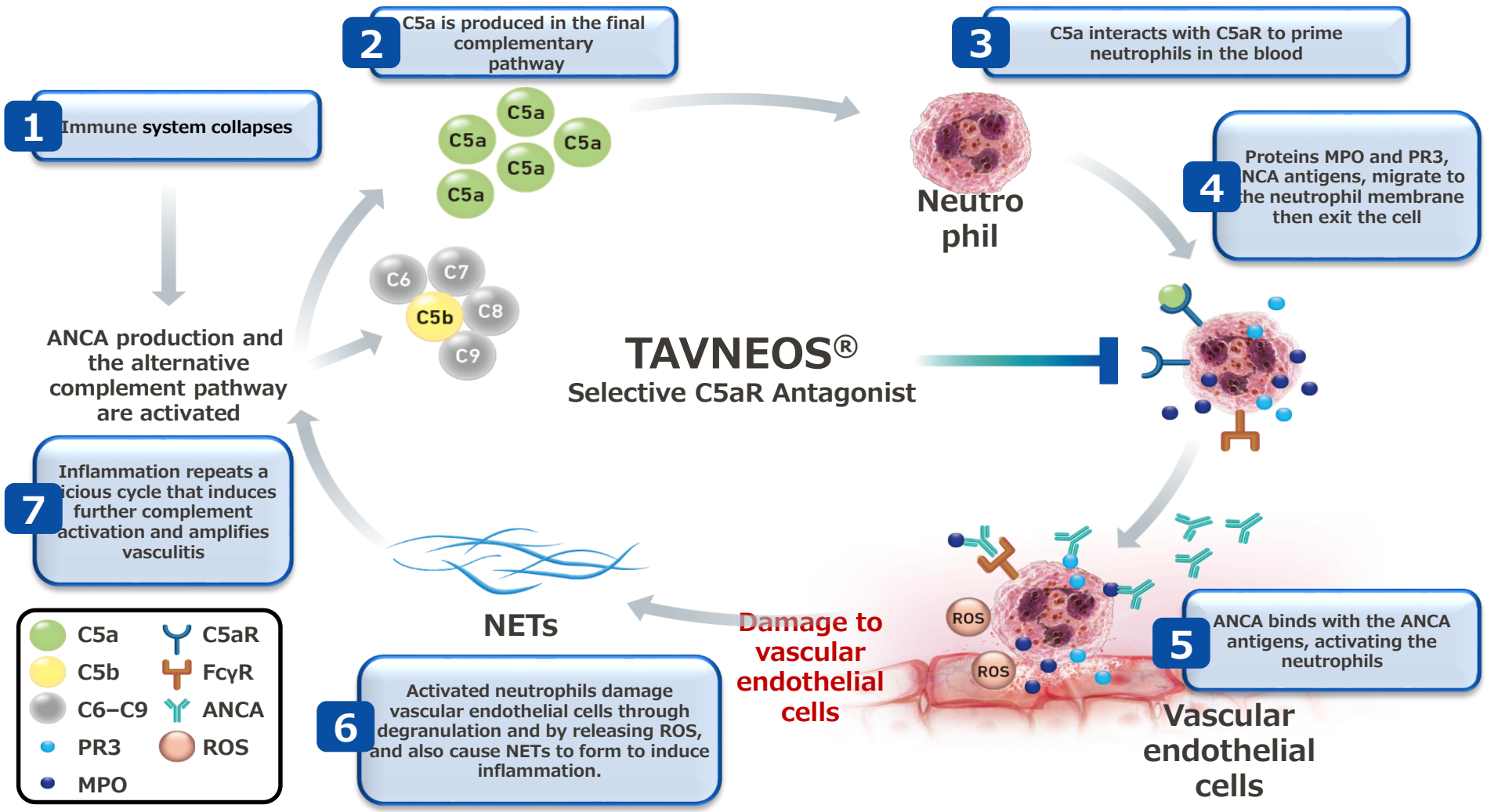
◆ Purchase and Disposal of Treasury Stock

We will implement the purchase and disposal of treasury stock in a flexible manner when, according to the resolution of the Board of Directors, it is deemed necessary in terms of business development and after first giving consideration to increasing shareholder value.

	Fiscal 2017	Fiscal 2018	Fiscal 2019	Fiscal 2020	Fiscal 2021	Fiscal 2022 (forecast)
Annual dividend per share	¥48.0	¥50.0	¥52.0	¥54.0	¥56.0	¥80.0
Dividend payout ratio (consolidated)	25.5%	42.6%	86.2%	47.7%	20.0%	36.9%
Treasury stock purchased (No. of shares)	¥4.4 billion (1.6 million)			¥1.3 billion (600,000)		
Disposal of treasury stock (No. of shares)	¥5.6 billion (2.5 million)					

Reference Materials

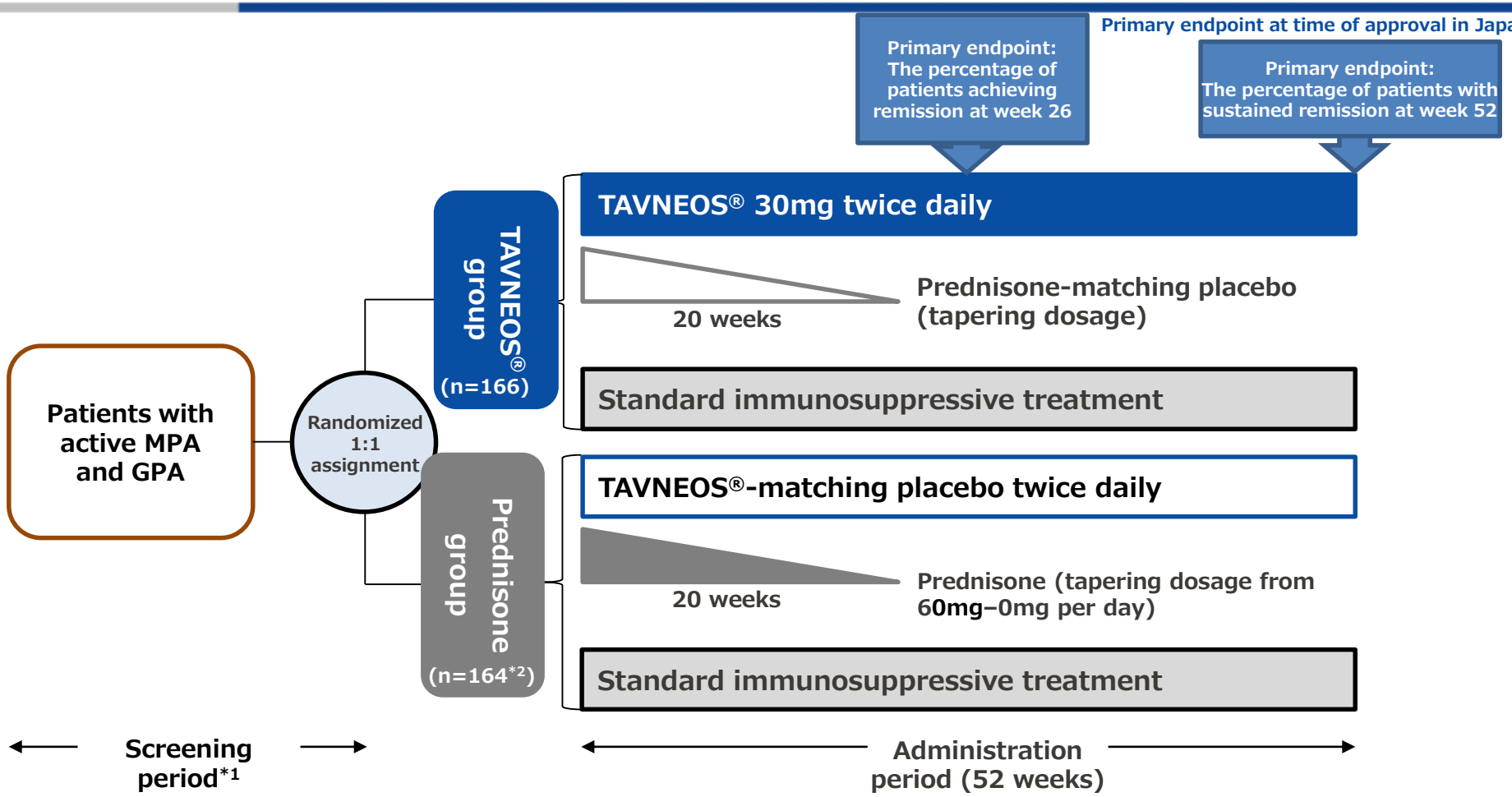
ANCA-Associated Vasculitis and TAVNEOS®'s Mechanism of Action



MPO: Myeloperoxidase; PR3: proteinase 3; C5aR: C5a receptor; NETs: Neutrophil extracelluar traps; ROS: Reactive oxygen species

Internal documents: Trials that support efficacy (mechanism of action), adapted from Chen M et al.: *Nat Rev Nephrol.* 13 : 359, 2017

Trial Design of Global Joint Phase III Clinical Trial ADVOCATE (CL010_168)



Note: Predisone not approved in Japan

*1 The screening period was not to exceed 14 days and allowed for intravenous glucocorticoids at a cumulative dose equivalent to a maximum of 3g of methylprednisone before and during screening. If a patient received oral glucocorticoids during the screening period, the dose needed to be tapered so as not to exceed 20mg of the prednisone equivalent on day one of the study.

*2 The prednisone group includes 164 subjects who received at least one dose of the drug. In the TAVNEOS® group, all subjects received doses of TAVNEOS®. One subject allocated to the prednisone group did not receive doses of the drug. The results from the subject's renal biopsy did not yield a clear diagnosis of vasculitis, and after consideration by the investigator, the subject was removed from the study.

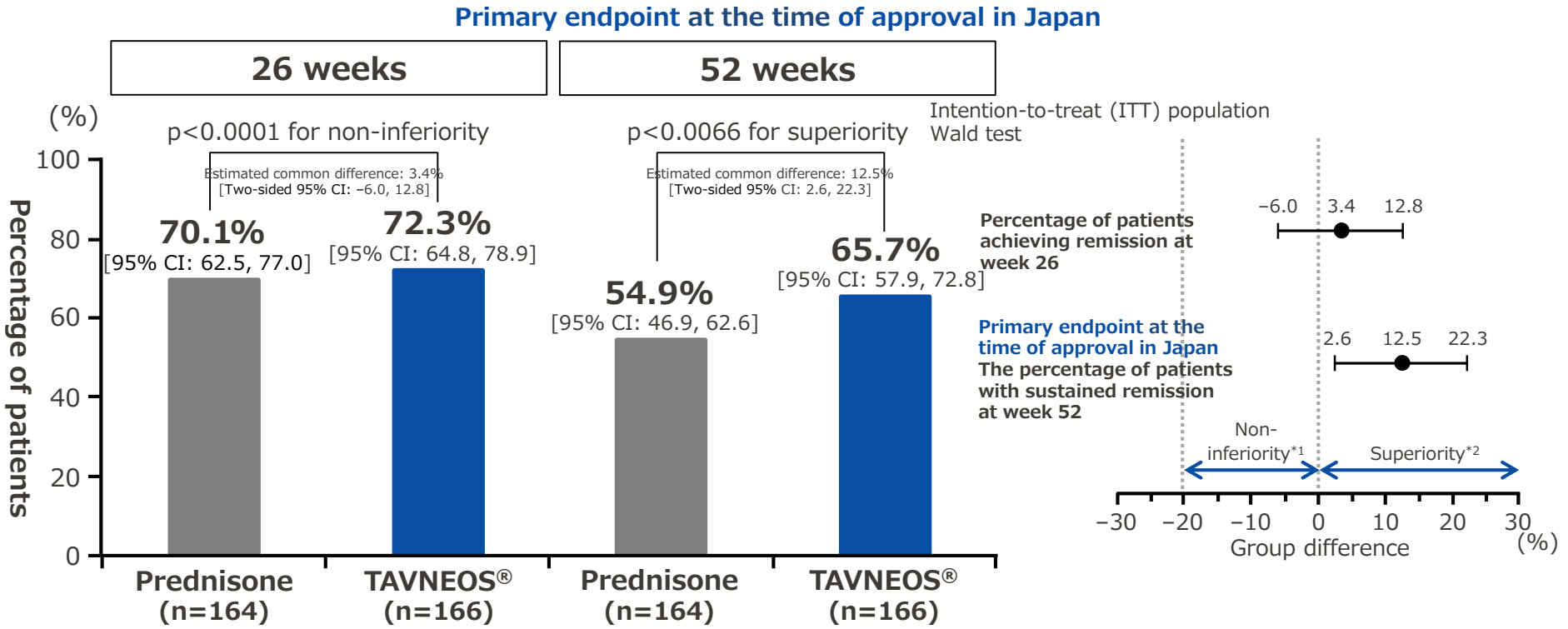
MPA: Microscopic polyangiitis; GPA: granulomatosis with polyangiitis

Internal document: Phase III Clinical Trial (CL010_168) (submitted as part of the application for marketing authorization approval) Jayne D.R.W. et al.: *N Engl J Med.* 384:599, 2021
Conflict of interest: Trial conducted by ChemoCentryx

The Percentage of Patients Achieving Remission at Week 26 and the Percentage of Patients with Sustained Remission at Week 52 (Primary Endpoints)

Global Joint Phase III Clinical Trial ADVOCATE (CLO10_168)

- **Superiority of TAVNEOS® to a tapered dose of prednisone was verified in terms of the percentage of patients with sustained remission at week 52, the primary endpoint at the time of approval in Japan, when the lower boundary of the two-sided 95% confidence interval (CI) of the test groups exceeded 0.0% (p=0.0066, Wald test).**
- **Non-inferiority of TAVNEOS® to prednisone was verified in terms of the percentage of patients who achieved remission at week 26, when the lower boundary of the two-sided 95% CI for the difference in remission between the TAVNEOS® and prednisone groups exceeded −20 percentage points (p<0.0001, Wald test).**



Note: Prednisone not approved in Japan

*1 If the lower boundary of the two-sided 95% CI for the difference between the two groups was above −20%, TAVNEOS® would be deemed not inferior to prednisone.

*2 If the lower boundary of the two-sided 95% CI for the difference between the two groups was above 0.0%, TAVNEOS® would be deemed superior to prednisone.

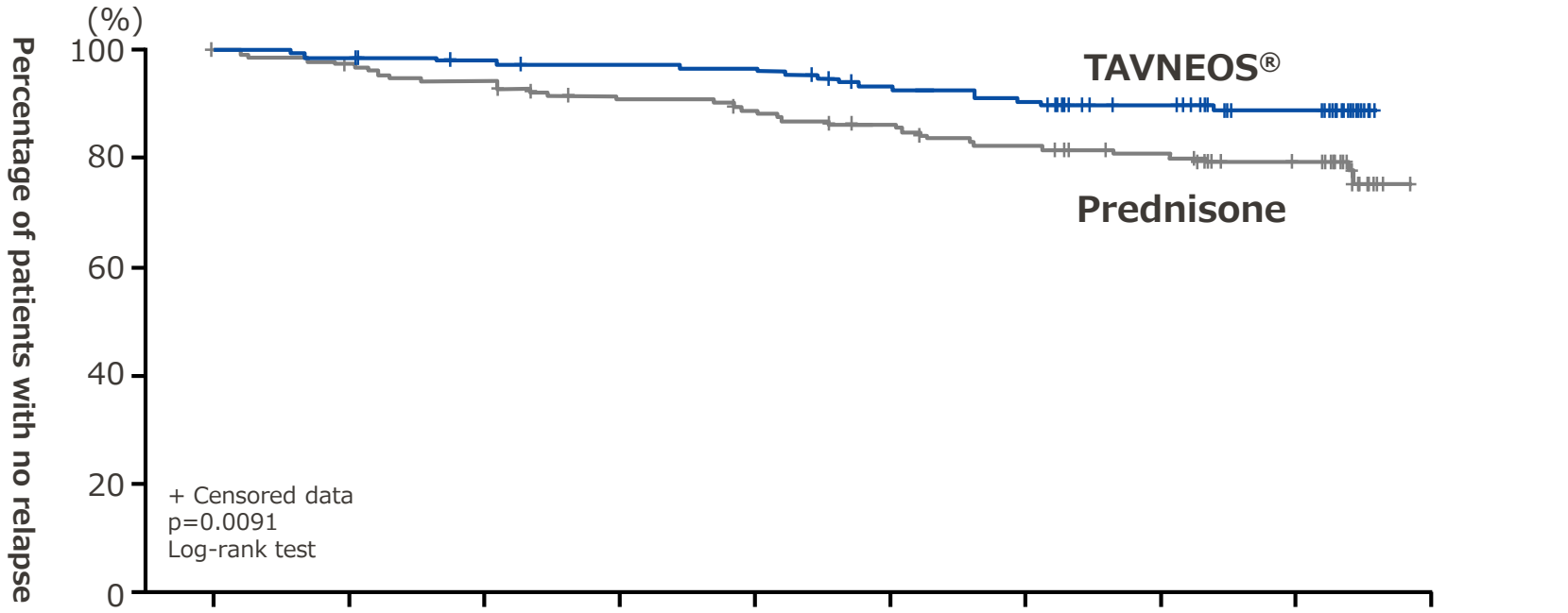
Internal document: Phase III Clinical Trial (CL010_168) (submitted as part of the application for marketing authorization approval) Jayne D.R.W. et al.: *N Engl J Med.* 384:599, 2021

Conflict of interest: Trial conducted by ChemoCentryx

Percentage of Patients Who Relapsed and Time Until Relapse (Secondary Endpoints)

Global Joint Phase III Clinical Trial ADVOCATE (CLO10_168)

- **At 26 weeks, the percentage of patients who relapsed after achieving remission was 12.2% for the prednisone group and 7.5% for the TAVNEOS® group, which was not a statistically significant difference (p=0.081, Wald test)**
- **The percentage of patients who relapsed during the trial after achieving a BVAS*1 of zero was 21.0% for the prednisone group and 10.1% for the TAVNEOS® group. A statistically significant difference was also observed in the period from achieving a BVAS of 0 to relapse.**
- **The hazard ratio for relapse after remission for TAVNEOS® versus prednisone was 0.46 (95% CI: 0.25, 0.84]. It is estimated that the risk of relapse was reduced by 54% in the TAVNEOS® Group compared with the prednisone group.**



TAVNEOS®	158	153	149	146	145	133	129	115	92	0
Prednisone	157	151	146	137	133	126	119	111	90	0

*1 Birmingham Vasculitis Activity Score

Internal document: Phase III Clinical Trial (CL010_168) (submitted as part of the application for marketing authorization approval) Jayne D.R.W. et al.: *N Engl J Med.* 384:599, 2021
Conflict of interest: Trial conducted by ChemoCentryx

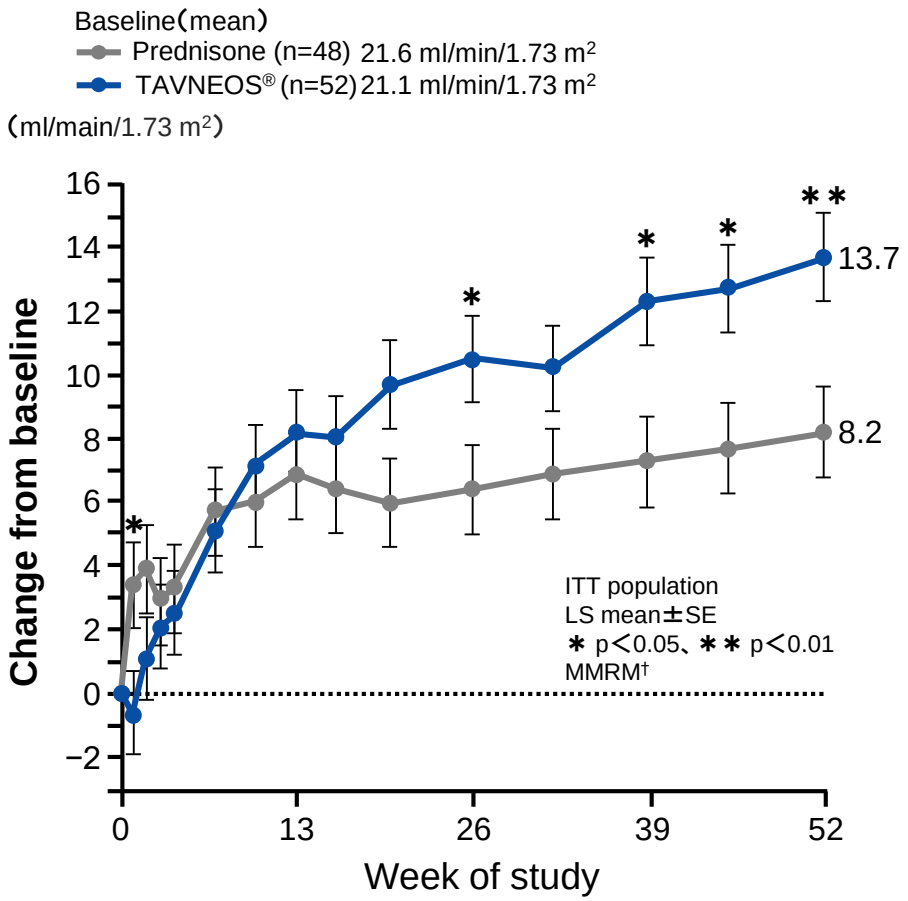
Improvement of Renal Function

Characteristics of Japanese patients according to epidemiological survey[1), 2)]

	Microscopic polyangiitis (MPA) (n=276)	Granulomatosis with polyangiitis (GPA) (n=86)
Male/Female	128/148	32/54
Mean Age	70.6	65.6
Mean Serum creatinine (mg/dL)	2.99	1.57
Occurrence of rapidly progressive glomerulonephritis	67.4%	38.4%

- Estimated glomerular filtration rate (eGFR), an indicator of renal function, increased significantly at 26 and 52 weeks compared with prednisone.
- Compared with the U.S. and Europe, Japanese patients are older, and those with MPA suffer from more severe renal dysfunction, meaning TAVNEOS® can contribute to the treatment of these patients.

Change in eGFR in patients with renal lesions and eGFR less than 30 ml/min/1.73 m²



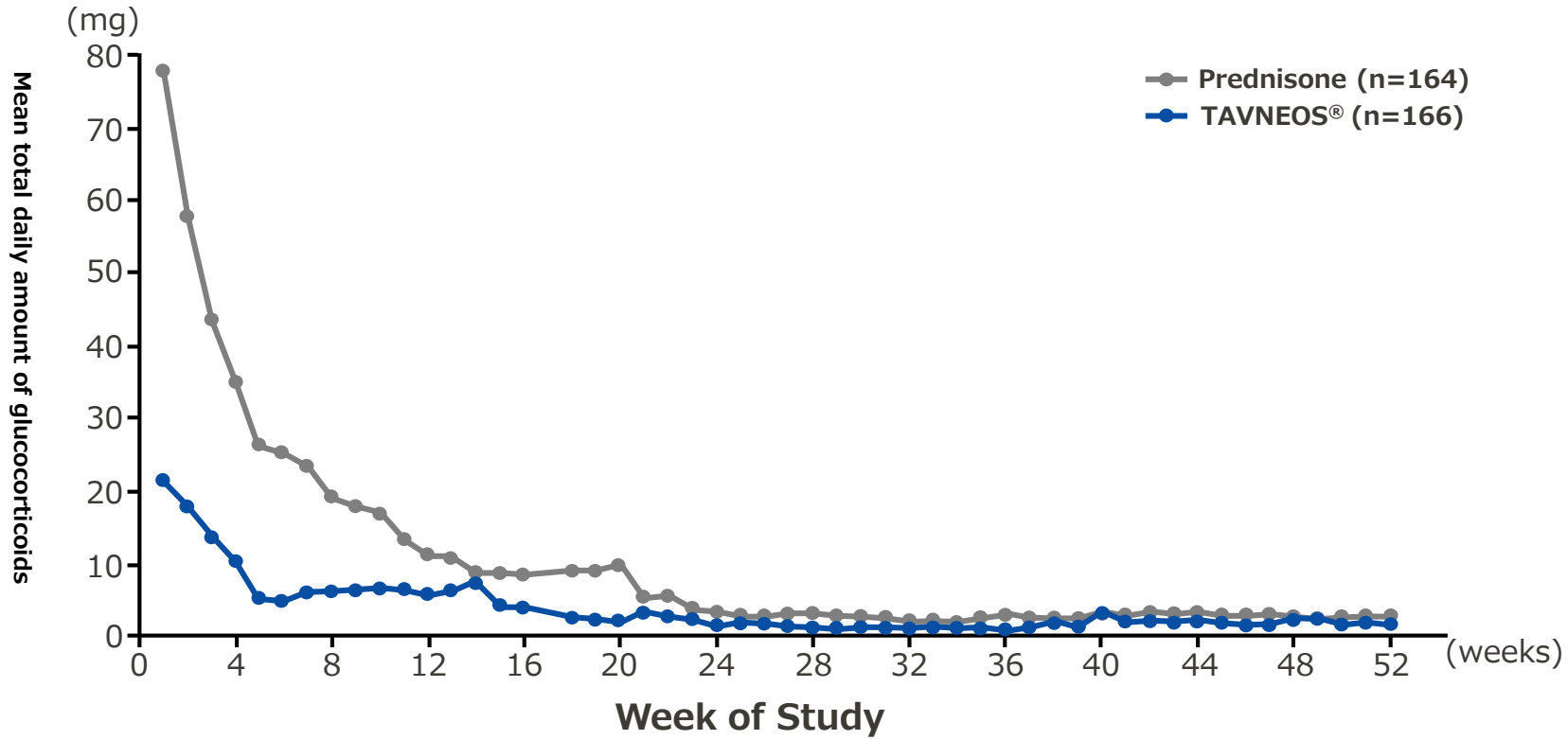
† With treatment group, study visit, treatment-by-visit interaction, and randomization stratum as factors and baseline as covariate
Note: Results from evaluation of the primary endpoints at 26 and 52 weeks are included

1) Sada KE et al.: *Arthritis Res Ther.* 16:R101, 2014
2) Sada KE et al.: *Mod Rheumatol.* 26:730, 2016

Patient Information / Mean Total Daily Glucocorticoid Administration per Week (Prednisone Equivalent)

Global Joint Phase III Clinical Trial ADVOCATE (CLO10_168)

Changes in the Mean Total Daily Amount of Glucocorticoids Administered Over the Course of 52 Weeks

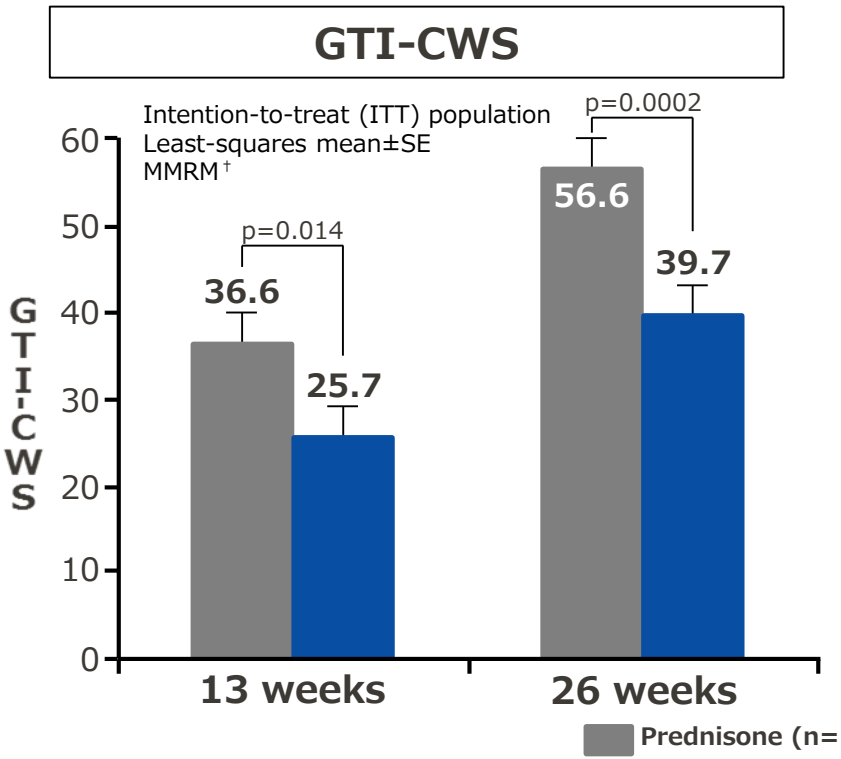


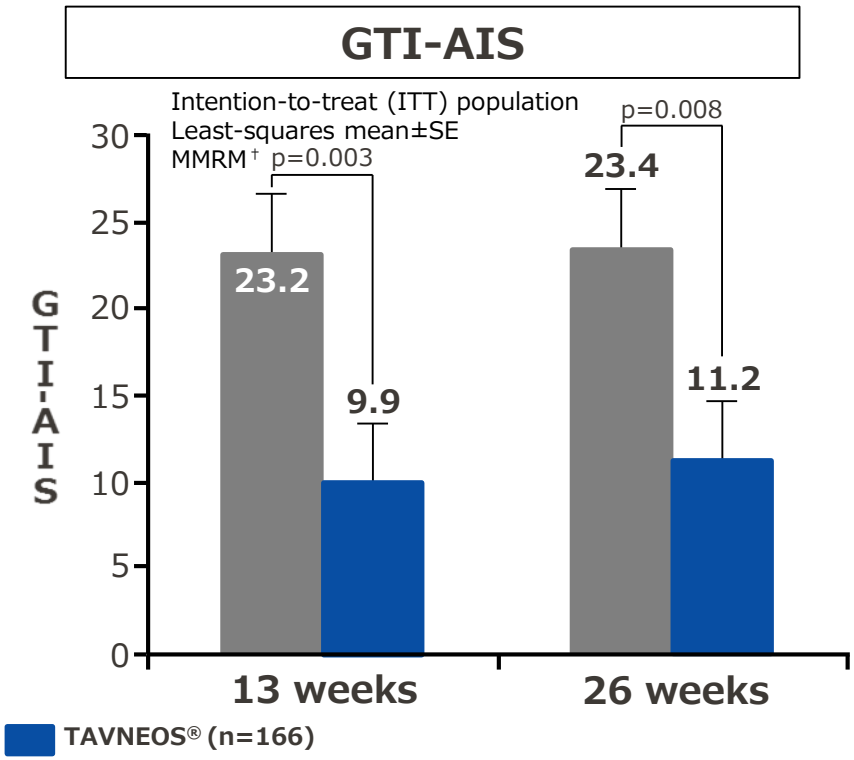
Internal document: Phase III Clinical Trial (CL010_168) (submitted as part of the application for marketing authorization approval) Jayne D.R.W. et al.: *N Engl J Med.* 384:599, 2021
Conflict of interest: Trial conducted by ChemoCentryx

Glucocorticoids Toxicity at 26 Weeks as Measured by GTI-CWS*1 and GTI-AIS*2 (Secondary Endpoint)

Global Joint Phase III Clinical Trial ADVOCATE (CLO10_168)

- **The least-squares mean for GTI-CWS at week 13 was 36.6 for the prednisone group and 25.7 for the TAVNEOS® group (p=0.014, MMRM), and 56.6 and 39.7 respectively at week 26 (p=0.0002, MMRM). The differences between groups at both week 13 and week 26 were recognized as statistically significant.**
- **The least-squares mean for GTI-AIS at week 13 was 23.2 for the prednisone group and 9.9 for the TAVNEOS® group (p=0.003, MMRM), and 23.4 and 11.2 respectively at week 26 (p=0.008, MMRM). The differences between groups at both week 13 and week 26 were recognized as statistically significant.**





Prednisone (n=164) TAVNEOS® (n=166)

Internal document: Phase III Clinical Trial (CL010_168) (submitted as part of the application for marketing authorization approval) Jayne D.R.W. et al.: *N Engl J Med.* 384:599, 2021

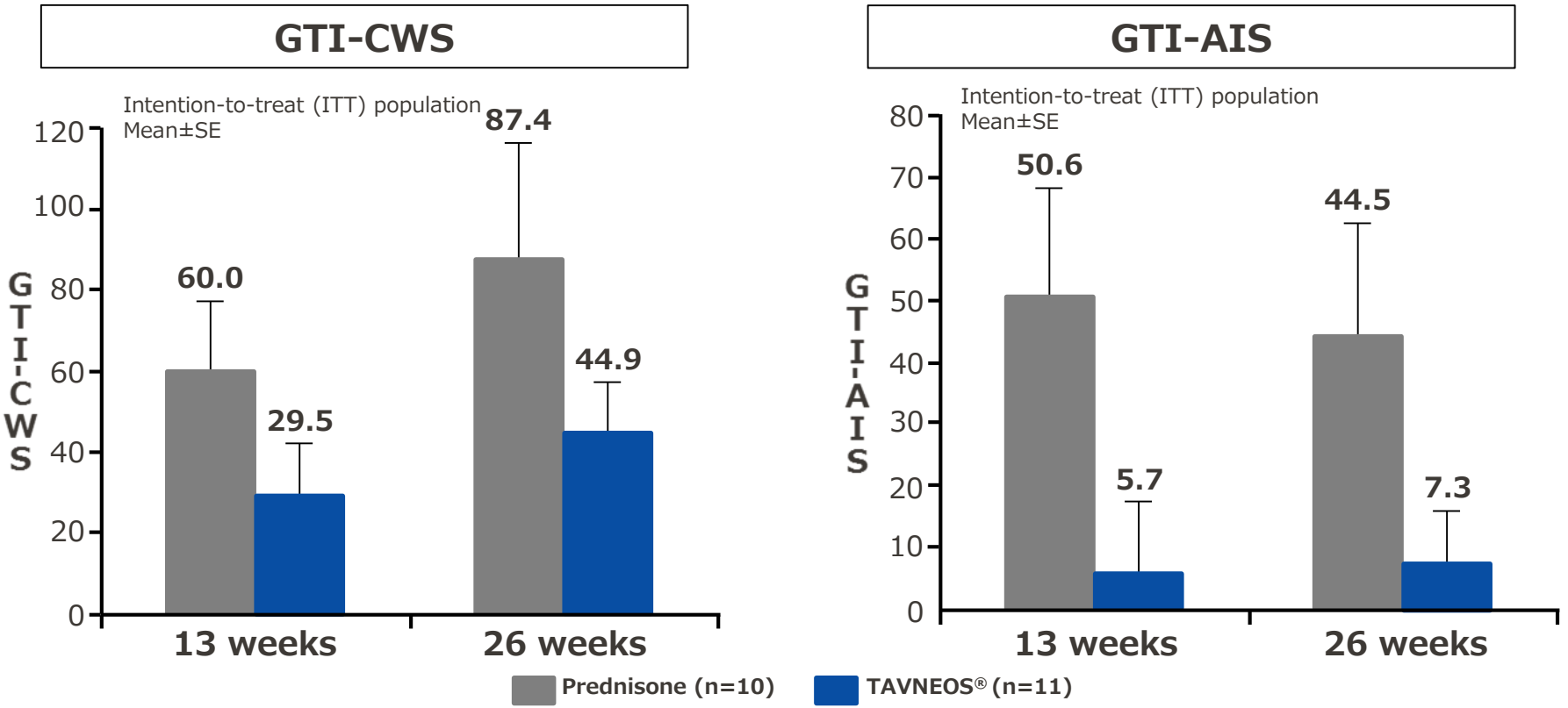
Conflict of interest: Trial conducted by ChemoCentryx

† With treatment group, study visit, treatment-by-visit interaction, and stratification factors as covariates
*1 Glucocorticoid Toxicity Index-Cumulative Worsening Score
*2 Glucocorticoid Toxicity Index-Aggregate Improvement Score

Glucocorticoids Toxicity at 26 Weeks as Measured by GTI-CWS*1 and GTI-AIS*2 (Secondary Endpoint)—Analysis of Japanese Patient Subgroup

Global Joint Phase III Clinical Trial ADVOCATE (CLO10_168)

- **The mean GTI-CWS among Japanese patients at week 13 was 60.0 for the prednisone group and 29.5 for the TAVNEOS® group, and 87.4 and 44.9 respectively at week 26.**
- **The mean GTI-AIS at week 13 among Japanese patients was 50.6 for the prednisone group and 5.7 for the TAVNEOS® group, and 44.5 and 7.3 respectively at week 26.**



*1 Glucocorticoid Toxicity Index-Cumulative Worsening Score
*2 Glucocorticoid Toxicity Index-Aggregate Improvement Score

Internal document: Phase III Clinical Trial (CL010_168) (submitted as part of the application for marketing authorization approval) Jayne D.R.W. et al.: *N Engl J Med.* 384:599, 2021
Conflict of interest: Trial conducted by ChemoCentryx

Adverse Events[1)]

Global Joint Phase III Clinical Trial ADVOCATE (CLO10_168)

- **Adverse events were recognized in 98.2% (161/164 patients) of the prednisone group and 98.8% (164/166 patients) in the TAVNEOS® group.**

Safety Analysis Target Group

	Prednisone (n=164)	TAVNEOS® (n=166)
Adverse events		
Number of patients (%)	161 (98.2)	164 (98.8)
Number of events	2,139	1,779
Life-threatening adverse events		
Number of patients (%)	14 (8.5)	8 (4.8)
Number of events	22	8
Deaths (%)	4 (2.4)	2 (1.2)
Serious adverse events*1		
Number of patients (%)	74 (45.1)	70 (42.2)
Number of events	166	116
Any serious event related to vasculitis worsening*2		
Number of patients (%)	23 (14.0)	17 (10.2)
Number of events	36	18
Any serious event not related to vasculitis worsening*2		
Number of patients (%)	64 (39.0)	62 (37.3)
Number of events	130	98
Any infection		
Number of patients (%)	124 (75.6)	113 (68.1)
Number of events	291	233
Any serious infection		
Number of patients (%)	25 (15.2)	22 (13.3)
Number of events	31	25

	Prednisone (n=164)	TAVNEOS® (n=166)
Any serious opportunistic infection	11 (6.7)	6 (3.6)
Deaths due to infection	2 (1.2)	1 (0.6)
Life-threatening infection	2 (1.2)	1 (0.6)
Serious adverse events of abnormality on liver-function testing	6 (3.7)	9 (5.4)
Adverse events potentially related to glucocorticoids*3	132 (80.5)	110 (66.3)
Cardiovascular	85 (51.8)	72 (43.4)
Infectious	25 (15.2)	22 (13.3)
Gastrointestinal	4 (2.4)	3 (1.8)
Psychological	39 (23.8)	27 (16.3)
Endocrine or metabolic	48 (29.3)	23 (13.9)
Dermatologic	28 (17.1)	14 (8.4)
Musculoskeletal	21 (12.8)	19 (11.4)
Ophthalmologic	12 (7.3)	7 (4.2)
Adverse events potentially related to glucocorticoids as assessed by investigators (%)	131 (79.9)	107 (64.5)
Serious adverse events potentially related to prednisone as assessed by investigators (%)	24 (14.6)	11 (6.6)

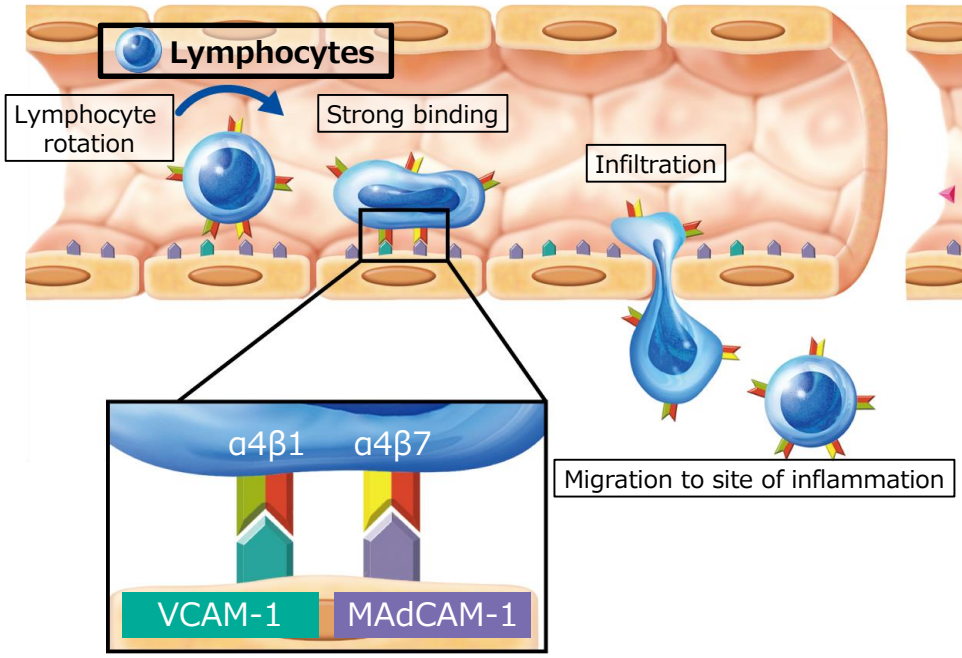
Number of cases/patients (%)

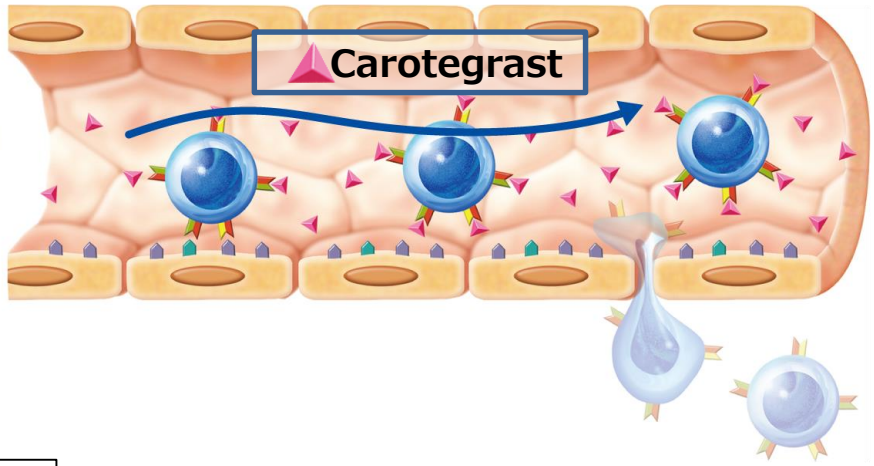
*1 Serious adverse events were defined as any adverse event that resulted in death, was immediately life-threatening, required or prolonged hospitalization, resulted in persistent or clinically significant disability or incapacity, was a birth defect, or was an important event that might jeopardize the patient or might have required intervention to prevent any of the above.
*2 Any serious event related to MPA or GPA worsening
*3 Potential of being related to glucocorticoids based on search criteria endorsed by the European League against Rheumatism (EULAR)[2)]

MPA: Microscopic polyangiitis; GPA: granulomatosis with polyangiitis

1)-Jayne D.R.W. et al.: *N Engl J Med.* 384:599, 2021 Conflict of interest: Trial conducted by ChemoCentryx
2) Duru N et al.: *Ann Rheum Dis* 72: 1905, 2013

Mechanism of Action





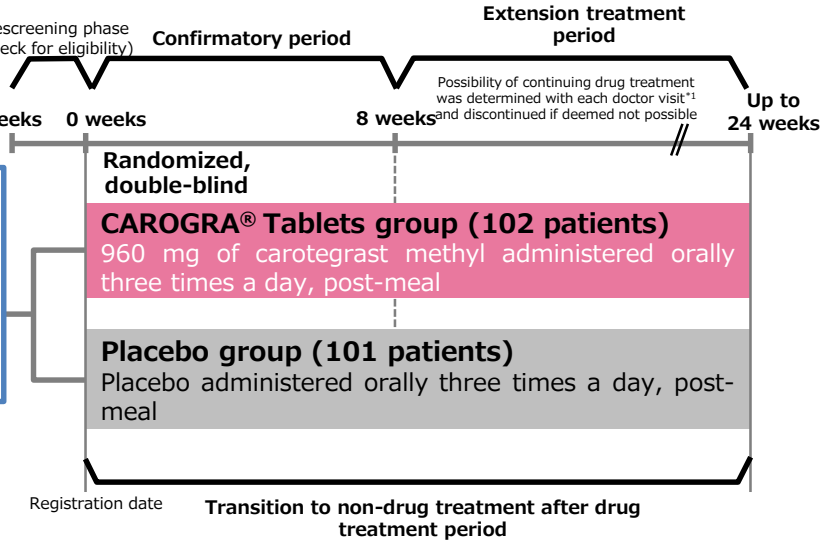
Carotegrast inhibits the binding of α4β1 integrins to VCAM-1 and α4β7 integrins to MAdCAM-1.

Produced with reference to Sugiura T, et al. : *J Crohns Colitis.* 2013 Dec; 7(11):e533-42
Conflict of interest : The authors of this study include employees of Ajinomoto Pharmaceuticals Co., Ltd.
The test drug was provided by Ajinomoto Pharmaceuticals Co., Ltd.

Domestic Phase III Clinical Trial (AJM300/CT3) (Confirmatory Trial)

Overview of Trial and Schedule (Initial Treatment Phase, Re-Treatment Phase)

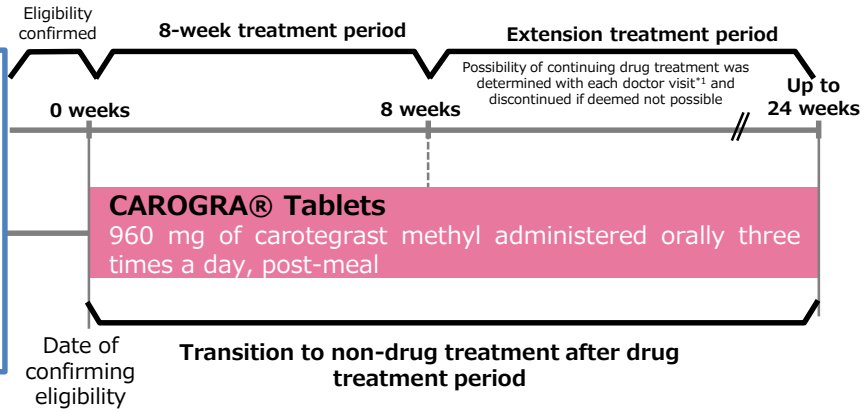
Initial Treatment Phase



203 patients with moderate active-period ulcerative colitis

・Insufficient response or intolerance to oral 5-ASA
・Mayo score of 6–10
・Endoscopic subscore of 2 or more
・Rectal bleeding subscore of 1 or more
etc.

Re-Treatment Phase



・Applicable to patients who completed 8-week drug treatment of the initial treatment phase
・Applicable to patients who matched any of the following criteria at the end of the initial treatment phase:
- Exhibited an improved Mayo score①
- Exhibited an improved partial Mayo score
- Had an endoscopic subscore of zero
- Had a rectal bleeding subscore of zero*2
・ Had a period of 8 weeks or more since completing the most recent dosage of the drug treatment and confirming eligibility for the re-treatment phase, etc.

Standards for Extended Treatment

Treatment was extended when patients exhibited an improved Mayo score①, but did not achieve an endoscopic subscore of zero. However, if patients exhibited an improved Mayo score① after eight weeks and wished to continue drug treatment, they were permitted to do so at the discretion of the principal investigator and the doctor in charge of the trial

*1 Discontinuation of treatment:
After 12 weeks, the feasibility of continuing administration of the drug was determined during each prescribed doctor visit and was discontinued if any of the following conditions were met:

- The patient is given an endoscopic subscore of 0 when colonoscopy is performed (initial treatment phase only)
- The patient is given a rectal bleeding subscore of zero
- The patient deviated from improvement standards laid out in the partial Mayo score

*2 Only for patients who enter the extension treatment period

7. Precautions regarding usage and dosage

7.1 If there is no improvement effect after eight weeks of administration of the drug, reconsider treatment methods, including whether or not to continue the drug.

7.2 Expression of progressive multifocal leukoencephalopathy (PML) has been reported in genetic recombinant natalizumab, another integrin antagonist. To reduce the risk of PML onset, the administration period of carotegrast methyl should be limited to six months, and administration should be terminated if remission is achieved within that time. Furthermore, when resuming treatment with the drug, a period of eight weeks should be given after the previous administration period. (See 5.2, 8.2, 9.1.1, 11.1.1])

Trial Overview / Evaluation Criteria (Mayo Score)

Item	Score
Stool frequency subscore*1	0 Normal number of stools
	1 1–2 stools/day above normal
	2 3–4 stools/day above normal
	3 5 or more stools/day above normal
Rectal bleeding subscore*2	0 No rectal bleeding
	1 Streaks of blood with stool less than half the time
	2 Obvious blood with stools in most cases
	3 Mainly blood
Endoscopic subscore*3	0 Normal mucosa or inactive disease
	1 Mild disease (erythema, decreased vascular pattern, mild friability)
	2 Moderate disease (marked erythema, absent vascular pattern, friability, erosions)
	3 Severe disease (spontaneous bleeding, ulceration)
Physician's global assessment subscore*4	0 Normal
	1 Mild disease
	2 Moderate disease
	3 Severe disease

Partial Mayo score: Comprises three of the Mayo score subscores, excluding the endoscopic subscore

*1 The mean value for the three days examined (rounded to the first decimal place) was compared with the normal number of stools and converted to a score.
*2 Of the three days examined, the day with the heaviest rectal bleeding was used as a score.
*3 During the colonoscopy given before administration of the investigational drug, the area where ulcerative colitis was most active was identified in the rectal and sigmoid colon (S, Rs, Ra, Rb) and those endoscopic findings were used to determine a score. These endoscopic findings were compared with endoscopy findings of the same area conducted after administration of the drug. If a colonoscopy could not be performed due to worsening ulcerative colitis after drug treatment began, the score was set at 3. Pre- and post-administration colonoscopies of the investigational drug were performed by the same doctor where possible.
*4 Scores were given with reference to the other three subscores and the results of an interview with the patient.

Domestic Phase III Clinical Trial (AJM300/CT3) (Confirmatory Trial)

Side Effects Experienced During the Initial Treatment Phase

Treatment phase		During initial treatment phase (Confirmatory period)		During initial treatment phase (including extension treatment period)	
Treatment group		CAROGRA® Tablets group	Placebo group	CAROGRA® Tablets group	Placebo group
Number of analysis targets		**102**	**101**	**102**	**101**
Total cases of side effects		**17 (16.7)**	**14 (13.9)**	**18 (17.6)**	**18 (17.8)**
Infections and parasitic disease		2 (2.0)	4 (4.0)	4 (3.9)	6 (5.9)
	Nasopharyngitis	2 (2.0)	3 (3.0)	3 (2.9)	4 (4.0)
	Gastroenteritis	0	0	1 (1.0)	0
	Influenza	0	1 (1.0)	0	2 (2.0)
Blood and lymphatic disorders		1 (1.0)	0	1 (1.0)	0
	Anemia	1 (1.0)	0	1 (1.0)	0
Immune system disorders		1 (1.0)	0	1 (1.0)	0
	Drug hypersensitivity	1 (1.0)	0	1 (1.0)	0
Nervous system disorders		1 (1.0)	1 (1.0)	2 (2.0)	2 (2.0)
	Headaches	1 (1.0)	1 (1.0)	2 (2.0)	1 (1.0)
	Dizziness	0	0	0	1 (1.0)
Ear and inner ear disorders		1 (1.0)	0	1 (1.0)	0
	Ear pain	1 (1.0)	0	1 (1.0)	0
Respiratory, chest, and mediastinal disorders		1 (1.0)	2 (2.0)	2 (2.0)	2 (2.0)
	Nosebleeds	0	0	1 (1.0)	0
	Sore throat or mouth	1 (1.0)	0	1 (1.0)	0
	Asthma	0	1 (1.0)	0	1 (1.0)
	Inflammation of the upper respiratory tract	0	1 (1.0)	0	1 (1.0)
Gastrointestinal		4 (3.9)	3 (3.0)	4 (3.9)	5 (5.0)
	Nausea	2 (2.0)	0	2 (2.0)	0
	Abdominal discomfort	1 (1.0)	0	1 (1.0)	0
	Mouth ulcers	1 (1.0)	1 (1.0)	1 (1.0)	1 (1.0)
	Upper abdominal pain	0	1 (1.0)	0	2 (2.0)
	Gingival pain	0	0	0	1 (1.0)
	Vomiting	0	1 (1.0)	0	1 (1.0)
Hepatobiliary disorders		2 (2.0)	1 (1.0)	2 (2.0)	1 (1.0)
	Abnormal liver function	2 (2.0)	1 (1.0)	2 (2.0)	1 (1.0)
Skin and hypodermal disorders		2 (2.0)	2 (2.0)	2 (2.0)	3 (3.0)
	Pyoderma gangrenosum	1 (1.0)	0	1 (1.0)	0
	Rashes	1 (1.0)	2 (2.0)	1 (1.0)	2 (2.0)
	Hives	1 (1.0)	0	1 (1.0)	0
	Itching	0	0	0	1 (1.0)
General disorders (full-body or centralized to dosage area)		1 (1.0)	1 (1.0)	1 (1.0)	1 (1.0)
	Fever	1 (1.0)	1 (1.0)	1 (1.0)	1 (1.0)
Clinical examinations		2 (2.0)	2 (2.0)	2 (2.0)	3 (3.0)
	Increased platelet count	1 (1.0)	0	1 (1.0)	0
	Liver enzyme abnormalities	1 (1.0)	0	1 (1.0)	0
	Increased blood creatine phosphokinase levels	0	1 (1.0)	0	1 (1.0)
	Increased blood lactate dehydrogenase levels	0	1 (1.0)	0	1 (1.0)
	Increased white blood cell count	0	1 (1.0)	0	1 (1.0)
	Increased blood alkaline phosphatase	0	0	0	1 (1.0)

Number of cases (%)
Based on *MedDRA/J* Ver.21.0

The forward-looking statements in these materials are based on Kissei's analysis of existing information and various trends as of May 2022. Actual results may differ from forecasts due to risks and uncertainties that may affect business.

Although drug information, including information pertaining to drugs under development, is reported in these materials, the contents are not intended as marketing or medical advice.