This content has been produced by Sanofi.
For Great Britain Healthcare Professionals only.

MAT-XU-2402610(v1.0)| July 2024
Prescribing information can be found on the last 2 pages.

REZUROCK® ▼
(belumosudil) tablets

ROCKSTAR STUDY

Explore when considering REZUROCK in the treatment of cGVHD for patients aged 12 years and older who have received at least two prior lines of systemic therapy.

sanofi

REZUROCK was evaluated in the **pivotal ROCKstar (KD025-213) study** for patients with cGVHD[1]

Patients received REZUROCK after failure of 2 to 5 previous lines of systemic therapy[1]

Study design[1]

ROCKstar was a pivotal phase 2, open-label, non-controlled, randomized, multicenter study that evaluated the efficacy and safety of REZUROCK in patients with cGVHD after receiving 2 to 5 prior lines of systemic therapy.

Treatment

Treatment consisted of REZUROCK 200 mg and was administered continuously until clinically significant progression of cGVHD or unacceptable toxicity.

Primary end point

- Best ORR at any time, defined as the proportion of subjects who achieved CR or PR according to the 2014 NIH cGVHD Consensus Criteria[1]

Prespecified key secondary end points (not powered to show statistical significance)

- Safety, DOR, TTR, LSS score, change in CS/CNI dose, FFS and OS[1]

cGVHD, chronic graft-versus-host disease; CNI, calcineurin inhibitor; CR, complete response; DOR, duration of response; FFS, failure-free survival; LSS, Lee Symptom Scale; NIH, National Institutes of Health; ORR, overall response rate; OS, overall survival; PR, partial response; TTR, time to response.

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2023. **3.** REZUROCK. Summary of Product Characteristics. **4.** Data on File. Sanofi. 2024. **5.** Lee SJ, Cutler C, Pavletic S, *et al*. Belumosudil for chronic graft-versus-host disease after 2 or more lines of systemic therapy: 3 year follow-up to the ROCKstar study. Poster presented at: Tandem Meetings; February 21, 2024; San Antonio, TX.

Select ROCKstar study patient baseline characteristics[1-5]

Characteristics	2021 ROCKstar study 200 mg once daily (n=66)[1-3,b]	3-year follow-up 200 mg once daily (n=77)[4,5,c]
Median age, y (range)	53 (21-77)	53 (21-77)
Male, n (%)	42 (64)	49 (64)
Median prior lines of systemic therapy, n	3	3
Median time from cGVHD diagnosis to enrollment, mo (range)	25 (2-162)	25 (2-162)
Median prednisone-equivalent dose at enrollment, mg/kg/d (range)	0.20 (0.03-0.95)	0.18 (0.03-0.66)
Concomitant PPI use, n (%)	33 (50)	39 (51)
≥4 organs involved, n (%)	33 (50)	40 (52)
Previous aGVHD, n (%)	42 (64)	50 (65)
Refractory to prior line of systemic therapy, n (%)	44 (79)	50 (81)
NIH-defined cGVHD severity, n (%)		
Severe	46 (70)	56 (73)
Moderate	18 (27)	19 (25)
Mild	2 (3)	2 (3)

- The most common prior systemic therapy[a] was corticosteroids (98%), followed by calcineurin inhibitors (tacrolimus 62% and sirolimus 47%), ECP (48%), ibrutinib (34%) and ruxolitinib (29%)[3]

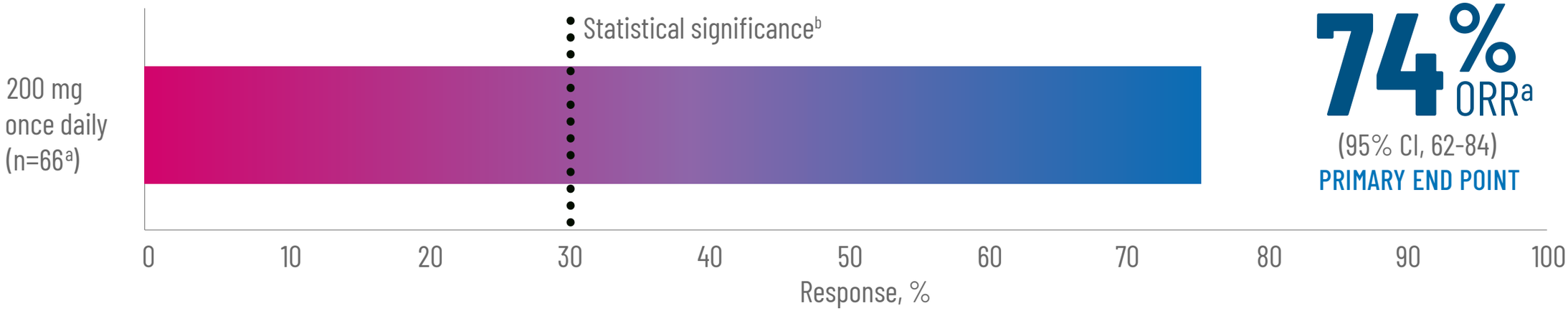
cGVHD, chronic graft-versus-host disease; NIH, National Institutes of Health; PPI, proton pump inhibitor; aGVHD, acute graft-versus-host disease; MHRA, Medicines and Healthcare Products Regulatory Agency.

[a]Some of these medicines do not have a licence in Great Britain for the treatment of cGvHD. [b]The final MHRA interpretation of the ROCKstar study omitted 1 patient from the REZUROCK200 mg once-daily arm. As a result, there are minor differences between the ROCKstar publication, where n=66, and the Summary of Product Characteristics, where n=65. [c]This analysis evaluated 152 participants in the mITT population (77 received belumosudil 200 mg once daily and 75 received belumosudil 200 mg twice daily), including 20 who were enrolled in a subsequent biomarker cohort after the August 19, 2020, ROCKstar publication data cutoff.[5]

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2023. **3.** REZUROCK. Summary of Product Characteristics. **4.** Data on File. Sanofi. 2024. **5.** Lee SJ, Cutler C, Pavletic S, *et al*. Belumosudil for chronic graft-versus-host disease after 2 or more lines of systemic therapy: 3 year follow-up to the ROCKstar study. Poster presented at: Tandem Meetings; February 21, 2024; San Antonio, TX.

Clinically meaningful **overall response rates**[1]

Statistically significant ORR[a] following treatment with REZUROCK 200 mg once daily[1]



74% ORR[a]
(95% CI, 62-84)
PRIMARY END POINT

Primary end point: Best ORR at any time, defined as the proportion of subjects who achieved CR or PR according to the 2014 NIH cGVHD Consensus Criteria[1]

CR, n=4 (6%). PR, n=45 (68%)[1]

AFTER 3 YEARS OF TREATMENT WITH REZUROCK,

THE BEST ORR[c] of 74% (95% CI, 63-83) was maintained in the 200-mg once-daily arm.[2]

cGVHD, chronic graft-versus-host disease; CR, complete response; NIH, National Institutes of Health; mITT, modified intent-to-treat; ORR, overall response rate; PR, partial response.

[a]Based on mITT population (n=66).[1]

[b]Statistical significance was achieved if the lower bound of the 95% CI of ORR exceeded 30%.[1] Clopper Pearson interval (exact) method used for calculation of 95% CIs, and p values are adjusted through Hochberg method of multiplicity correction corresponding to the null hypothesis of ORR ≤30%.[1]

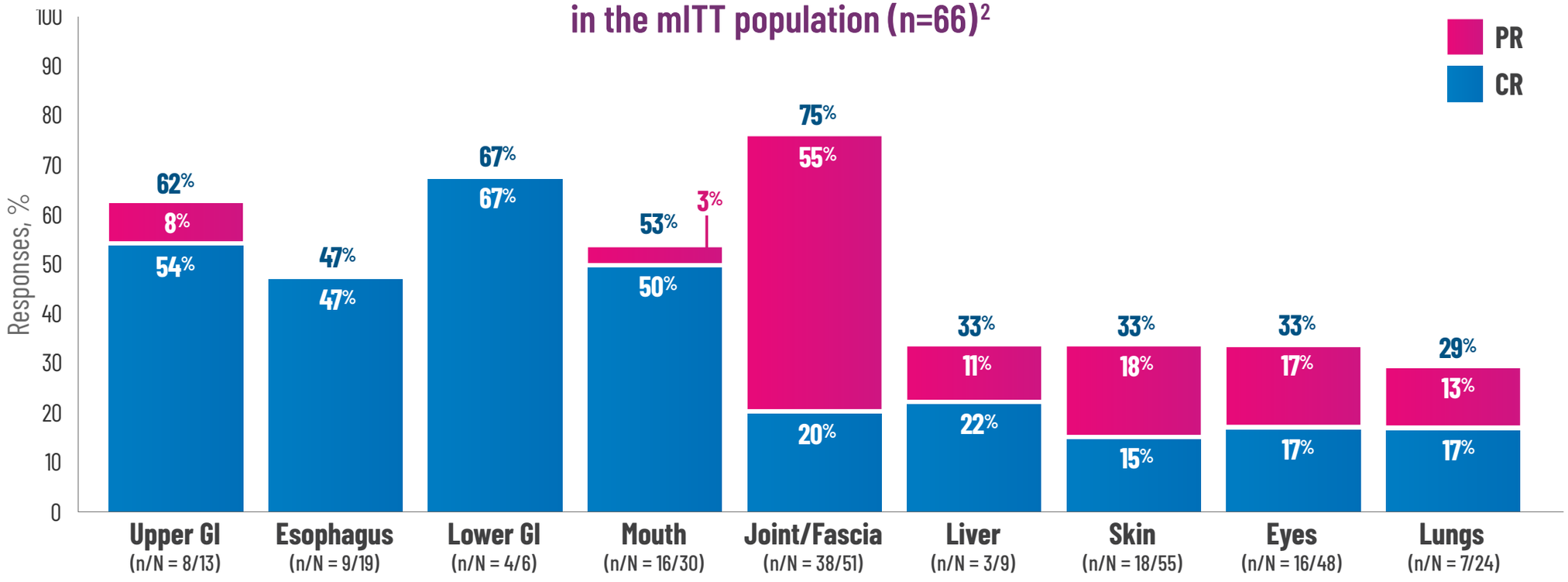
[c]Based on mITT population (n=77).[3]

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2024.

Response across **all evaluated organs**[1,2]

1-year data | 3-year data

Responses by organ system[a] with REZUROCK 200 mg once daily in the mITT population (n=66)[2]



Secondary end point: Response rate by organ system.[1]

CR, complete response; GI, gastrointestinal; mITT, modified intent-to-treat; PR, partial response.

[a]Primary end point was best ORR at any time, defined as the proportion of subjects who achieved CR or PR according to the 2014 NIH cGVHD Consensus Criteria.[1] CR defined as the resolution of all manifestations in each organ or site. PR defined as improvement in ≥1 organs or sites without progression in any other organ or site.[3,4]

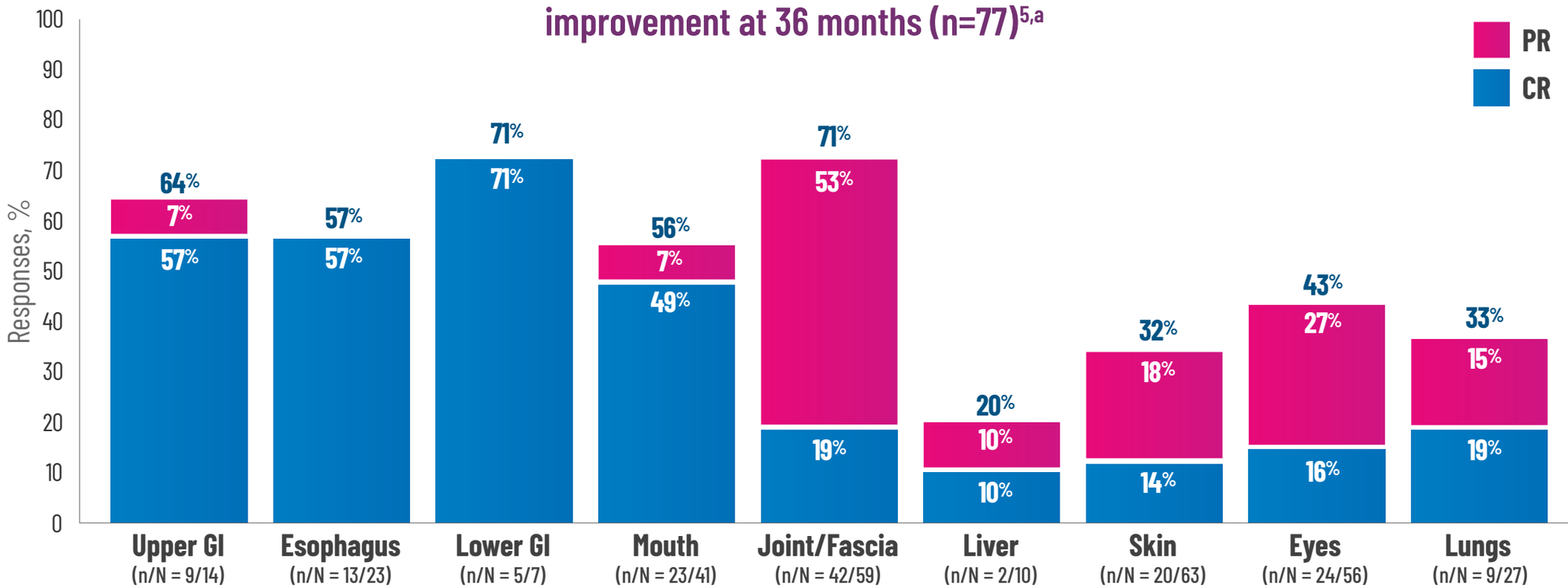
Percentages may not add up to the total due to rounding.

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. Supplementary Appendix. **3.** Lee SJ, Wolff D, Kitko C, *et al.* Measuring therapeutic response in chronic graft-versus host disease. National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: IV. The 2014 Response Criteria Working Group report. *Biol Blood Marrow Transplant* 2015;21(6):984-999. doi:10.1016/j.bbmt.2015.02.025. **4.** REZUROCK. Summary of Product Characteristics. **5.** Data on File. Sanofi. 2024.

Response across **all evaluated organs**[1,2]

1-year data | 3-year data

The majority of evaluated organs demonstrated further improvement at 36 months (n=77)[5,a]



Secondary end point: Response rate by organ system.[1]

CR, complete response; GI, gastrointestinal; mITT, modified intent-to-treat; PR, partial response.

[a]Primary end point was best ORR at any time, defined as the proportion of subjects who achieved CR or PR according to the 2014 NIH cGVHD Consensus Criteria.[1] CR defined as the resolution of all manifestations in each organ or site. PR defined as improvement in ≥1 organs or sites without progression in any other organ or site.[3,4]

Percentages may not add up to the total due to rounding.

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. Supplementary Appendix. **3.** Lee SJ, Wolff D, Kitko C, *et al.* Measuring therapeutic response in chronic graft-versus host disease. National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: IV. The 2014 Response Criteria Working Group report. *Biol Blood Marrow Transplant* 2015;21(6):984-999. doi:10.1016/j.bbmt.2015.02.025. **4.** REZUROCK. Summary of Product Characteristics. **5.** Data on File. Sanofi. 2024.

Most responses were seen **between 4 and 8 weeks**[1]

Cumulative response rates over time in the responder population with REZUROCK 200 mg once daily (n/N=48/66)[1]

4.4 WEEKS

Median time to response was 4.4 weeks (3.7-40.6)[2]

100.3 WEEKS

Median time from first response to the initiation of new systemic cGVHD therapy was 100.3 weeks (54.14-NA)[1]

63% OF RESPONSES

were observed between **weeks 4 and 8**[1]

96% OF RESPONSES

were observed by **weeks 24**[1]

After 3 years, the median DOR was

69.9 WEEKS[3]

References: 1. Data on File. Sanofi. 2023. **2.** REZUROCK. Summary of Product Characteristics. **3.** Data on File. Sanofi. 2024.

Responses were seen **across all patient types**[1-3]

Best ORRs observed across key subgroups in the 200 mg once-daily arm[1-3]

The subgroups have limited numbers and were not powered for planned efficacy comparisons or inference. These are therefore exploratory.

1-year data | 3-year data

EARLIER REZUROCK INITIATION[2]

86% ORR

Defined as ≤29-month duration of cGVHD before enrollment

(n/N=30/35)

SEVERE cGVHD[2]

74% ORR

(n/N=34/46)

CHRONIC GVHD INVOLVING ≥4 ORGANS[2]

70% ORR

(n/N=23/33)

>3 PRIOR LINES OF SYSTEMIC THERAPY[2]

67% ORR

(n/N=20/30)

cGVHD, chronic graft-versus-host disease; ORR, overall response rate.

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2023. **3.** Data on File. Sanofi. 2024. **4.** Chen Y-B. Highlights in graft-versus-host disease from the 2023 Tandem Meetings I Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR: commentary. *Clin Adv Hematol Oncol*. 2023;21 suppl 4(4):19-23.

Responses were seen **across all patient types**[1-3]

Best ORRs observed across key subgroups in the 200 mg once-daily arm[1-3]

The subgroups have limited numbers and were not powered for planned efficacy comparisons or inference. These are therefore exploratory.

1-year data | 3-year data

WITHIN 36 MONTHS (n=77)[3]

EARLIER REZUROCK INITIATION

83% ORR

Defined as ≤28-month duration of cGVHD before enrollment

(n/N=34/41)

WITHIN 36 MONTHS (n=77)[3]

SEVERE cGVHD

75% ORR

(n/N=42/56)

WITHIN 36 MONTHS (n=77)[3]

CHRONIC GVHD INVOLVING ≥4 ORGANS

75% ORR

(n/N=30/40)

WITHIN 36 MONTHS (n=77)[3]

>3 PRIOR LINES OF SYSTEMIC THERAPY

74% ORR

(n/N=25/34)

HOW SOON YOU TREAT MAY BE JUST AS IMPORTANT AS HOW YOU TREAT

Earlier treatment of GVHD may offer better outcomes by preventing end-organ damage.[4]

cGVHD, chronic graft-versus-host disease; ORR, overall response rate.

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2023. **3.** Data on File. Sanofi. 2024. **4.** Chen Y-B. Highlights in graft-versus-host disease from the 2023 Tandem Meetings I Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR: commentary. *Clin Adv Hematol Oncol*. 2023;21 suppl 4(4):19-23.

Change in **QOL scores**

Improvements in patient-reported QOL[1]

≥7-point reduction in LSS summary score with REZUROCK 200 mg once daily in the mITT population in an exploratory analysis[1]

- Both responders (69%) and non responders (29%) had improved QOL scores[1]

The Lee Symptom Scale (LSS) is a 30-item, 7-subscale symptom scale and QOL measurement tool that evaluates the AEs of cGVHD in the categories of skin, vitality, lung, nutritional status, psychological functioning,eye and mouth.[2]

These were not tested for statistical significance.

59% (n/N=39/66) **12 MONTHS**[1,a]

58% (n/N=45/77) **36 MONTHS**[3,b]

AE, adverse event; cGVHD, chronic graft-versus-host disease; LSS, Lee Symptom Scale; mITT, modified intent-to-treat; QOL, quality of life.

[a]Based on mITT population (n=66).[1]

[b]Based on mITT population (n=77).[3]

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Lee SJ, Cook EF, Soiffer R, Antin JH. Development and validation of a scale to measure symptoms of chronic graft-versus-host disease. *Biol Blood Marrow Transplant*.2002;8(8):444-452. doi:10.1053/bbmt.2002.v8.pm12234170. **3.** Data on File. Sanofi. 2024.

Change in dependence on **CS and CNI therapies**

Change in use of CS and CNI therapies[1, 2, 4]

This data is descriptive.

1-year data[a] | **3-year data[b]**

CS reductions and discontinuations were observed in the 200-mg once-daily arm[1]

64% (n/N=42/66) of patients reduced their **CS DOSE.**

20% (n/N=13/66) of patients **DISCONTINUED CS THERAPY** during treatment with REZUROCK.

CNI reductions and disontinuations were observed in the 200-mg once-daily arm[4]

29% (n/N=7/24) of patients reduced their **CNI DOSE.**

8% (n/N=2/24) of patients successfully **DISCONTINUED CNI THERAPY.**

CNI, calcineurin inhibitor; CR, complete response; CS, corticosteroid; mITT, modifiedintent-to-treat; PR, partial response.

[a]Based on mITT population (n=66).[1,3]

[b]Based on mITT population (n=77).[4]

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138 (22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2023. **3.** Cutler C, Lee SJ, Arai S, *et al*; on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. Supplementary Appendix. *Blood.* 2021;138{22):2278-2289. doi:10.1182/blood.2021012021. **4.** Data on File. Sanofi. 2024.

Change in dependence on **CS and CNI therapies**

Change in use of CS and CNI therapies[1, 2, 4]

This data is descriptive.

1-year data[a] | **3-year data[b]**

Higher rates of CS reductions and discontinuations were observed in the 200-mg once-daily arm over 3 years[4]

65% (n/N=50/76) of patients reduced their **CS DOSE.**

27% (n/N=21/73) of patients **DISCONTINUED CS THERAPY** during treatment with REZUROCK.

Higher rates of CNI reductions and discontinuations were observed in the 200-mg once-daily arm over 3 years[4]

47% (n/N=15/32) of patients reduced their **CNI DOSE.**

22% (n/N=7/32) of patients successfully **DISCONTINUED CNI THERAPY.**

CNI, calcineurin inhibitor; CR, complete response; CS, corticosteroid; mITT, modifiedintent-to-treat; PR, partial response.

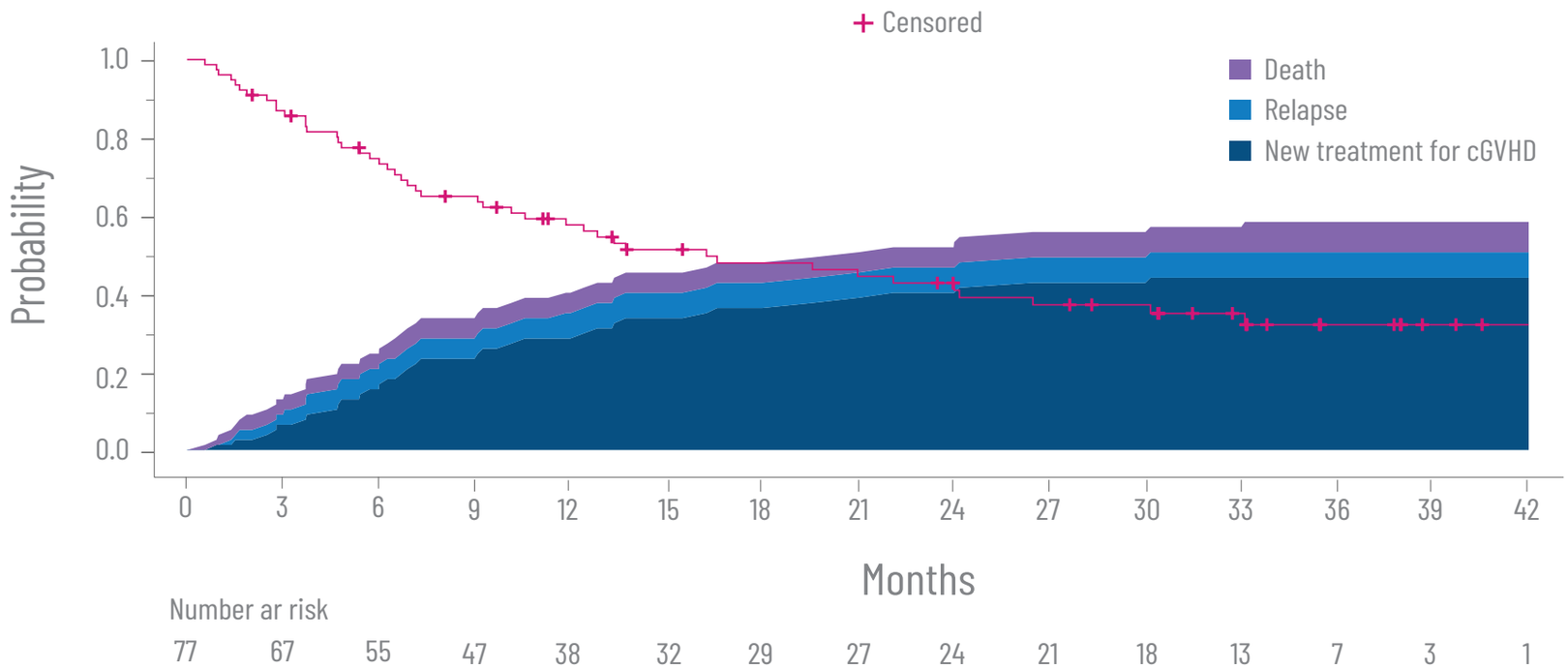
[a]Based on mITT population (n=66).[1,3]

[b]Based on mITT population (n=77).[4]

References: 1. Cutler C, Lee SJ, Arai S, *et al;* on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood.* 2021;138 (22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2023. **3.** Cutler C, Lee SJ, Arai S, *et al*; on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. Supplementary Appendix. *Blood.* 2021;138{22):2278-2289. doi:10.1182/blood.2021012021. **4.** Data on File. Sanofi. 2024.

FFS rates with REZUROCK

FFS[a] with REZUROCK 200 mg once daily in the mITT population[2]



FSS was maintained throughout the 36-month period.[2]

The FSS rate was

73%
(95% CI, 61-83) at 6 months.[1]

57%
(95% CI, 44-68) at 12 months.[1]

42%
(n/N=32/77) at 36 months.[2]

Secondary end point: FFS, defined as the absence of relapse, nonrelapse mortality or a need for additional systemic therapy.[1]

Adapted from Data on File, Sanofi[2]

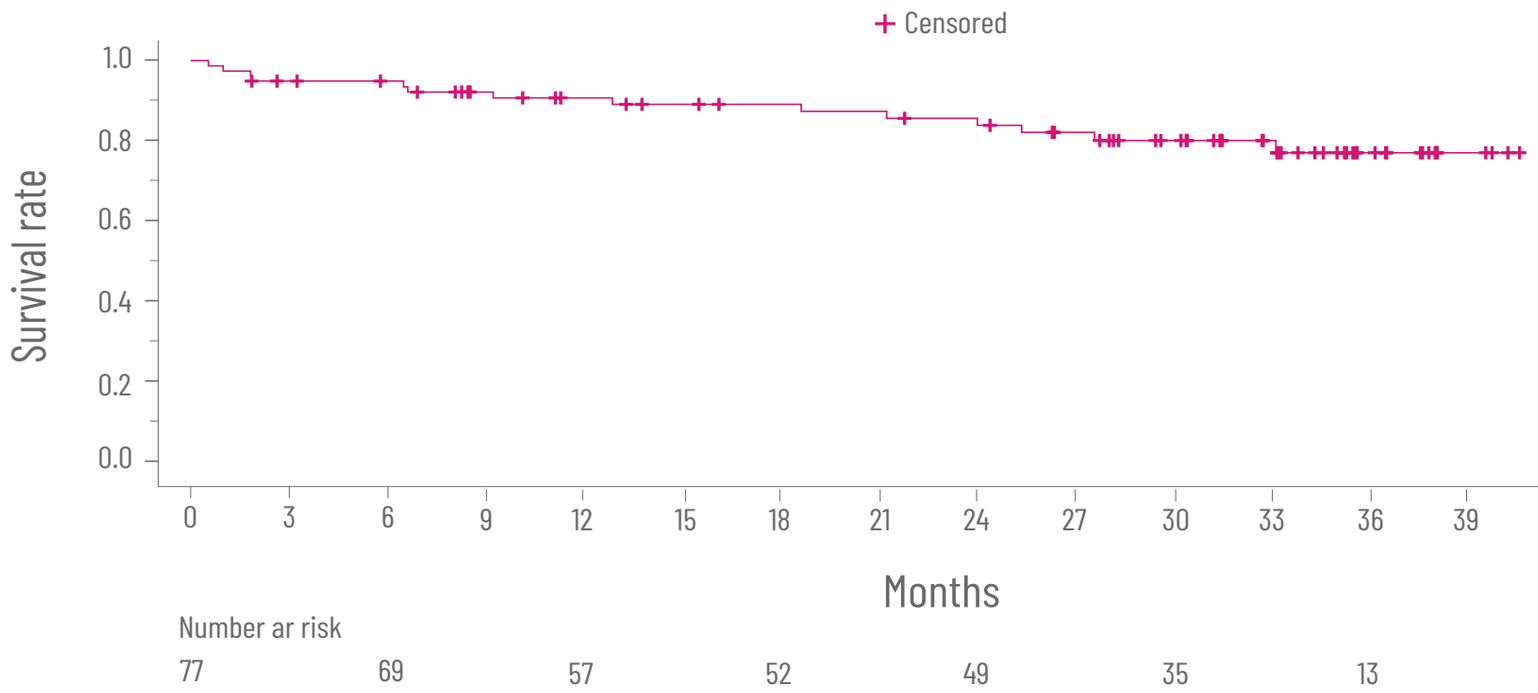
cGVHD, chronic graft-versus-host disease; FFS, failure-free survival; mITT, modified intent-to-treat.

[a]Kaplan-Meier curve of estimated FFS.

References: 1. Cutler C, Lee SJ, Arai S, *et al*; on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood*. 2021;138(22):2278-2289. doi:10.1182/blood.2021012021. **2.** Data on File. Sanofi. 2024.

Estimated OS rates with REZUROCK

OS[a] with REZUROCK 200 mg once daily in the mITT population[1]



The estimated 2-year OS rate was

86%

(95% CI, 75-92).[1]

Secondary end point: OS, defined as the time from the first dose of REZUROCK to the date of death due to any cause.[2,3]

Adapted from Data on File, Sanofi.[1]

mITT, modified intent-to-treat; OS, overall survival.

[a]Kaplan-Meier curve of estimated OS.

References: 1. Data on File. Sanofi. 2024. **2.** Data on File. Sanofi. 2023. **3.** Cutler C, Lee SJ, Arai S, *et al*; on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood*. 2021;138(22):2278-2289. doi:10.1182/blood.2021012021.

The ROCKstar study: **safety and tolerability profile**[1]

AEs were overall consistent with those expected in patients with cGVHD receiving corticosteroids and other immunosuppressants.

Data up to 19 August 2020 included.[1]

- There was 1 reported case of Epstein-Barr virus and 1 reported case of CMV reactivation

Commonly reported AEs, n (%)	REZUROCK 200 mg QD (n=66)	REZUROCK 200 mg BID (n=66)	Overall (N=132)
All grades in ≥20% of patients			
Fatigue	**30 (46)**	20 (30)	50 (38)
Diarrhoea	**23 (35)**	21 (32)	44 (33)
Nausea	**23 (35)**	18 (27)	41 (31)
Cough	**20 (30)**	17 (26)	37 (28)
Upper respiratory tract infection	**17 (26)**	18 (27)	35 (27)
Dyspnea	**21 (32)**	12 (18)	33 (25)
Headache	**13 (20)**	18 (27)	31 (24)
Peripheral edema	**17 (26)**	13 (20)	30 (23)
Vomiting	**18 (27)**	10 (15)	28 (21)
Muscle spasms	**13 (20)**	13 (20)	26 (20)
Grade ≥3 in ≥5% of patients			
Pneumonia	**6 (9)**	4 (6)	10 (8)
Hypertension	**4 (6)**	4 (6)	8 (6)
Hyperglycemia	**3 (5)**	3 (5)	6 (5)

Safety overview	REZUROCK 200 mg QD (n=66)	REZUROCK 200 mg BID (n=66)	Overall (N=132)
Median duration of treatment, mo	**9.4**	11.8	10.4
Any AE, n (%)	**65 (99)**	66 (100)	131 (99)
Grade ≥3 AEs, n (%)	**37 (56)**	34 (52)	71 (54)
SAEs, n (%)	**27 (41)**	23 (35)	50 (38)
Drug-related AEs, n (%)			
Any related AE	**49 (74)**	40 (61)	89 (67)
Related SAEs	**5 (8)**	2 (3)	7 (5)
Deaths[a], n (%)	**8 (12)**	6 (9)	14 (11)

[a]Six subjects died during long-term follow-up (>28 days after the last dose).

According to the Summary of Product Characteristics, the dosage of REZUROCK should be increased to 200 mg twice daily when co-administered with strong CYP3A inducers or proton pump inhibitors (PPIs).

AE, adverse event; cGVHD, chronic graft-versus-host disease; CMV, cytomegalovirus; SAE, serious adverse event.

Reference: 1. Cutler C, Lee SJ, Arai S, *et al*; on behalf of the ROCKstar Study Investigators. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. *Blood*. 2021;138(22):2278-2289. doi:10.1182/blood.2021012021.

Prescribing Information: REZUROCK (belumosudil) ▼ 200mg film coated tablets (Licence valid in GB only)

Therapy should be initiated and supervised by physicians experienced in the management of chronic GVHD. Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each film-coated tablet contains belumosudil mesilate, equivalent to 200mg belumosudil.
Indication: Rezurock is indicated for the treatment of patients aged 12 years and older with chronic graft-versus- host disease (chronic GVHD) who have received at least two prior lines of systemic therapy.
Dosage and Administration: The recommended dose of Rezurock is 200mg administered orally once daily at approximately the same time with a meal. The film-coated tablet should not be broken, crushed or chewed. Treatment should continue until disease progression or unacceptable toxicity. A complete blood cell count and liver function test must be performed before initiating therapy with Rezurock. Perform liver function tests at least monthly throughout treatment. Dose modification due to hepatotoxicity and other adverse reactions: For Grade 3 alanine aminotransferase (ALT) or aspartate aminotransferase (AST) (>5 – 20 × upper limit of normal (ULN)) or Grade 2 bilirubin (>1.5 – 3 × ULN) or other Grade 3 adverse reactions, hold Rezurock until recovery to ≤Grade 1, then resume Rezurock at the recommended dose at physician's discretion. For Grade 4 ALT or AST (>20 × ULN) or Grade ≥3 bilirubin (>3 × ULN) or other Grade 4 adverse reactions, permanently discontinue Rezurock. Dose modification due to drug interactions: *Strong CYP3A Inducers:* Increase the dosage of Rezurock to 200mg twice daily when co-administered with strong CYP3A inducers. *Proton Pump Inhibitors:* Increase the dosage of Rezurock to 200mg twice daily when co- administered with proton pump inhibitors. Delayed or missed dose: If a dose is missed or delayed for <12 hours after the scheduled dose, the dose should be taken as soon as possible on the same day with a return to the normal schedule the following day. If a dose is missed or delayed for >12 hours after the scheduled dose, the dose should be taken at the usual time the following day. If a patient vomits following the intake of a dose, the next dose should be taken at the usual time the following day. Patients should not take extra doses to make up the missed dose.
Special Populations: Hepatic impairment: Dose modification is not recommended when administering belumosudil to patients with mild or moderate hepatic impairment (Child-Pugh A and B). Belumosudil is not recommended in patients with severe hepatic impairment. The safety and efficacy of belumosudil in severe (Child-Pugh C) hepatic impairment has not been evaluated. For patients with pre-existing severe hepatic impairment (Child-Pugh C), consider the risks and potential benefits before initiating treatment with belumosudil. Monitor patients frequently for adverse reactions.
Renal impairment: No dose modification of Rezurock is required in patients with mild or moderate renal impairment (creatine clearance ≥30 mL/min). No data are available for patients with severe renal impairment (creatine clearance<30 mL/min) or for patients with end-stage renal disease on dialysis. Use with caution. Elderly patients (≥65 years): No additional dose adjustments are recommended for elderly patients. Paediatric population: The posology is the same in adults and adolescents aged 12 – 18 years. The safety and efficacy of Rezurock in children and adolescents aged below 12 years of age have not been established. No data are available.
Contraindications: Pregnancy. Hypersensitivity to the active substance or to any of the excipients.
Precautions and Warnings: Female patients of childbearing potential and male patients with female partners of childbearing potential: Women of childbearing potential (WOCBP) should be advised to avoid becoming pregnant while they or their male partner are taking belumosudil and of the potential risk to a fetus. WOCBP should be advised to have a pregnancy test prior to starting treatment with belumosudil. WOCBP and male patients with female partners of childbearing potential must use a highly effective method of contraception during treatment with belumosudil and for at least one week after the last dose of belumosudil. Hepatotoxicity: Increases in liver function tests were observed in clinical studies with belumosudil and generally occurred early during treatment with the incidence decreasing thereafter. Liver function tests should be performed prior to the initiation of treatment with belumosudil and monitored at least monthly during treatment with belumosudil and the dose should be adjusted for ≥Grade 2 toxicities. Sodium: This product is essentially sodium free. **Interactions:** Effect of CYP3A inhibitors on belumosudil: The co-administration of multiple doses of itraconazole did not alter exposure to belumosudil to any clinically relevant extent. Effect of CYP3A inducers on belumosudil: The co- administration of multiple doses of rifampin decreased belumosudil Cmax by 59% and AUC by 72%. The co- administration of strong CYP3A4 inducers with belumosudil may decrease belumosudil exposure. Increase the dose of belumosudil to 200mg twice daily. The co-administration of moderate CYP3A4 inducers e.g., efavirenz is predicted to have a reduced effect on belumosudil as compared to strong CYP3A4 inducers. The co-administration of moderate CYP3A4 inducers with belumosudil may decrease belumosudil exposure. No dose adjustment is recommended. Effect of proton pump inhibitors on belumosudil: The co-administration of multiple doses of rabeprazole decreased belumosudil Cmax by 87% and AUC by 80%. The co-administration of multiple doses of omeprazole decreased belumosudil Cmax by 68% and AUC by 47%. The co-administration of proton pump inhibitors with belumosudil may decrease belumosudil exposure. Increase the dose of belumosudil to 200mg twice daily. Effect of other gastric acid reducing agents on belumosudil: The co-administration of belumosudil with gastric acid reducing agents other than proton pump inhibitors may decrease belumosudil exposure. No dose adjustment is recommended, however belumosudil and the gastric acid reducing agent should be taken 12 hours apart. In vitro studies: *Effect of belumosudil on CYP3A substrates:* The co- administration of belumosudil is predicted to increase midazolam Cmax and AUC approximately 1.3- and 1.5-fold, respectively. No dose adjustment is recommended.

Prescribing Information: REZUROCK (belumosudil) ▼ 200mg film coated tablets (Licence valid in GB only)

Therapy should be initiated and supervised by physicians experienced in the management of chronic GVHD. Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

The co- administration of belumosudil may increase exposure of sensitive CYP3A4 substrates with a narrow therapeutic index such as ciclosporin and tacrolimus. No dose adjustment is recommended. *Effect of belumosudil on CYP2C9 substrates*: The co-administration of belumosudil is not expected to have clinically meaningful effect on the exposure of CYP2C9 substrates (such as warfarin). *Effect of belumosudil on CYP2C8 substrates*: The co-administration of belumosudil is not expected to have clinically meaningful effect on the exposure of CYP2C8 substrates that are not an OATP1B1 substrate. *Effect of belumosudil on UGT1A1 substrates*: Belumosudil is a weak inhibitor of UGT1A1, the clinical consequences are not known. *Transporters*: Belumosudil is a substrate of P-gp. Belumosudil inhibits BCRP, P-gp, and OATP1B1. The co-administration of oral BCRP, P-gp and OATP1B1 substrates with belumosudil may increase the concentrations of the substrate drugs (such as digoxin and docetaxel).

Pregnancy: There are no data on the use of belumosudil in pregnant women. Belumosudil can cause fetal harm based on findings from animal studies and its mechanism of action. As a precautionary measure, belumosudil is contraindicated in pregnancy. **Breast-feeding:** It is unknown whether belumosudil or its metabolites are excreted in human milk. No data are available regarding the presence of belumosudil or its metabolites in animal or human milk or its effects on the breast-fed child, or on milk production. A risk to the infant cannot be excluded. Because of the potential for serious adverse reactions in a breast-fed child, breast-feeding should be discontinued during treatment with belumosudil and for at least one week after the last dose. **Fertility:** There are no human data on the effect of belumosudil on fertility. Based on findings from animal studies, belumosudil may impair male and female fertility at dose levels above the recommended clinical dose. The effects on fertility are reversible.

Adverse Reactions: Very common: Nausea, asthenia. Common: upper and lower respiratory tract infections, anaemia, leukopenia, platelet count decreased, decreased appetite, hyperglycaemia, headache, neuropathy peripheral, dizziness, hypertension, dyspnoea, cough, diarrhoea, vomiting, abdominal pain, constipation, AST and ALT increased, gamma-glutamyltransferase increased, pruritus, musculoskeletal pain, muscle spasms, blood alkaline phosphatase increased, blood creatine phosphokinase increased, blood creatinine increased, oedema, pyrexia, weight decreased. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal Category: POM

GB List Price and Marketing Authorisation Number:
200mg x 30 tablets (PLGB 04425/0902): £6708.

Marketing Authorisation Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.

Further information is available from: Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.
uk-medicalinformation@sanofi.com

Date of preparation: January 2024

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com.

REZUROCK® ▼
(belumosudil) tablets