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**REZUROCK**<sup>®</sup> ▼  
(belumosudil) tablets

# MECHANISM OF ACTION

**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.

Adverse events should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://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](mailto:UK-drugsafety@sanofi.com).

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# REZUROCK targets both the inflammatory and fibrotic processes of cGVHD<sup>1-3</sup>

REZUROCK is an immunomodulator that selectively inhibits the ROCK2 pathway<sup>1-3</sup>



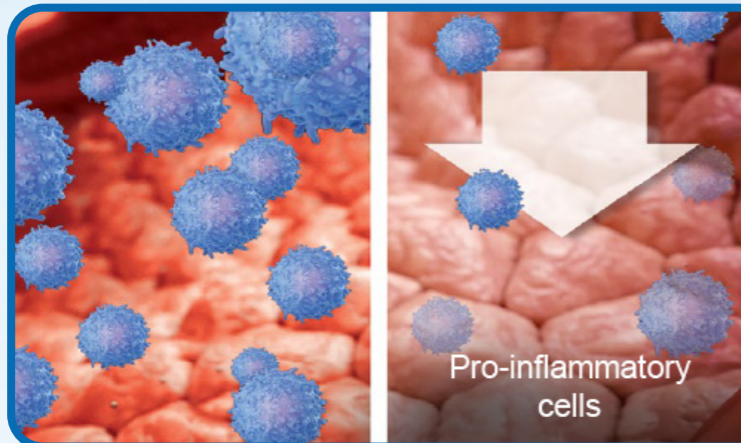
As an oral selective ROCK2 inhibitor, REZUROCK is an innovative treatment designed to restore **immune homeostasis** and to **downregulate the fibrotic processes** of cGVHD.<sup>1-3</sup>

The mechanism of action of belumosudil was studied through *ex vivo* or *in vitro* human T-cell assays and in animal models of chronic GvHD. The clinical significance of ROCK2 inhibition data is not known.

cGVHD, chronic graft-versus-host disease; ROCK2, rho-associated coiled-coil-containing protein kinase-2.

**References:** **1.** REZUROCK Summary of Product Characteristics. **2.** Zanin Zhorov A, Weiss JM, Nyuydzefe MS, et al. *Proc Natl Acad Sci USA* 2014;111(47):16814-16819. doi:10.1073/pnas.1414189111. **3.** Flynn R, Paz K, Du J, et al. *Blood* 2016;127(17):2144-2154. doi:10.1182/blood-2015-10-678706. **4.** Weiss JM, Chen W, Nyuydzefe MS, et al. *Sci Signal* 2016;9(437):ra73. doi:10.1126/scisignal.aad8953. **5.** Chen W, Nyuydzefe MS, Weiss JM, et al. *Sci Rep* 2018;8(1):16636. doi:10.1038/s41598-018-35109-9. **6.** Riches DWH, Backos DS and Redente EF. *Am J Pathol* 2015;185(4):909-12. doi:10.1016/j.ajpath.2015.01.005.

## How does REZUROCK impact inflammation?



Decreases the activation of STAT3, triggering the **significant downregulation of both Th17 and Tfh cells**, leading to the decreased production of pro-inflammatory cytokines<sup>2,4</sup>



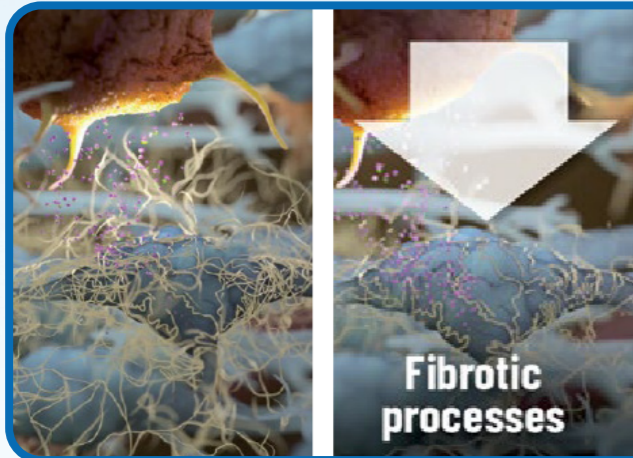
Increases the phosphorylation of STAT5, causing the **upregulation of Treg cells**<sup>5</sup>

**Reduces inflammation** via its immunomodulatory effect on STAT3 and STAT5 phosphorylation<sup>2,4</sup>

STAT3, signal transducer and activator of transcription 3; STAT5, signal transducer and activator of transcription 5; Tfh, follicular helper T [cell]; Th17, type 17 helper T [cell]; Treg, regulatory T [cell].

**References:** **1.** REZUROCK Summary of Product Characteristics. **2.** Zanin Zhorov A, Weiss JM, Nyuydzefe MS, et al. *Proc Natl Acad Sci USA* 2014;111(47):16814-16819. doi:10.1073/pnas.1414189111. **3.** Flynn R, Paz K, Du J, et al. *Blood* 2016;127(17):2144-2154. doi:10.1182/blood-2015-10-678706. **4.** Weiss JM, Chen W, Nyuydzefe MS, et al. *Sci Signal* 2016;9(437):ra73. doi:10.1126/scisignal.aad8953. **5.** Chen W, Nyuydzefe MS, Weiss JM, et al. *Sci Rep* 2018;8(1):16636. doi:10.1038/s41598-018-35109-9. **6.** Riches DWH, Backos DS and Redente EF. *Am J Pathol* 2015;185(4):909-12. doi:10.1016/j.ajpath.2015.01.005.

## How does REZUROCK impact fibrosis?



**Prevents the polymerization of G-actin to F-actin** as well as MRTF changes to profibrotic gene expression<sup>6</sup>

**Downregulates fibrosis**, as evidenced by decreased collagen deposition around the bronchioles and the delayed progression of scleroderma in animal cGVHD models<sup>3</sup>

cGVHD, chronic graft-versus-host disease; MRTF, myocardin-related transcription factor.

**References:** **1.** REZUROCK Summary of Product Characteristics. **2.** Zanin Zhorov A, Weiss JM, Nyuydzefe MS, et al. *Proc Natl Acad Sci USA* 2014;111(47):16814-16819. doi:10.1073/pnas.1414189111. **3.** Flynn R, Paz K, Du J, et al. *Blood* 2016;127(17):2144-2154. doi:10.1182/blood-2015-10-678706. **4.** Weiss JM, Chen W, Nyuydzefe MS, et al. *Sci Signal* 2016;9(437):ra73. doi:10.1126/scisignal.aad8953. **5.** Chen W, Nyuydzefe MS, Weiss JM, et al. *Sci Rep* 2018;8(1):16636. doi:10.1038/s41598-018-35109-9. **6.** Riches DWH, Backos DS and Redente EF. *Am J Pathol* 2015;185(4):909-12. doi:10.1016/j.ajpath.2015.01.005.