NOW APPROVED

GOMEKLI™
(mirdametinib)
1 mg tablets for oral suspension
1 mg and 2 mg capsules

HELP PATIENTS SEE BEYOND THE LIMITS OF NF1-PN SO THEY CAN

GO. BE.

Actor portrayal.

GOMEKLI: The **FIRST AND ONLY** treatment approved for both adults and children with NF1-PN[1]

Indication

GOMEKLI (mirdametinib) is indicated for the treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection.

Important Safety Information

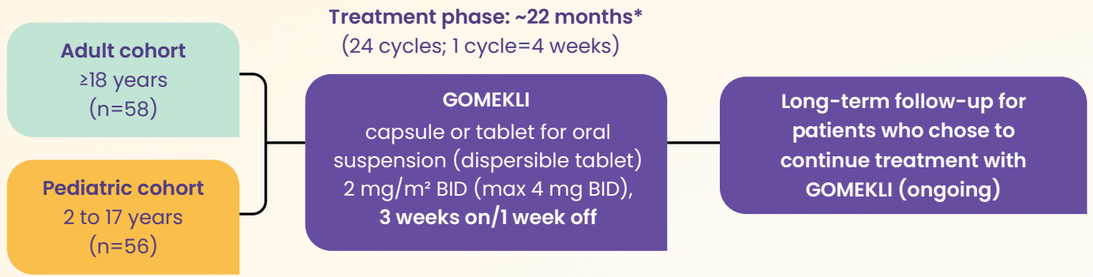
Warnings and Precautions associated with GOMEKLI include Ocular Toxicity, Left Ventricular Dysfunction, Dermatologic Adverse Reactions, and Embryo-Fetal Toxicity.

Adverse Reactions (>25%) in both adult and pediatric patients include rash, diarrhea, musculoskeletal pain, vomiting, and nausea, as well as fatigue in adult patients and abdominal pain, headache, paronychia, and left ventricular dysfunction in pediatric patients.

Please see Important Safety Information throughout and on pages 16-17, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

The efficacy and safety of GOMEKLI were evaluated in both adult and pediatric patients

ReNeu: A pivotal, phase 2b, single-arm study conducted in 114 patients across 37 sites[1,2]



Patients had to be ≥2 years of age and have NF1 with a symptomatic, inoperable PN.[1,†]

Primary endpoint[1]

Confirmed overall response rate (ORR), defined as the proportion of patients with complete response (disappearance of the target PN) or partial response (≥20% reduction) on MRI of the target PN volume from baseline to Cycle 24 (treatment phase) as assessed by blinded independent central review (BICR) on ≥2 consecutive scans within 2 to 6 months

Secondary endpoints[1,2]

- Duration of response
- Change in patient-reported outcomes, including worst tumor pain severity (NRS-11), pain interference (PII), and HRQoL (PedsQL), from baseline to Cycle 13
- Safety and tolerability

Across adult and pediatric cohorts, the majority of patients who completed the treatment phase (including those with and without a confirmed response) chose to remain on GOMEKLI treatment for long-term follow-up.[2]

*Patients were required to return for a safety follow-up 30 days after their last dose of study treatment.[2]
†Patients were excluded if they had lymphoma, leukemia, or any malignancy (including malignant glioma or MPNST) within the past 5 years; breast cancer within the past 10 years; or evidence of an active optic glioma or other low-grade glioma requiring treatment with chemotherapy or radiation therapy.[2]

BID=twice daily; HRQoL=health-related quality of life; MRI=magnetic resonance imaging; MPNST=malignant peripheral nerve sheath tumor; NRS=numeric rating scale; PedsQL=Pediatric Quality of Life Inventory; PII=Pain Interference Index.

Important Safety Information (cont'd)

Warnings and Precautions

Ocular Toxicity: GOMEKLI can cause ocular toxicity including retinal vein occlusion (RVO), retinal pigment epithelium detachment (RPED), and blurred vision. In the adult pooled safety population, ocular toxicity occurred in 28% of patients treated with GOMEKLI: 21% were Grade 1, 5% were Grade 2 and 1.3% were Grade 3. RVO occurred in 2.7%, RPED occurred in 1.3%, and blurred vision occurred in 9% of adult patients. In the

The ReNeu study included adult and pediatric patients with a broad range of baseline characteristics[2]

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	Adult cohort (n=58)	Pediatric cohort (n=56)
Median age at enrollment (range)	34 years (18-69)	10 years (2-17)
Sex		
Male	36%	46%
Female	64%	54%
Target PN progressing at study entry	53%	62%
Location of target PN		
Head and neck	48%	50%
Lower extremities	26%	7%
Paraspinal	9%	7%
Chest wall	7%	4%
Mesentery and pelvis	2%	9%
Upper extremities	3%	7%
Abdominal wall	0%	2%
Other	5%	14%
Type of PN-related morbidity‡		
Pain	90%	70%
Disfigurement or major deformity	52%	50%
Motor dysfunction	40%	27%
Airway dysfunction	5%	12%
Other	17%	21%
Previous PN treatment		
Surgery	69%	36%
Targeted medications/therapies	19%	14%
Radiotherapy	2%	0%

Many of the morbidities seen in ReNeu are often seen in clinical practice.[2-4]

‡Morbidities were clinician determined. Patients may have had more than 1 reported morbidity.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

pediatric pooled safety population, ocular toxicity occurred in 19% of patients: 17% were Grade 1 and 1.7% were Grade 2. Conduct comprehensive ophthalmic assessments prior to initiating GOMEKLI, at regular intervals during treatment, and to evaluate any new or worsening visual changes such as blurred vision. Continue, withhold, reduce the dose, or permanently discontinue GOMEKLI as clinically indicated.

Please see Important Safety Information throughout and on pages 16-17, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

Adult cohort

Only GOMEKLI is proven to shrink PNs in adults with NF1-PN

Primary endpoint: confirmed overall response rate (ORR)[1,*]

41% (24/58)

achieved a confirmed response[†]
(≥20% reduction in PN volume on consecutive scans)
(95% CI: 29-55)

Of the patients with a confirmed response:

62% (15/24)

had a deep response
(>50% reduction in PN volume)[2]
(This analysis was post hoc and exploratory)

GOMEKLI is the first and only FDA-approved treatment proven to shrink PNs in adult patients with NF1.[1]

In a post hoc subgroup analysis

Patients who achieved a deep response had a longer duration of treatment than those who did not[5]

The median duration of treatment for patients with a deep response was 37 months (range: 20 to 46 months) vs 26 months (range: 7 to 33 months) for those with a 20% to 50% reduction in PN volume.

*Confirmed ORR defined as the proportion of patients with complete response (disappearance of the target PN) or partial response (≥20% reduction) on MRI of the target PN volume from baseline to Cycle 24 (treatment phase) as assessed by BICR on ≥2 consecutive scans within 2 to 6 months.[1]
†All partial responses.[1]
FDA=Food and Drug Administration.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Left Ventricular Dysfunction: GOMEKLI can cause left ventricular dysfunction. GOMEKLI has not been studied in patients with a history of clinically significant cardiac disease or LVEF <55% prior to initiation of treatment. In the ReNeu study, decreased LVEF of 10 to <20% occurred in 16% of adult patients treated with GOMEKLI. Five patients (9%) required dose interruption, one patient (1.7%) required a dose reduction, and one patient required permanent discontinuation of GOMEKLI. The median time to first onset of decreased LVEF in adult patients was 70 days. Decreased LVEF of 10 to <20% occurred in 25%, and decreased LVEF of

Depth of response achieved by adults

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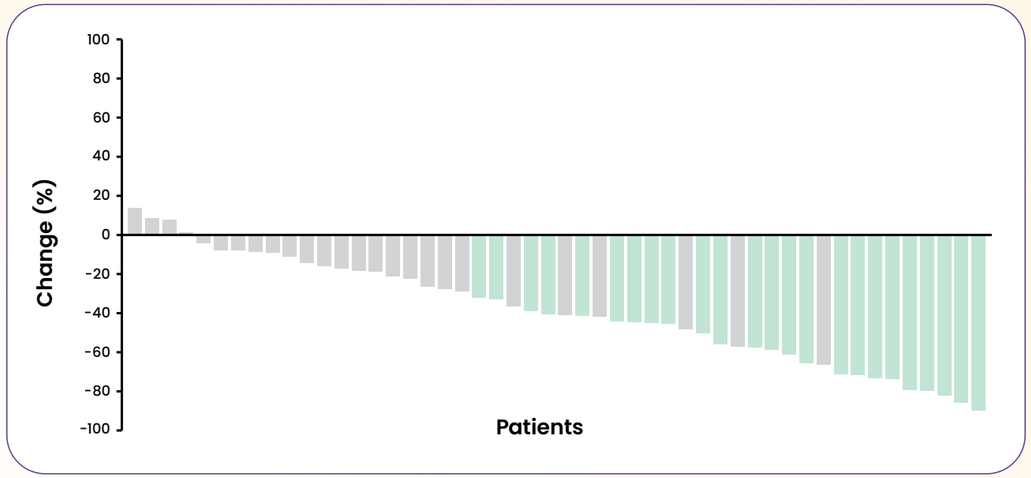
Best percent change in PN volume[2,6]



Data for 50 out of 58 patients shown here; 8 patients did not have postbaseline MRI assessments. Green bars represent those patients who had a confirmed overall response (≥20% reduction in PN volume on consecutive MRI scans). Gray bars represent nonresponders who had a best overall response of stable disease or progressive disease.

Median best change in PN volume from baseline[2]:

−41%

(range: -90% to 13%)

Maximum best change in PN volume from baseline[2]:

−90%

Analysis of best change was a prespecified exploratory endpoint

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

≥20% occurred in 1.8% of pediatric patients treated with GOMEKLI. One patient (1.8%) required dose interruption of GOMEKLI. The median time to first onset of decreased LVEF in pediatric patients was 132 days. All patients with decreased LVEF were identified during routine echocardiography, and decreased LVEF resolved in 75% of patients. Before initiating GOMEKLI, assess ejection fraction (EF) by echocardiogram. Monitor EF every 3 months during the first year and then as clinically indicated. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Please see Important Safety Information throughout and on pages 16-17, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

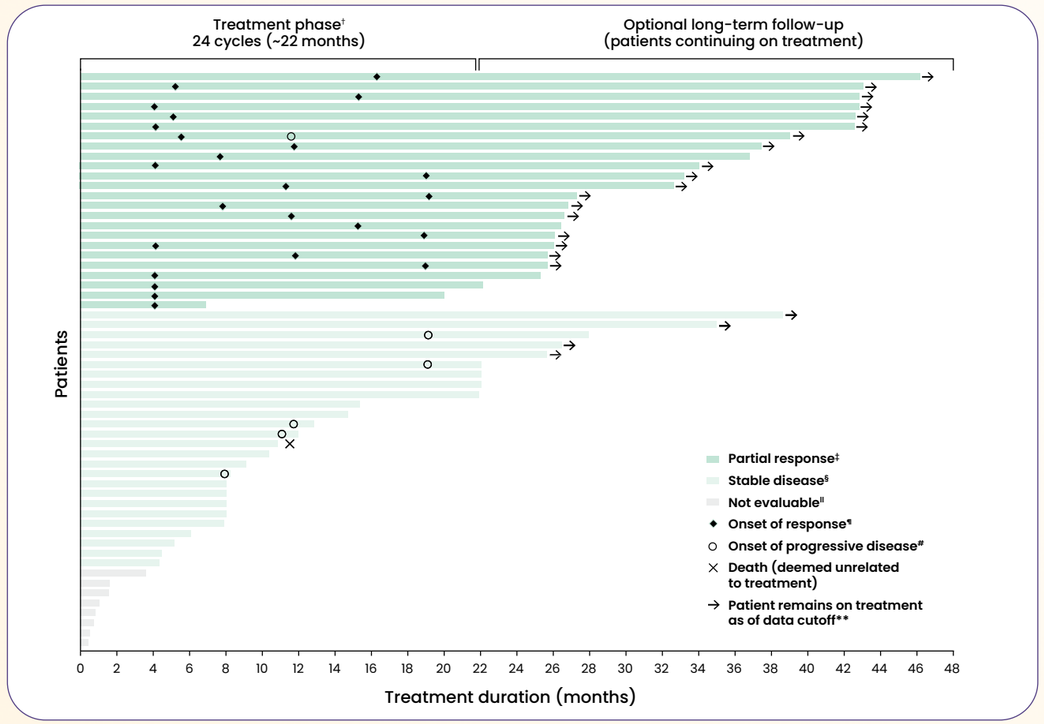
Adult cohort

Durable response in adults

88% (21/24) of the confirmed overall responses remained durable for ≥12 months[1,*]

- 50% (12/24) of the confirmed overall responses remained durable for ≥24 months[1,*]
- **46% of responders (11/24) had onset of response at Cycle 5, the first on-treatment assessment (based on a post hoc analysis)[6]**
- Median time to first confirmed response was 7.8 months (range: 4 to 19 months)[1]

Treatment duration and response[2]



84% of patients (26/31) who completed the treatment phase chose to remain on GOMEKLI for long-term follow-up.[2]

*Duration of response was assessed based on observed time.[1]
†Four-week cycles of 3 weeks on/1 week off. The treatment phase ends 3 weeks into the final cycle.[2]
‡Partial response corresponds with confirmed overall response of ≥20% reduction in target PN volume from baseline.[1]
§Stable disease is defined as a <20% increase or a <20% decrease in target PN volume from baseline.[2]
‖Patients who were not evaluable were those for whom no postbaseline volumetric data were collected.[6]
¶Responses were confirmed on a subsequent scan within 2 to 6 months.[2]
#Progressive disease is defined as a ≥20% increase in target PN volume from baseline.[2]
**Data cutoff was September 20, 2023.[2]

A manageable safety profile in adults

GOMEKLI™ (mirdametinib)
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1 mg and 2 mg capsules

The majority of adverse reactions in ReNeu were mild to moderate[1]

Adverse reactions (≥20%) in adult patients who received GOMEKLI (n=58)[1]

	All grades	Grades 3 or 4††
Skin and subcutaneous tissue disorders		
Rash‡‡	90%	10%
Gastrointestinal (GI) disorders		
Diarrhea§§	59%	0%
Nausea	52%	0%
Vomiting	38%	0%
Abdominal pain‖‖	24%	3%
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain¶¶	41%	5%
General disorders and administration site conditions		
Fatigue	29%	2%
Infections and infestations		
COVID-19##	22%	5%
Nervous system disorders		
Peripheral neuropathy***	21%	0%

Low rates of severe (Grade 3) adverse reactions were observed with GOMEKLI.[1]

GOMEKLI has no contraindications.[1]

††All reactions were Grade 3 except one fatal case of COVID-19 in an adult.
‡‡Rash includes dermatitis acneiform, eczema, maculo-papular rash, pustular rash, dermatitis, erythematous rash, palmar-plantar erythrodysesthesia syndrome, exfoliative rash, skin exfoliation, pruritic rash, papule, papular rash, and macular rash.
§§Diarrhea includes frequent bowel movements.
‖‖Abdominal pain includes upper abdominal pain, gastrointestinal pain, and abdominal discomfort.
¶¶Musculoskeletal pain includes noncardiac chest pain, back pain, pain in extremity, neck pain, musculoskeletal chest pain, myalgia, arthralgia, and bone pain.
##Includes one fatal case in an adult.
***Peripheral neuropathy includes paresthesia, hypoesthesia, neuralgia, and peripheral sensory neuropathy.

Please see Important Safety Information throughout and on pages 16-17, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

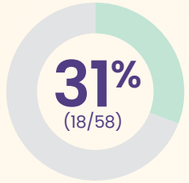
Adult cohort

Additional safety information in adults

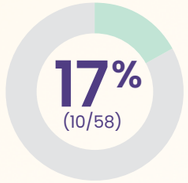
Laboratory abnormalities[1,*,†,‡]

The select all-grade laboratory abnormalities (≥15%) that worsened from baseline in adult patients were increased creatine phosphokinase (55%), increased triglycerides (29%), decreased calcium (23%),[§] increased cholesterol (23%), decreased hemoglobin (21%), increased aspartate aminotransferase (AST) (18%), and decreased lymphocytes (16%). The most common Grade 3 or 4 laboratory abnormality (>2%) was increased creatine phosphokinase.

Dose interruption, reduction, and discontinuation due to adverse reactions[1]



31% (18/58) of patients had a dose interruption



17% (10/58) of patients had a dose reduction

Adverse reactions that required dose interruption in ≥5% of adult patients included left ventricular dysfunction and COVID-19. Adverse reactions that required dose reductions in ≥5% of patients included rash.

22% (13/58) of patients permanently discontinued treatment

Adverse reactions that resulted in permanent discontinuation of GOMEKLI in ≥1% of adult patients were rash, diarrhea, nausea, abdominal pain, alopecia, dry skin, left ventricular dysfunction, cough, wheezing, COVID-19, peripheral swelling, retinal vein occlusion, dizziness, and vomiting.

*The denominator used to calculate the rate was 56 based on the number of patients with a baseline value and at least 1 posttreatment value.
†Graded per NCI-CTCAE version 5.0.
‡No Grade 5 laboratory abnormalities were reported in the ReNeu study.
§Calcium corrected for albumin (mmol/L).

CTCAE=Common Terminology Criteria for Adverse Events; NCI=National Cancer Institute.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Dermatologic Adverse Reactions: GOMEKLI can cause dermatologic adverse reactions including rash. The most frequent rashes included dermatitis acneiform, rash, eczema, maculo-papular rash and pustular rash. In the pooled adult safety population, rash occurred in 92% of patients treated with GOMEKLI (37% were Grade 2 and 8% were Grade 3) and resulted in permanent discontinuation in 11% of patients. In the pooled pediatric safety population, rash occurred in 72% of patients treated with GOMEKLI (22% were Grade 2 and 3.4% were Grade 3) and resulted in permanent discontinuation in 3.4% of patients. Initiate supportive care at first signs of dermatologic adverse reactions. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Pediatric cohort

GOMEKLI shrank PNs in pediatric patients with NF1-PN

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Primary endpoint: confirmed overall response rate (ORR)[1,‖]

52% (29/56) **achieved a confirmed response**[¶]
(≥20% reduction in PN volume on consecutive scans)
(95% CI: 38-65)

Of the patients with a confirmed response:

52% (15/29) **had a deep response**
(>50% reduction in PN volume)[2]
(This analysis was post hoc and exploratory)

In a post hoc subgroup analysis

Patients who achieved a deep response had a longer duration of treatment than those who did not[5]

The median duration of treatment for patients with a deep response was 27 months (range: 22 to 39 months) vs 25 months (range: 12 to 40 months) for those with a 20% to 50% reduction in PN volume.

‖Confirmed ORR defined as the proportion of patients with complete response (disappearance of the target PN) or partial response (≥20% reduction) on MRI of the target PN volume from baseline to Cycle 24 (treatment phase) as assessed by BICR on ≥2 consecutive scans within 2 to 6 months.[1]
¶All partial responses.[1]

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

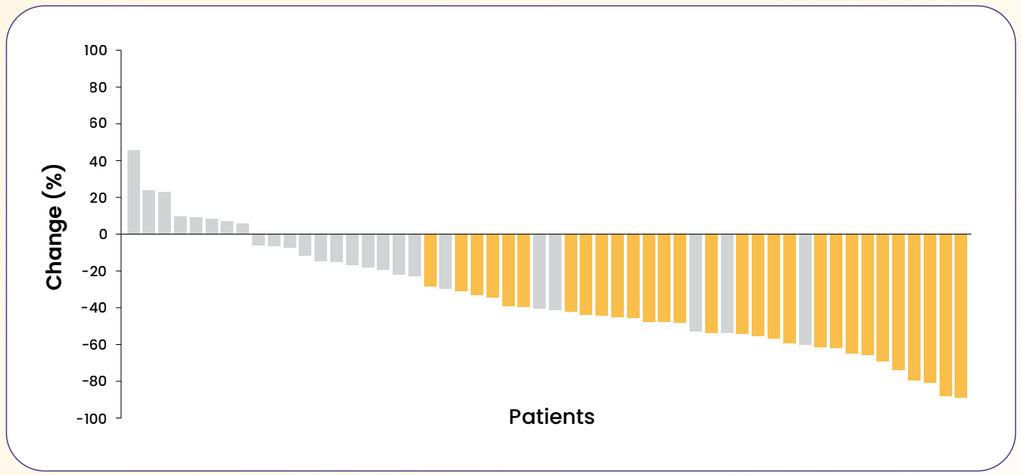
Embryo-Fetal Toxicity: GOMEKLI can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to the initiation of GOMEKLI. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Also advise patients to use effective contraception during treatment with GOMEKLI and for 6 weeks after the last dose (females) or 3 months after the last dose (males).

Please see Important Safety Information throughout and on pages 16-17, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

Pediatric cohort

Depth of response achieved by pediatric patients

Best percent change in PN volume[2,6]



Data for 54 out of 56 patients shown here; 2 patients did not have postbaseline MRI assessments. Gold bars represent those patients who had a confirmed overall response (≥20% reduction in PN volume on consecutive MRI scans). Gray bars represent nonresponders who had a best overall response of stable disease or progressive disease.

Median best change in PN volume from baseline[2]:

−42%

(range: -91% to 48%)

Maximum best change in PN volume from baseline[2]:

−91%

Analysis of best change was a prespecified exploratory endpoint

Important Safety Information (cont'd)

Adverse Reactions

The most common adverse reactions (>25%) in adult patients were rash (90%), diarrhea (59%), nausea (52%), musculoskeletal pain (41%), vomiting (38%), and fatigue (29%). Serious adverse reactions occurred in 17% of adult patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormality (>2%) was increased creatine phosphokinase.

Durable response in pediatric patients

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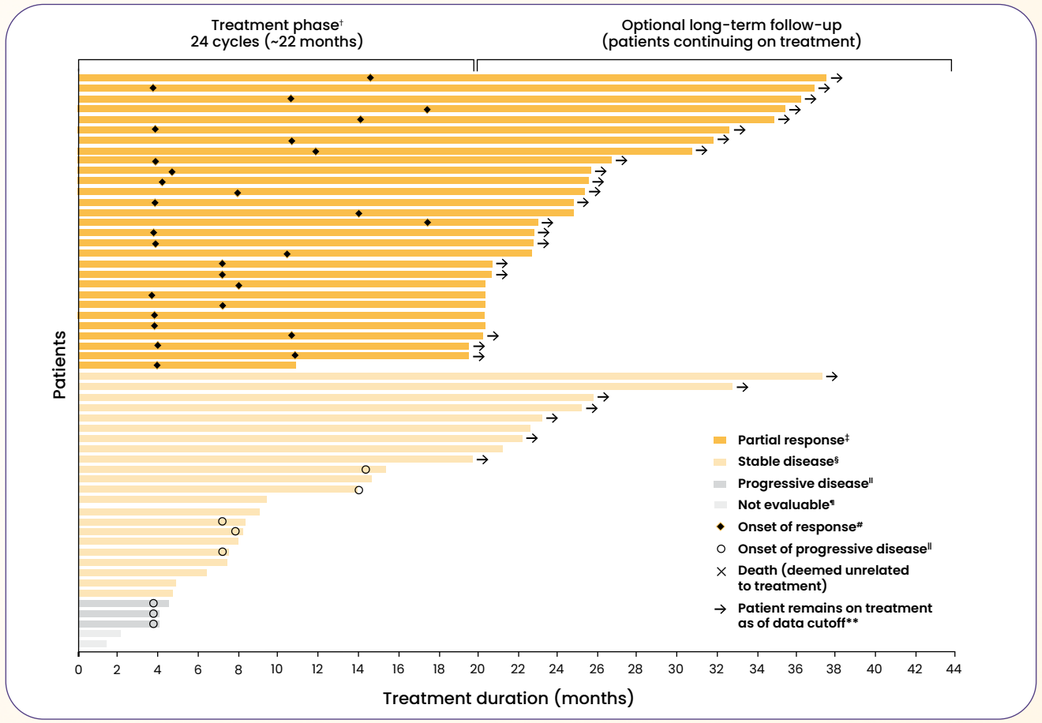
90% (26/29) of the confirmed overall responses remained durable for ≥12 months[1,*]

- 48% (14/29) of the confirmed overall responses remained durable for ≥24 months[1,*]
- **45% of responders (13/29) had onset of response at Cycle 5, the first on-treatment assessment (based on a post hoc analysis)[6]**
- Median time to first confirmed response was 7.9 months (range: 4.1 to 18.8 months)[1]

Treatment duration and response[2]



85% of patients (28/33) who completed the treatment phase chose to remain on GOMEKLI for long-term follow-up.[2]

*Duration of response was assessed based on observed time.[1]
†Four-week cycles of 3 weeks on/1 week off. The treatment phase ends 3 weeks into the final cycle.[2]
‡Partial response corresponds with confirmed overall response of ≥20% reduction in target PN volume from baseline.[1]
§Stable disease defined as a <20% increase or a <20% decrease in target PN volume from baseline.[2]
‖Progressive disease defined as a ≥20% increase in target PN volume from baseline.[2]
¶Patients who were not evaluable were those for whom no postbaseline volumetric data were collected.[6]
#Responses were confirmed on a subsequent scan within 2 to 6 months.[2]
**Data cutoff was September 20, 2023.[2]

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Pediatric cohort

A manageable safety profile in pediatric patients

The majority of adverse reactions in ReNeu were mild to moderate[1]

Adverse reactions (≥20%) in pediatric patients who received GOMEKLI (n=56)[1]

	All grades	Grades 3 or 4*
Skin and subcutaneous tissue disorders		
Rash†	73%	4%
Gastrointestinal (GI) disorders		
Diarrhea‡	55%	5%
Nausea	27%	0%
Vomiting	39%	0%
Abdominal pain§	39%	4%
Stomatitis‖	20%	0%
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain¶	41%	2%
General disorders and administration site conditions		
Pyrexia	20%	0%
Infections and infestations		
COVID-19#	25%	0%
Paronychia	32%	0%
Upper respiratory tract infection	23%	0%
Nervous system disorders		
Headache**	34%	2%
Cardiac disorders		
Left ventricular dysfunction	27%	2%
Respiratory, thoracic, and mediastinal disorders		
Cough††	21%	0%

Low rates of severe (Grade 3) adverse reactions were observed with GOMEKLI.[1]

*All reactions were Grade 3 except one fatal case of COVID-19 in an adult.
†Rash includes dermatitis acneiform, eczema, maculo-papular rash, pustular rash, dermatitis, erythematous rash, palmar-plantar erythrodysesthesia syndrome, exfoliative rash, skin exfoliation, pruritic rash, papule, papular rash, and macular rash.
‡Diarrhea includes frequent bowel movements.
§Abdominal pain includes upper abdominal pain, gastrointestinal pain, and abdominal discomfort.
‖Stomatitis includes mouth ulceration and aphthous ulcer.
¶Musculoskeletal pain includes noncardiac chest pain, back pain, pain in extremity, neck pain, musculoskeletal chest pain, myalgia, arthralgia, and bone pain.

Additional safety information in pediatric patients

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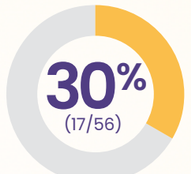
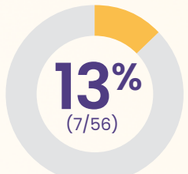
Laboratory abnormalities[1,‡‡,§§,‖‖]

The select all-grade laboratory abnormalities (≥15%) that worsened from baseline in pediatric patients were increased creatine phosphokinase (59%), increased triglycerides (45%), decreased leukocytes (40%), decreased glucose (36%), decreased neutrophils (31%), increased creatinine (30%), increased alkaline phosphatase (29%), decreased hemoglobin (29%), increased lymphocytes (27%), decreased bicarbonate (21%), increased alanine aminotransferase (ALT) (21%), decreased calcium (20%),¶¶ and increased cholesterol (16%). The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased neutrophil count and increased creatine phosphokinase.

Dose interruption, reduction, and discontinuation due to adverse reactions[1]



of patients had a dose interruption



of patients had a dose reduction

Adverse reactions that required dose interruption in ≥5% of patients included COVID-19. Adverse reactions that required dose reduction in ≥3% of pediatric patients were rash and decreased neutrophil count.

9% (5/56) of patients permanently discontinued treatment

Adverse reactions that required permanent discontinuation of GOMEKLI in ≥1% of patients were urticaria, rash, abdominal pain, constipation, and diarrhea.

#Includes one fatal case in an adult.
**Headache includes migraine.
††Cough includes upper-airway cough syndrome.
‡‡The denominator used to calculate the rate varied from 55 to 56 based on the number of patients with a baseline value and at least 1 posttreatment value.
§§Graded per NCI-CTCAE version 5.0.
‖‖No Grade 5 laboratory abnormalities were reported in the ReNeu study.
¶¶Calcium corrected for albumin (mmol/L).

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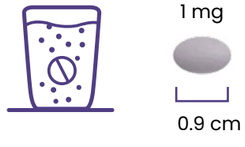
GOMEKLI dosing was designed with patient needs in mind

GOMEKLI is taken on a 3-weeks-on/ 1-week-off dosing schedule[1]

- The recommended dose is 2 mg/m^2 twice daily, with a maximum dose of 4 mg twice daily
- GOMEKLI can be taken with or without food
- Continue treatment with GOMEKLI until disease progression or unacceptable toxicity

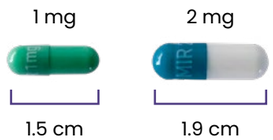
GOMEKLI is available in 2 dose formulations[1]

A tablet that can be dispersed in water or swallowed whole



Liquid can be orally administered by cup or syringe

A capsule that comes in 2 sizes



The tablet for oral suspension (dispersible tablet) may help more patients[2]

PNs on the head and neck may interfere with the functions of the surrounding anatomical structures, including swallowing. In a study of patients with NF1-PN, 23% (8/35) of adults reported difficulty swallowing.[7,8,*]

*An exploratory, cross-sectional, noninterventional study consisting of 2 anonymous surveys directed at adult patients with NF1-PN and caregivers of pediatric patients with NF1-PN.[8]

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

The most common adverse reactions (>25%) in pediatric patients were rash (73%), diarrhea (55%), musculoskeletal pain (41%), abdominal pain (39%), vomiting (39%), headache (34%), paronychia (32%), left ventricular dysfunction (27%), and nausea (27%). Serious adverse reactions occurred in 14% of pediatric patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased neutrophil count and increased creatine phosphokinase.

Getting patients started with personalized support

GOMEKLI™ (mirdametinib)
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1 mg and 2 mg capsules

SpringWorks CareConnections™ provides personalized support services and resources to help your patients get started and stay on track with GOMEKLI

Coverage and access support

- We offer support to help navigate insurance coverage, including prior authorization requirements and appeal processes for GOMEKLI
- Field Access Managers (FAMs) can provide in-person or virtual support to help facilitate access to GOMEKLI by providing you and your office staff with regional payer education and timely responses to questions

Financial assistance

- Financial support options for eligible patients

Personalized educational and emotional support

- SpringWorks CareConnections Nurse Advocates serve as a single point of contact for your patients throughout the treatment journey with GOMEKLI and can provide personalized educational and emotional support upon request[†]

Acquisition and ordering information

- GOMEKLI is available through a limited Specialty Pharmacy network
- GOMEKLI is also available for eligible medically integrated dispensing (MID) pharmacies by ordering directly through one of our Specialty Distributor partners

SpringWorks CareConnections representatives are available Monday - Friday, 8AM to 10PM ET. Click here to learn more.

[†]The SpringWorks CareConnections Patient Support Program is not intended to take the place of a healthcare provider, and our team of Nurse Advocates cannot provide medical or clinical advice.

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Important Safety Information

GOMEKLI™ (mirdametinib)
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1 mg and 2 mg capsules

Warnings and Precautions

Ocular Toxicity: GOMEKLI can cause ocular toxicity including retinal vein occlusion (RVO), retinal pigment epithelium detachment (RPED), and blurred vision. In the adult pooled safety population, ocular toxicity occurred in 28% of patients treated with GOMEKLI: 21% were Grade 1, 5% were Grade 2 and 1.3% were Grade 3. RVO occurred in 2.7%, RPED occurred in 1.3%, and blurred vision occurred in 9% of adult patients. In the pediatric pooled safety population, ocular toxicity occurred in 19% of patients: 17% were Grade 1 and 1.7% were Grade 2. Conduct comprehensive ophthalmic assessments prior to initiating GOMEKLI, at regular intervals during treatment, and to evaluate any new or worsening visual changes such as blurred vision. Continue, withhold, reduce the dose, or permanently discontinue GOMEKLI as clinically indicated.

Left Ventricular Dysfunction: GOMEKLI can cause left ventricular dysfunction. GOMEKLI has not been studied in patients with a history of clinically significant cardiac disease or LVEF <55% prior to initiation of treatment. In the ReNeu study, decreased LVEF of 10 to <20% occurred in 16% of adult patients treated with GOMEKLI. Five patients (9%) required dose interruption, one patient (1.7%) required a dose reduction, and one patient required permanent discontinuation of GOMEKLI. The median time to first onset of decreased LVEF in adult patients was 70 days. Decreased LVEF of 10 to <20% occurred in 25%, and decreased LVEF of ≥20% occurred in 1.8% of pediatric patients treated with GOMEKLI. One patient (1.8%) required dose interruption of GOMEKLI. The median time to first onset of decreased LVEF in pediatric patients was 132 days. All patients with decreased LVEF were identified during routine echocardiography, and decreased LVEF resolved in 75% of patients. Before initiating GOMEKLI, assess ejection fraction (EF) by echocardiogram. Monitor EF every 3 months during the first year and then as clinically indicated. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Dermatologic Adverse Reactions: GOMEKLI can cause dermatologic adverse reactions including rash. The most frequent rashes included dermatitis acneiform, rash, eczema, maculo-papular rash and pustular rash. In the pooled adult safety population, rash occurred in 92% of patients treated with GOMEKLI (37% were Grade 2 and 8% were Grade 3) and resulted in permanent discontinuation in 11% of patients. In the pooled pediatric safety population, rash occurred in 72% of patients treated with GOMEKLI (22% were Grade 2 and 3.4% were Grade 3) and resulted in permanent discontinuation in 3.4% of patients. Initiate supportive care at first signs of dermatologic adverse reactions. Withhold, reduce the dose, or permanently discontinue GOMEKLI based on severity of adverse reaction.

Embryo-Fetal Toxicity: GOMEKLI can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to the initiation of GOMEKLI. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Also advise patients to use effective contraception during treatment with GOMEKLI and for 6 weeks after the last dose (females) or 3 months after the last dose (males).

Adverse Reactions

The most common adverse reactions (>25%) in adult patients were rash (90%), diarrhea (59%), nausea (52%), musculoskeletal pain (41%), vomiting (38%), and fatigue (29%). Serious adverse reactions occurred in 17% of adult patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormality (>2%) was increased creatine phosphokinase.

The most common adverse reactions (>25%) in pediatric patients were rash (73%), diarrhea (55%), musculoskeletal pain (41%), abdominal pain (39%), vomiting (39%), headache (34%), paronychia (32%), left ventricular dysfunction (27%), and nausea (27%). Serious adverse reactions occurred in 14% of pediatric patients who received GOMEKLI. The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased neutrophil count and increased creatine phosphokinase.

Use in Specific Populations

Verify the pregnancy status of patients of reproductive potential prior to initiating GOMEKLI. Due to the potential for adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with GOMEKLI and for 1 week after the last dose.

Please click here for full Prescribing Information, including Patient Information and Instructions for Use.

References: 1. GOMEKLI. Prescribing Information. SpringWorks Therapeutics, Inc. **2.** Moertel CL, Hirbe AC, Shuhaiber HH, et al. ReNeu: a pivotal, phase IIb trial of mirdametinib in adults and children with symptomatic neurofibromatosis type I-associated plexiform neurofibroma. *J Clin Oncol*. Published online November 8, 2024. doi org/10.1200/JCO.24.01034 **3.** Darrigo LG Jr, Ferraz VEF, Cormedi MCV, et al. Epidemiological profile and clinical characteristics of 491 Brazilian patients with neurofibromatosis type 1. *Brain Behav*. 2022;12(6):e2599. **4.** Gross AM, Singh G, Akshintala S, et al. Association of plexiform neurofibroma volume changes and development of clinical morbidities in neurofibromatosis 1. *Neuro Oncol*. 2018;20(12):1643-1651. **5.** Gershon T, Moertel C, McNall-Knapp RY, et al. Pivotal, phase 2b ReNeu trial of mirdametinib in children and adults with neurofibromatosis type 1-associated plexiform neurofibroma (NF1-PN): a spotlight on patients achieving deep response. Poster presented at: 29th Annual Meeting of the Society for Neuro-Oncology; November 21-24, 2024; Houston, TX. **6.** Data on file: SpringWorks Therapeutics, Inc. **7.** Rapado F, Simo R, Small M. Neurofibromatosis type 1 of the head and neck: dilemmas in management. *J Laryngol Otol*. 2001;115(2):151-154. **8.** Yoo HK, Porteous A, Ng A, et al. Impact of neurofibromatosis type 1 with plexiform neurofibromas on the health-related quality of life and work productivity of adult patients and caregivers in the UK: a cross-sectional survey. *BMC Neurol*. 2023;23(1):419.

GOMEKLI is the **FIRST and ONLY** FDA-approved treatment for both adult and pediatric patients 2 years and older who have NF1 with symptomatic PNs not amenable to complete resection[1]

- **Deep responses seen in a portion of patients[2]**
- **The majority of eligible patients chose to remain on GOMEKLI for long-term follow-up[2]**
- **Most adverse reactions across both cohorts were mild to moderate[1]**
- **Available in 2 dosing formulations designed with patient needs in mind[1]**

Learn more at **GOMEKLI.com/hcp**

Important Safety Information

Warnings and Precautions associated with GOMEKLI include Ocular Toxicity, Left Ventricular Dysfunction, Dermatologic Adverse Reactions, and Embryo-Fetal Toxicity.

Adverse Reactions (>25%) in both adult and pediatric patients include rash, diarrhea, musculoskeletal pain, vomiting, and nausea, as well as fatigue in adult patients and abdominal pain, headache, paronychia, and left ventricular dysfunction in pediatric patients.

Please see Important Safety Information throughout and on pages 16-17, and click here for full Prescribing Information, including Patient Information and Instructions for Use.

SpringWorks THERAPEUTICS

GOMEKLI™
(mirdametinib)
1 mg tablets for oral suspension
1 mg and 2 mg capsules