Deploy DANYELZA

Battle bone and bone marrow metastases

DANYELZA® (naxitamab-gqgk) 40mg/10mL Injection

At incomplete response* to induction or relapse therapy, recruit the only FDA-approved immunotherapy to treat disease in bone and/or bone marrow.[1]

*Incomplete response is defined as partial response (PR), minor response (MR), or stable disease (SD) to prior therapy.

INDICATION

DANYELZA is indicated, in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), for the treatment of pediatric patients 1 year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFUSION-RELATED REACTIONS and NEUROTOXICITY

Serious Infusion-Related Reactions

- **DANYELZA can cause serious infusion reactions, including cardiac arrest, anaphylaxis, hypotension, bronchospasm, and stridor. Infusion reactions of any Grade occurred in 94-100% of patients. Severe infusion reactions occurred in 32-68% and serious infusion reactions occurred in 4-18% of patients in DANYELZA clinical studies.**
- **Premedicate prior to each DANYELZA infusion as recommended and monitor patients for at least 2 hours following completion of each infusion. Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity.**

Neurotoxicity

- **DANYELZA can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis and reversible posterior leukoencephalopathy syndrome (RPLS). Pain of any Grade occurred in 94-100% of patients in DANYELZA clinical studies.**
- **Premedicate to treat neuropathic pain as recommended. Permanently discontinue DANYELZA based on the adverse reaction and severity.**

Please see additional Important Safety Information inside. Please see full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

Half of neuroblastoma is classified as high-risk, with bone and bone marrow as common sites of metastases[2,3]

Neuroblastoma is the most common pediatric extracranial solid tumor[4]

INRG staging, age, MYCN status, and tumor histology are key factors for stratifying risk[5]

- **Half of neuroblastoma cases are** classified as **high-risk**, which typically involves metastatic disease[2,5]

Bone marrow and bone are the most common sites of metastatic neuroblastoma[3,6]

- In children presenting with metastatic disease, **70%** of metastases involve bone marrow and **55%** involve cortical bone[3]

Approximately **1 in 3 patients has a complete metastatic response** during induction therapy.[7]
Despite intensive multimodal frontline therapy, **2 in 5 patients relapse**[8]

INRG=International Neuroblastoma Risk Group.

Bone/BM in NB

Reducing or eliminating disease in the bone and bone marrow is a goal of high-risk neuroblastoma treatment[2]

Assessing disease in bone or bone marrow requires both biopsy and imaging[2]

- **Bilateral aspirates** and **bilateral trephine biopsies** detect and quantify neuroblastoma cells in the bone marrow
- **^{123}I-MIBG imaging** detects the presence of metastases in the bone for MIBG-avid tumors, with FDG-PET or PET/CT scans used for MIBG nonavid tumors
  - MIBG imaging is widely used as a diagnostic and prognostic indicator for high-risk neuroblastoma[9]

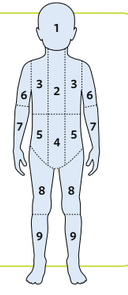
Curie score (CS) uses MIBG imaging to quantify metastatic disease in the bone and soft tissue, which can have prognostic implications[2, 9-11]

The body is subdivided into 10 regions: 9 skeletal regions, 1 soft tissue region[9]

Each region is designated a score of 0-3 points, with a maximum collective score of 30 points (higher score indicates greater extent of disease)

Up to 27 points may be assigned to skeletal regions

Up to 3 points may be assigned to soft tissue regions



An absolute CS of 0-2 prior to transplant has been shown to be more clinically prognostic than relative reduction in CS[9-11]

Please see Important Safety Information throughout. Please see full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

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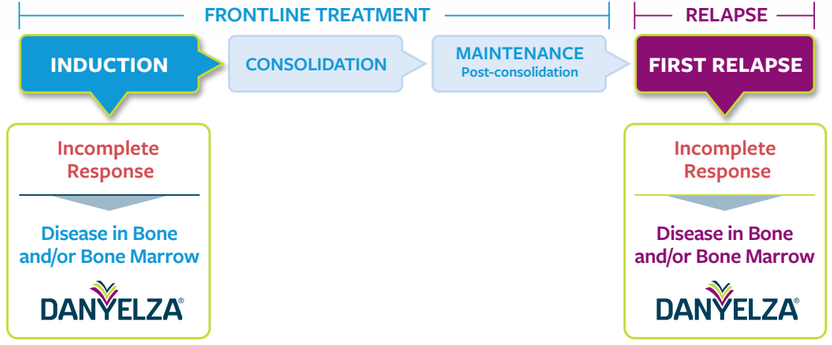
When response is incomplete, consider the only FDA-approved humanized immunotherapy for patients with R/R high-risk neuroblastoma in bone and/or bone marrow[1]



Incomplete response is defined as partial response (PR), minor response (MR), or stable disease (SD) to prior therapy

R/R=relapsed or refractory.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

DANYELZA is contraindicated in patients with a history of severe hypersensitivity reaction to naxitamab-gqgk. Reactions have included anaphylaxis.

WARNINGS AND PRECAUTIONS

Serious Infusion-Related Reactions

DANYELZA can cause serious infusion reactions requiring urgent intervention including fluid resuscitation, administration of bronchodilators and corticosteroids, intensive care unit admission, infusion rate reduction or interruption of DANYELZA infusion. Infusion-related reactions included hypotension, bronchospasm, hypoxia, and stridor.

Serious infusion-related reactions occurred in 4% of patients in Study 201 and in 18% of patients in Study 12-230. Infusion-related reactions of any Grade occurred in 100% of patients in Study 201 and 94% of patients in Study 12-230. Hypotension of any grade occurred in 100% of patients in Study 201 and 89% of patients in Study 12-230.

Please see additional Important Safety Information throughout. Please see full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

DANYELZA with GM-CSF was granted accelerated approval based on two clinical studies[1]

STUDY 12-230

Phase 1/2, open-label, single-arm, single-center trial (N=72)

- Efficacy analysis included only patients with evaluable disease at baseline (n=38)

STUDY 201

Phase 2, open-label, single-arm, global, multicenter trial (initial analysis: N=25)[1]

- **A pre-specified interim analysis for Study 201 was conducted (N=74), with trial sites in the US, Canada, Denmark, Germany, Italy, Spain, and Hong Kong[12]**
- Efficacy analysis included only patients with evaluable disease in bone and/or bone marrow at baseline (initial analysis: n=22; interim analysis: n=52)[1,12]

INCLUSION CRITERIA (both studies)[1,12]

- HR-NB patients ≥12 months of age with bone/bone marrow involvement who had incomplete response to induction or relapse therapy
- Evaluable disease in bone and/or bone marrow
- Patients with prior anti-GD2 therapy permitted
- At least one prior systemic therapy to treat disease outside of the bone and/or bone marrow

EXCLUSION CRITERIA (both studies)[1]

- Actively progressing disease
- Evaluable NB outside of the bone/bone marrow

PRIMARY ENDPOINT[1,12]

- Overall response rate (ORR)

SECONDARY ENDPOINTS

- Duration of response (DOR)
- Complete response (CR)
- Safety

Accelerated approval is based on overall response rate and duration of response.
Continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Treatment with DANYELZA is backed by more than a decade of clinical trial experience and was approved by the FDA in 2020[13]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Serious Infusion-Related Reactions (cont)

In Study 201, 68% of patients experienced Grade 3 or 4 infusion reactions; and in Study 12-230, 32% of patients experienced Grade 3 or 4 infusion reactions. Anaphylaxis occurred in 12% of patients and two patients (8%) permanently discontinued DANYELZA due to anaphylaxis in Study 201. One patient in Study 12-230 (1.4%) experienced a Grade 4 cardiac arrest 1.5 hours following completion of DANYELZA infusion.

In Study 201, infusion reactions generally occurred within 24 hours of completing a DANYELZA infusion, most often within 30 minutes of initiation. Infusion reactions were most frequent during the first infusion of DANYELZA in each cycle. Eighty percent of patients required reduction in infusion rate and 80% of patients had an infusion interrupted for at least one infusion-related reaction.

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Baseline patient and disease characteristics in DANYELZA with GM-CSF trials[1,12]

		Initial Analysis[1]	Pre-specified Interim Analysis[12]
	STUDY 12-230[1] Efficacy Analysis (n=38)	STUDY 201 Efficacy Analysis (n=22)	STUDY 201 Efficacy Analysis (n=52)
DISEASE TYPE			
Refractory (incomplete response to induction)	45% (n=17)	64% (n=14)	50% (n=26)
Relapsed	55% (n=21)	36% (n=8)	50% (n=26)
Median age (range)	5 years (2 to 23 years)	5 years (3 to 10 years)	6 years (2 to 18 years)
MYCN amplification	16%	14%	14%
INSS Stage 4	95%	86%	89%
DISEASE SITES			
Bone marrow only	11%	9%	4%
Bone only	50%	59%	56%
Both	39%	32%	40%
PRIOR TREATMENTS			
Surgery	100%	91%	89%
Chemotherapy	100%	95%	100%
Radiation	47%	36%	40%
ASCT	42%	18%	27%
Anti-GD2 antibody treatment	58%	18%	25%

ASCT=autologous stem cell transplant; INSS=International Neuroblastoma Staging System.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Serious Infusion-Related Reactions (cont)

Premedicate with an antihistamine, acetaminophen, an H2 antagonist and corticosteroid as recommended. Monitor patients closely for signs and symptoms of infusion reactions during and for at least 2 hours following completion of each DANYELZA infusion in a setting where cardiopulmonary resuscitation medication and equipment are available.

Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity and institute appropriate medical management as needed.

Neurotoxicity

DANYELZA can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis, and reversible posterior leukoencephalopathy syndrome.

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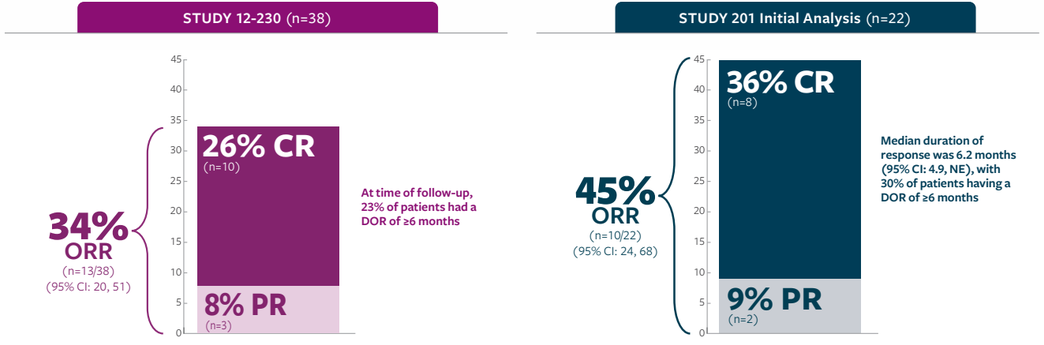
In both studies, more than 1/3 of patients responded and more than 1/4 achieved *complete* response with DANYELZA with GM-CSF[1]



ORR was defined as a CR or PR according to the revised INRC (2017) *and confirmed by at least 1 subsequent assessment.*

Effectiveness of DANYELZA with GM-CSF was evaluated by independent pathology and imaging review. Responses were observed in the bone, bone marrow, or both bone and bone marrow.[1]

CI=confidence interval; CR=complete response; DOR=duration of response; INRC=International Neuroblastoma Response Criteria; NE=not estimable; ORR=overall response rate; PR=partial response.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Neurotoxicity (cont)

Pain

Pain, including abdominal pain, bone pain, neck pain, and extremity pain, occurred in 100% of patients in Study 201 and 94% of patients in Study 12-230. Grade 3 pain occurred in 72% of patients in Study 201. One patient in Study 201 (4%) required interruption of an infusion due to pain. Pain typically began during the infusion of DANYELZA and lasted a median of less than one day in Study 201 (range less than one day and up to 62 days).

Premedicate with drugs that treat neuropathic pain (e.g., gabapentin) and oral opioids. Administer intravenous opioids as needed for breakthrough pain. Permanently discontinue DANYELZA based on severity.

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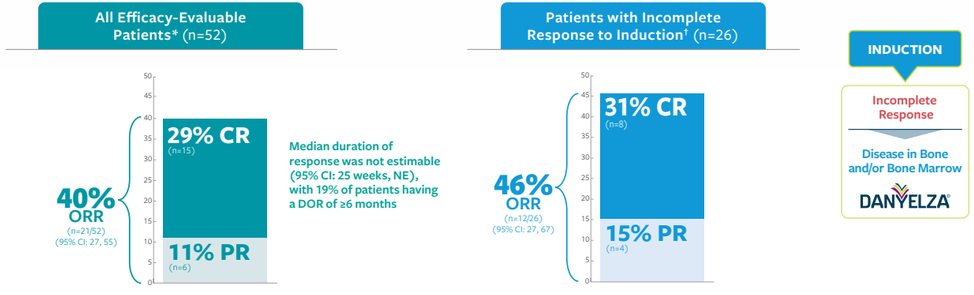
Study 201 pre-specified interim analysis



ORR was defined as a CR or PR according to the revised INRC (2017) *and confirmed by at least 1 subsequent assessment.*

Effectiveness of DANYELZA with GM-CSF was evaluated by independent pathology and imaging review. Responses were observed in the bone, bone marrow, or both bone and bone marrow.[12]

***Median follow-up: 5.9 months (range: 0.6–17.8).**

For the primary endpoint, a sample size of at least 37 patients in the efficacy population is sufficient to ensure at least 90% power to exclude an ORR of 20% or less at the two-sided 5% level.[12]
Limitations: Interim analysis may not be representative of the final analysis.

†Study design: These data underwent pre-specified analyses, including subgroup analyses of the primary endpoint.[12]
Limitation: These subgroup results are based on small sample sizes and could represent chance findings, and they were not adjusted for multiplicity; interpret with caution.[12]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Neurotoxicity (cont)

Transverse Myelitis

Transverse myelitis has occurred with DANYELZA. Permanently discontinue DANYELZA in patients who develop transverse myelitis.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

Reversible posterior leukoencephalopathy syndrome (RPLS) (also known as posterior reversible encephalopathy syndrome or PRES) occurred in 2 (2.8%) patients in Study 12-230. Events occurred 2 and 7 days following completion of the first cycle of DANYELZA. Monitor blood pressure during and following DANYELZA infusion and assess for neurologic symptoms. Permanently discontinue DANYELZA in case of symptomatic RPLS.

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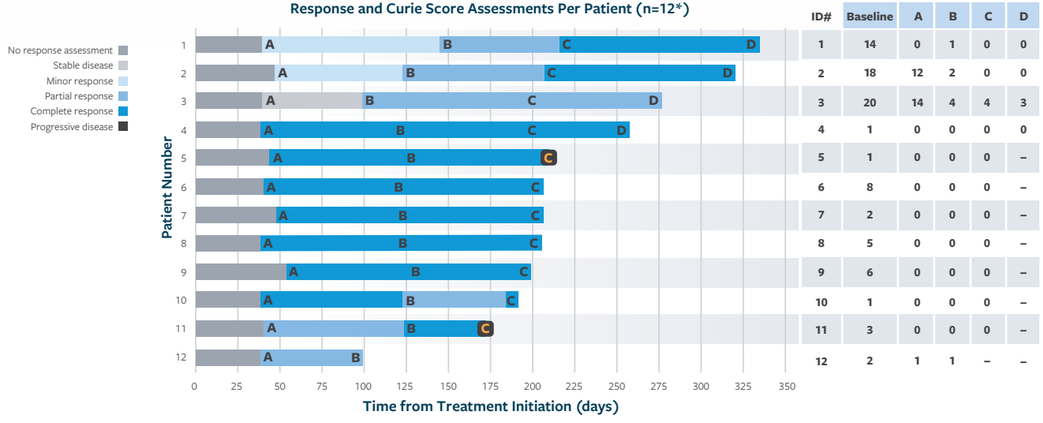
Study 201 pre-specified interim analysis: swimmer plot of patients with incomplete response to induction[12]



*Patients with a best response of minor response (MR), stable disease (SD), or progressive disease (PD) to DANYELZA with GM-CSF are excluded from the swimmer plot.

Limitation: Patient-level data are for descriptive purposes and should not be considered indicative of typical product efficacy or duration; interpret with caution.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Neurotoxicity (cont)

Peripheral Neuropathy

Peripheral neuropathy, including peripheral sensory neuropathy, peripheral motor neuropathy, paresthesia, and neuralgia, occurred in 32% of patients in Study 201 and in 25% of patients in Study 12-230. Most signs and symptoms of neuropathy began on the day of the infusion and neuropathy lasted a median of 5.5 days (range 0 to 22 days) in Study 201 and 0 days (range 0 to 22 days) in Study 12-230.

Permanently discontinue DANYELZA based on severity.

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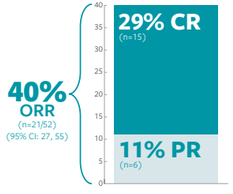
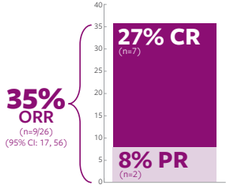
Study 201 pre-specified interim analysis

All Efficacy-Evaluable Patients* (n=52)



Median duration of response was not estimable (95% CI: 25 weeks, NE), with 19% of patients having a DOR of ≥6 months

Patients with Incomplete Response to Relapse Therapy† (n=26)



RELAPSE

Incomplete Response

Disease in Bone and/or Bone Marrow

DANYELZA

ORR was defined as a CR or PR according to the revised INRC (2017) *and confirmed by at least 1 subsequent assessment.*

Effectiveness of DANYELZA with GM-CSF was evaluated by independent pathology and imaging review. Responses were observed in the bone, bone marrow, or both bone and bone marrow.[12]

***Median follow-up: 5.9 months (range: 0.6–17.8).**

For the primary endpoint, a sample size of at least 37 patients in the efficacy population is sufficient to ensure at least 90% power to exclude an ORR of 20% or less at the two-sided 5% level.[12]
Limitations: Interim analysis may not be representative of the final analysis.

†Study design: These data underwent pre-specified analyses, including subgroup analyses of the primary endpoint.[12]
Limitation: These subgroup results are based on small sample sizes and could represent chance findings, and they were not adjusted for multiplicity; interpret with caution.[12]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Neurotoxicity (cont)

Neurological Disorders of the Eye

Neurological disorders of the eye including unequal pupils, blurred vision, accommodation disorder, mydriasis, visual impairment, and photophobia occurred in 24% of patients in Study 201 and 19% of patients in Study 12-230. Neurological disorders of the eye lasted a median of 17 days (range 0 to 84 days) in Study 201 with two patients (8%) experiencing an event that had not resolved at the time of data cutoff, and a median of 1 day (range less than one day to 21 days) in Study 12-230. Permanently discontinue DANYELZA based on severity.

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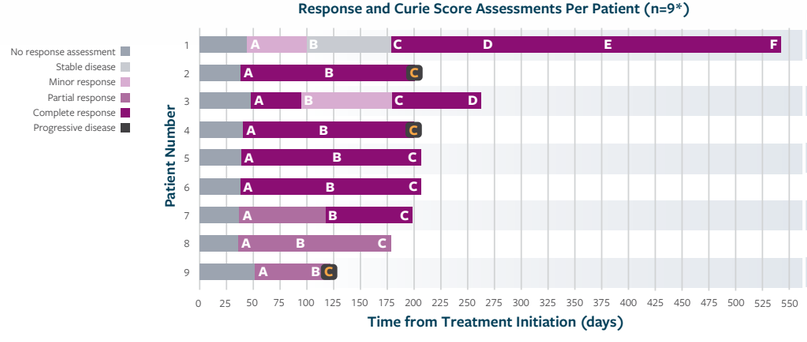
Study 201 pre-specified interim analysis: swimmer plot of patients with incomplete response to relapse therapy[12]



Curie Score Assessments

ID#	Baseline	A	B	C	D	E	F
1	4	3	3	0	0	0	0
2	1	0	0	1	–	–	–
3	1	0	1	0	0	–	–
4	1	0	0	2	–	–	–
5	1	0	0	0	–	–	–
6	2	0	0	0	–	–	–
7	17	1	0	0	–	–	–
8	3	1	1	1	–	–	–
9	4	1	2	3	–	–	–

*Patients with a best response of minor response (MR), stable disease (SD), or progressive disease (PD) to DANYELZA with GM-CSF are excluded from the swimmer plot.

Limitation: Patient-level data are for descriptive purposes and should not be considered indicative of typical product efficacy or duration; interpret with caution.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Neurotoxicity (cont)

Prolonged Urinary Retention

Urinary retention occurred in 1 (4%) patient in Study 201 and in 3 patients (4%) in Study 12-230. All events in both studies occurred on the day of an infusion of DANYELZA and lasted between 0 and 24 days. Permanently discontinue DANYELZA in patients with urinary retention that does not resolve following discontinuation of opioids.

Embryo-Fetal Toxicity

Based on its mechanism of action, DANYELZA may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential, including pregnant women, of the potential risk to a fetus. Advise females of reproductive potential to use effective contraceptive during treatment with DANYELZA and for two months after the final dose.

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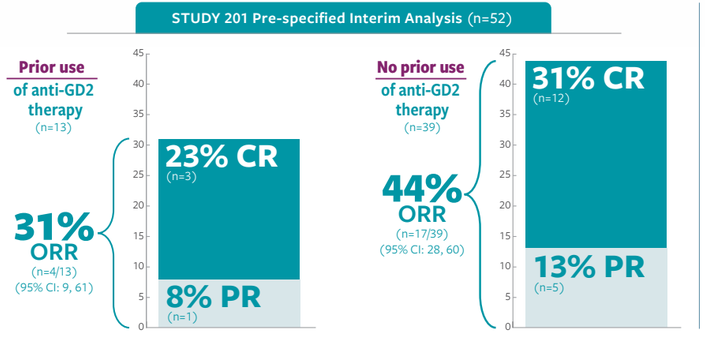
Study 201 pre-specified interim analysis: patients by prior use of anti-GD2 therapy and patients with development of anti-drug antibodies (ADAs)[12]



Patients who had developed anti-drug antibodies (ADAs) (n=18)

22% (4/18) responded

17% (3/18) achieved a CR

ORR was defined as a CR or PR according to the revised INRC (2017) *and confirmed by at least 1 subsequent assessment.*

Effectiveness of DANYELZA with GM-CSF was evaluated by independent pathology and imaging review. Responses were observed in the bone, bone marrow, or both bone and bone marrow.[12]

DANYELZA is the only FDA-approved anti-GD2 immunotherapy approved for this patient population (ie, R/R high-risk neuroblastoma in the bone or bone marrow).[1]

Study design: These data underwent pre-specified analyses, including subgroup analyses of the primary endpoint.[12]

Limitation: These subgroup results are based on small sample sizes and could represent chance findings, and they were not adjusted for multiplicity; interpret with caution.[12]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypertension

Hypertension occurred in 44% of patients in Study 201 and 28% of patients in Study 12-230 who received DANYELZA. Grade 3 or 4 hypertension occurred in 4% of patients in Study 201 and 7% of patients in Study 12-230. Four patients (6%) in Study 12-230 permanently discontinued DANYELZA due to hypertension. In both studies, most events occurred on the day of DANYELZA infusion and occurred up to 9 days following an infusion of DANYELZA.

Do not initiate DANYELZA in patients with uncontrolled hypertension. Monitor blood pressure during infusion, and at least daily on Days 1 to 8 of each cycle of DANYELZA and evaluate for complications of hypertension including RPLS. Interrupt DANYELZA infusion and resume at a reduced rate, or permanently discontinue DANYELZA based on the severity.

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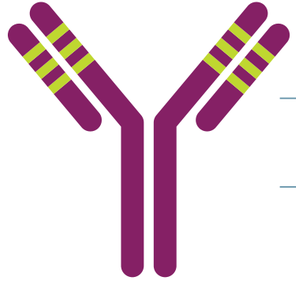
DANYELZA is the only humanized GD2-binding monoclonal antibody approved by the FDA[1*]



Neuroblastoma is characterized by an overexpression of GD2, a disialoganglioside also found in the central nervous system and on peripheral nerves[1]

Antibody structure[14]

- 92% human framework
- 8% murine framework

~10-fold higher binding affinity to the GD2 receptor due to a slower off-rate than approved chimeric anti-GD2 antibodies shown in *in vitro* studies.[15] Clinical significance and product comparisons of efficacy or safety should not be inferred

*In refractory or relapsed high-risk neuroblastoma.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

The most common adverse reactions in Studies 201 and 12-230 (≥25% in either study) were infusion-related reaction, pain, tachycardia, vomiting, cough, nausea, diarrhea, decreased appetite, hypertension, fatigue, erythema multiforme, peripheral neuropathy, urticaria, pyrexia, headache, injection site reaction, edema, anxiety, localized edema and irritability. The most common Grade 3 or 4 laboratory abnormalities (≥5% in either study) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased platelet count, decreased potassium, increased alanine aminotransferase, decreased glucose, decreased calcium, decreased albumin, decreased sodium and decreased phosphate.

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Safety analysis of patients who received DANYELZA with GM-CSF

DANYELZA can cause serious infusion reactions, including hypotension, bronchospasm, hypoxia, and stridor, as well as severe neurotoxicity, including pain[1]:

- Any-grade infusion-related reactions occurred in **94%–100%** of patients
  - Any-grade hypotension occurred in **89%–100%** of patients
- Any-grade pain occurred in **94%–100%** of patients

The most common ARs in Studies 12-230 and 201 (both analyses) (≥25% in either study)[1,12]

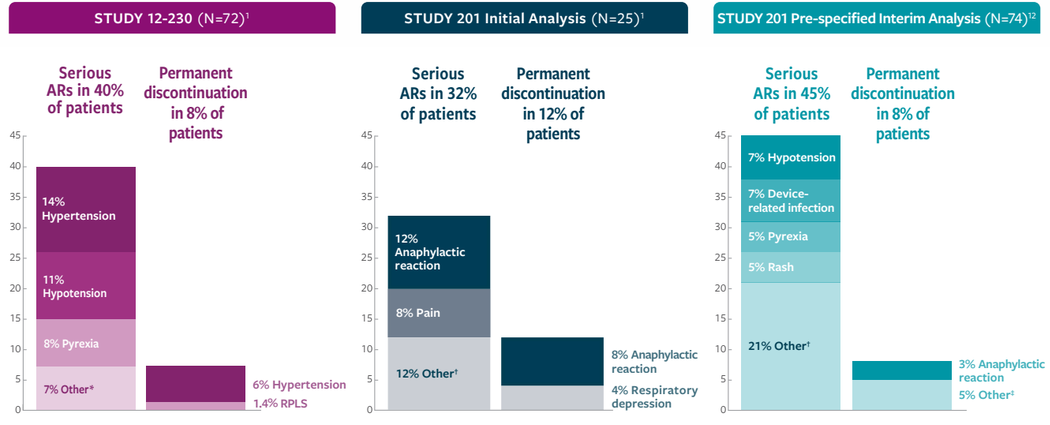
- Infusion-related reaction
- Pain
- Tachycardia
- Vomiting
- Cough
- Pruritus
- Nausea
- Diarrhea
- Decreased appetite
- Hypertension
- Fatigue
- Erythema multiforme
- Peripheral neuropathy
- Urticaria
- Pyrexia
- Headache
- Injection site reaction
- Edema
- Anxiety
- Localized edema
- Irritability
- Anemia

Total DANYELZA exposure across Studies 12-230 and 201[1,12]

- Of the 72 patients in Study 12-230, 32% were exposed to DANYELZA with GM-CSF for ≥6 months and 8% for >1 year[1]
- Of the 25 patients in Study 201 (initial analysis), an ongoing multicenter trial, 12% were exposed to DANYELZA with GM-CSF for ≥6 months and 0% for >1 year[1]
- Of the 74 patients in the Study 201 pre-specified interim analysis, 18% were exposed to DANYELZA with GM-CSF for ≥6 months and 3% for ≥1 year[12]

AR=adverse reaction.

Some patients experienced serious adverse reactions that led to permanent discontinuation[1,12]



- In the Study 201 initial analysis, dose interruptions due to an AR occurred in 84% of patients. ARs requiring dosage interruption in >10% of patients included hypotension and bronchospasm[1]
- In the Study 201 pre-specified interim analysis, dose interruptions due to an AR occurred in 69% of patients. ARs requiring dosage interruption in >10% of patients included hypotension, pain, and bronchospasm[12]

*Serious ARs occurring in <5% of patients.
†Serious ARs occurring in only 1 patient.
‡1% each: respiratory depression, myocarditis, hypotension, RPLS, and urticaria.
RPLS=reversible posterior leukoencephalopathy syndrome.

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When to permanently discontinue DANYELZA[1]

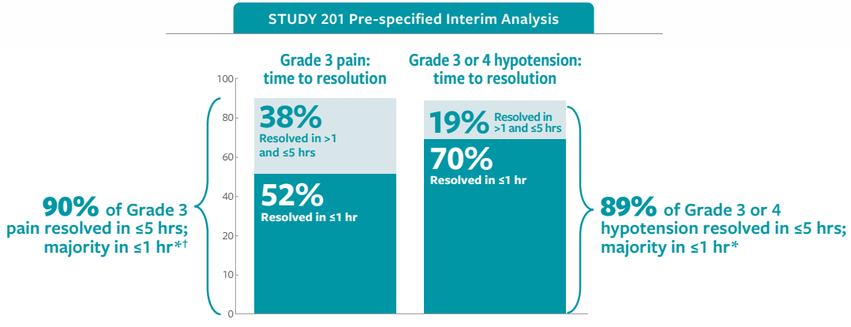
DANYELZA should be discontinued in the case of*:

Infusion-related reactions	■ Grade 4, Grade 3 and not responding to medical intervention, or Grade 3-4 anaphylaxis	**Neurological disorders of the eye**	■ Grade 2-4 not resolving within 2 weeks or upon recurrence; any grade with subtotal or total vision loss
Pain	■ Grade 3 and unresponsive to maximum supportive measures	**Prolonged urinary retention**	■ Persisting following discontinuation of opioids
Reversible posterior leukoencephalopathy syndrome (RPLS)	■ All grades	**Hypertension**	■ Grade 4, or Grade 3 and not responding to medical intervention
Transverse myelitis	■ All grades	**Other ARs**	■ Grade 4, or Grade 3 not resolving to Grade ≤2 within 2 weeks
Peripheral neuropathy	■ Grade ≥2 motor neuropathy or Grade 3-4 sensory neuropathy		

*Based on Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

Safety

Study 201 pre-specified interim analysis: resolution of select Grade 3 or 4 adverse reactions[12]



*Incidence of events related to DANYELZA or DANYELZA with GM-CSF occurring on day of infusion, after start of infusion.
† Excludes procedural pain and vessel puncture site pain.

DANYELZA® (naxitamab-gqgk) 40mg/10mL Injection

DANYELZA can offer the flexibility of inpatient or outpatient administration, at the treating physician's discretion[12]

>90% of infusions were given in an outpatient setting in the Study 201 pre-specified interim analysis[12]*

Pretreatment[1]

- **Five days before first infusion in each cycle:** initiate GM-CSF and a 12-day course (Day -4 through Day 7) of gabapentin or other prophylactic medication for neuropathic pain

Infusion days[1]

- DANYELZA is given on **Days 1, 3, and 5 of each 28-day cycle** until disease progression or unacceptable toxicity
- In preparation for each DANYELZA dose:
  - **2 hours to 30 min before DANYELZA:** premedicate
  - **≥1 hour before infusion** on Days 1, 3, 5 of each cycle: administer GM-CSF
- Administer DANYELZA 3 mg/kg/infusion (up to 150 mg/day) on Days 1, 3, 5 (9 mg/kg/cycle), given as IV infusion after dilution and in combination with GM-CSF subcutaneously. Do not administer DANYELZA as IV push or bolus
  - **60-min first infusion** (Cycle 1, Day 1) and subsequently 30-60 min as tolerated
  - **Observation required for at least 2 hours after** the DANYELZA infusion in a setting where cardiopulmonary resuscitation medication and equipment are available

***Out of 1,237 infusions, 92.5% (1,144) were outpatient and 7.5% (93) were inpatient.[12]**
†For more details, refer to the GM-CSF Prescribing Information.
IV=intravenous.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFUSION-RELATED REACTIONS and NEUROTOXICITY

Serious Infusion-Related Reactions

- **DANYELZA can cause serious infusion reactions, including cardiac arrest, anaphylaxis, hypotension, bronchospasm, and stridor. Infusion reactions of any Grade occurred in 94-100% of patients. Severe infusion reactions occurred in 32-68% and serious infusion reactions occurred in 4-18% of patients in DANYELZA clinical studies.**
- **Premedicate prior to each DANYELZA infusion as recommended and monitor patients for at least 2 hours following completion of each infusion. Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity.**

Please see additional Important Safety Information throughout. Please see full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

Administer DANYELZA until CR or PR and follow treatment course shown below[1]

Treatment Course[1]

Continue 28-day cycles until CR or PR	Repeat for 5 more 28-day cycles	May switch to 8-week cycles
Administer 28-day cycles of DANYELZA with GM-CSF until CR or PR	Following response, maintain 28-day cycle for an additional 5 cycles	At physician's discretion, subsequently shift to 8-week cycle and discontinue for disease progression or unacceptable toxicity

If a DANYELZA dose is missed[1]

- Administer the missed dose the following week by Day 10
- Administer GM-CSF 500 µg/m²/day on the first day of the DANYELZA infusion, and on the day before and the days of the second and third infusions, respectively (ie, a total of 5 days with 500 µg/m²/day)

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFUSION-RELATED REACTIONS and NEUROTOXICITY (cont)

Neurotoxicity

- **DANYELZA can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis and reversible posterior leukoencephalopathy syndrome (RPLS). Pain of any Grade occurred in 94-100% of patients in DANYELZA clinical studies.**
- **Premedicate to treat neuropathic pain as recommended. Permanently discontinue DANYELZA based on the adverse reaction and severity.**

CONTRAINDICATION

DANYELZA is contraindicated in patients with a history of severe hypersensitivity reaction to naxitamab-gqgk. Reactions have included anaphylaxis.

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DANYELZA® (naxitamab-gqgk) 40mg/10mL Injection

Y-mAbs Connect® is a patient support program that provides information about access, insurance, financial support, and other resource programs for qualifying patients

Y-mAbs Connect®

Your link to patient support

ymabsconnect.com or **1-833-33YMABS, option 2**

Healthcare professionals get help with:

- Summary of Benefits for health insurance coverage of DANYELZA, including assistance in determining when a prior authorization or appeal may be needed
- Information on ordering DANYELZA

Patients get help with:

- Determining eligibility for Y-mAbs Connect Patient Support Programs
- Information on third-party organizations* that may help with logistical and other support

*Third-party organizations are not associated with Y-mAbs Therapeutics, Inc.; specific details and eligibility requirements may vary by organization.

DANYELZA J-code: J9348

Information about Y-mAbs Connect can be found at ymabsconnect.com or by calling Y-mAbs Connect at 1-833-33YMABS, option 2 between 8:00 am – 8:00 pm ET, Monday – Friday. Closed on weekends and major holidays.

References

1. DANYELZA® [package insert]. New York, NY: Y-mAbs Therapeutics, Inc.; 2020. Available online at https://labeling.ymabs.com/danyelza. **2.** Park JR, Bagatell R, Cohn SL, et al. *J Clin Oncol.* 2017;35(22):2580-2587. **3.** DuBois SG, Kalika Y, Lukens JN, et al. *J Pediatr Hematol Oncol.* 1999;21(3):181-189. **4.** Smith V, Foster J. *Children* (Basel). 2018;5(9):114. **5.** Irwin MS, Naranjo A, Zhang FF, et al. *J Clin Oncol.* 2021;39:3229-3241. **6.** Sharp SE, Trout AT, Weiss BD, et al. *Radiographics.* 2016;36:258-278. **7.** Garaventa A, Poetschger U, Valteau-Couanet D, et al. *J Clin Oncol.* 2021;39(23):2552-2563. **8.** Pinto N, Naranjo A, Hibbitts E, et al. *Eur J Cancer.* 2019;112:66-79. **9.** Yanik GA, Parisi MT, Naranjo A, et al. *J Nucl Med.* 2018;59:502-508. **10.** Yanik GA, Parisi MT, Shulkin BL, et al. *J Nucl Med.* 2013;54(4):541-548. **11.** Streby KA, Parisi MT, Shulkin BL, et al. *Pediatr Blood Cancer.* 2023;e30418. https://doi.org/10.1002/pbc.30418. **12.** Data on file. Y-mAbs Therapeutics, Inc. **13.** NIH US National Library of Medicine. https://clinicaltrials.gov/ct2/show/NCT01419834?term=NCT01419834&draw=2&rank=1. Accessed June 15, 2023. **14.** Cheung N-KV, Guo H, Hu J, et al. *Oncoimmunology.* 2012;1(4):477-486. **15.** Lisby S, Liebenberg N, Bukrinski J, et al. Presented at the SIOP virtual congress. Abstract #945. October 16, 2020.

Please see Important Safety Information throughout. Please see full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

Indication and Important Safety Information

INDICATION

DANYELZA is indicated, in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), for the treatment of pediatric patients 1 year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFUSION-RELATED REACTIONS and NEUROTOXICITY

Serious Infusion-Related Reactions

- **DANYELZA can cause serious infusion reactions, including cardiac arrest, anaphylaxis, hypotension, bronchospasm, and stridor. Infusion reactions of any Grade occurred in 94-100% of patients. Severe infusion reactions occurred in 32-68% and serious infusion reactions occurred in 4-18% of patients in DANYELZA clinical studies.**
- **Premedicate prior to each DANYELZA infusion as recommended and monitor patients for at least 2 hours following completion of each infusion. Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity.**

Neurotoxicity

- **DANYELZA can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis and reversible posterior leukoencephalopathy syndrome (RPLS). Pain of any Grade occurred in 94-100% of patients in DANYELZA clinical studies.**
- **Premedicate to treat neuropathic pain as recommended. Permanently discontinue DANYELZA based on the adverse reaction and severity.**

CONTRAINDICATION

DANYELZA is contraindicated in patients with a history of severe hypersensitivity reaction to naxitamab-gqgk. Reactions have included anaphylaxis.

WARNINGS AND PRECAUTIONS

Serious Infusion-Related Reactions

DANYELZA can cause serious infusion reactions requiring urgent intervention including fluid resuscitation, administration of bronchodilators and corticosteroids, intensive care unit admission, infusion rate reduction or interruption of DANYELZA infusion. Infusion-related reactions included hypotension, bronchospasm, hypoxia, and stridor.

Serious infusion-related reactions occurred in 4% of patients in Study 201 and in 18% of patients in Study 12-230. Infusion-related reactions of any Grade occurred in 100% of patients in Study 201 and 94% of patients in Study 12-230. Hypotension of any grade occurred in 100% of patients in Study 201 and 89% of patients in Study 12-230.

In Study 201, 68% of patients experienced Grade 3 or 4 infusion reactions; and in Study 12-230, 32% of patients experienced Grade 3 or 4 infusion reactions. Anaphylaxis occurred in 12% of patients and two patients (8%) permanently discontinued DANYELZA due to anaphylaxis in Study 201. One patient in Study 12-230 (1.4%) experienced a Grade 4 cardiac arrest 1.5 hours following completion of DANYELZA infusion.

In Study 201, infusion reactions generally occurred within 24 hours of completing a DANYELZA infusion, most often within 30 minutes of initiation. Infusion reactions were most frequent during the first infusion of DANYELZA in each cycle. Eighty percent of patients required reduction in infusion rate and 80% of patients had an infusion interrupted for at least one infusion-related reaction.

Premedicate with an antihistamine, acetaminophen, an H2 antagonist and corticosteroid as recommended. Monitor patients closely for signs and symptoms of infusion reactions during and for at least 2 hours following completion of each DANYELZA infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity and institute appropriate medical management as needed.

Please see full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

Important Safety Information

Indication and Important Safety Information (cont)

Neurotoxicity

DANYELZA can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis, and reversible posterior leukoencephalopathy syndrome.

Pain

Pain, including abdominal pain, bone pain, neck pain, and extremity pain, occurred in 100% of patients in Study 201 and 94% of patients in Study 12-230. Grade 3 pain occurred in 72% of patients in Study 201. One patient in Study 201 (4%) required interruption of an infusion due to pain. Pain typically began during the infusion of DANYELZA and lasted a median of less than one day in Study 201 (range less than one day and up to 62 days).

Premedicate with drugs that treat neuropathic pain (e.g., gabapentin) and oral opioids. Administer intravenous opioids as needed for breakthrough pain. Permanently discontinue DANYELZA based on severity.

Transverse Myelitis

Transverse myelitis has occurred with DANYELZA. Permanently discontinue DANYELZA in patients who develop transverse myelitis.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

Reversible posterior leukoencephalopathy syndrome (RPLS) (also known as posterior reversible encephalopathy syndrome or PRES) occurred in 2 (2.8%) patients in Study 12-230. Events occurred 2 and 7 days following completion of the first cycle of DANYELZA. Monitor blood pressure during and following DANYELZA infusion and assess for neurologic symptoms. Permanently discontinue DANYELZA in case of symptomatic RPLS.

Peripheral Neuropathy

Peripheral neuropathy, including peripheral sensory neuropathy, peripheral motor neuropathy, paresthesia, and neuralgia, occurred in 32% of patients in Study 201 and in 25% of patients in Study 12-230. Most signs and symptoms of neuropathy began on the day of the infusion and neuropathy lasted a median of 5.5 days (range 0 to 22 days) in Study 201 and 0 days (range 0 to 22 days) in Study 12-230.

Permanently discontinue DANYELZA based on severity.

Neurological Disorders of the Eye

Neurological disorders of the eye including unequal pupils, blurred vision, accommodation disorder, mydriasis, visual impairment, and photophobia occurred in 24% of patients in Study 201 and 19% of patients in Study 12-230. Neurological disorders of the eye lasted a median of 17 days (range 0 to 84 days) in Study 201 with two patients (8%) experiencing an event that had not resolved at the time of data cutoff, and a median of 1 day (range less than one day to 21 days) in Study 12-230. Permanently discontinue DANYELZA based on severity.

Prolonged Urinary Retention

Urinary retention occurred in 1 (4%) patient in Study 201 and in 3 patients (4%) in Study 12-230. All events in both studies occurred on the day of an infusion of DANYELZA and lasted between 0 and 24 days. Permanently discontinue DANYELZA in patients with urinary retention that does not resolve following discontinuation of opioids.

Hypertension

Hypertension occurred in 44% of patients in Study 201 and 28% of patients in Study 12-230 who received DANYELZA. Grade 3 or 4 hypertension occurred in 4% of patients in Study 201 and 7% of patients in Study 12-230. Four patients (6%) in Study 12-230 permanently discontinued DANYELZA due to hypertension. In both studies, most events occurred on the day of DANYELZA infusion and occurred up to 9 days following an infusion of DANYELZA.

Do not initiate DANYELZA in patients with uncontrolled hypertension. Monitor blood pressure during infusion, and at least daily on Days 1 to 8 of each cycle of DANYELZA and evaluate for complications of hypertension including RPLS. Interrupt DANYELZA infusion and resume at a reduced rate, or permanently discontinue DANYELZA based on the severity.

Embryo-Fetal Toxicity

Based on its mechanism of action, DANYELZA may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential, including pregnant women, of the potential risk to a fetus. Advise females of reproductive potential to use effective contraceptive during treatment with DANYELZA and for two months after the final dose.

ADVERSE REACTIONS

The most common adverse reactions in Studies 201 and 12-230 (≥25% in either study) were infusion-related reaction, pain, tachycardia, vomiting, cough, nausea, diarrhea, decreased appetite, hypertension, fatigue, erythema multiforme, peripheral neuropathy, urticaria, pyrexia, headache, injection site reaction, edema, anxiety, localized edema and irritability. The most common Grade 3 or 4 laboratory abnormalities (≥5% in either study) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased platelet count, decreased potassium, increased alanine aminotransferase, decreased glucose, decreased calcium, decreased albumin, decreased sodium and decreased phosphate.

Please click for full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

To review important state-specific disclosure information for licensed healthcare practitioners, please visit https://www.ymabs.com/information-for-prescribers

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In the battle against relapsed/refractory high-risk neuroblastoma...

- Reducing or eliminating disease in the **bone and bone marrow** is a goal of high-risk neuroblastoma treatment[2]
- DANYELZA is the **only FDA-approved therapy** indicated to treat high-risk neuroblastoma in the bone and/or bone marrow when response to induction or relapse therapy is incomplete[1]
- DANYELZA is a **structurally distinct** humanized anti-GD2 monoclonal antibody that provides another immunotherapeutic option[1,15]
- DANYELZA can offer the **flexibility** to be administered in either an **inpatient or outpatient** hospital setting, at the treating physician's discretion[12]

When response to induction or first relapse therapy is incomplete, **DEPLOY DANYELZA**

Administered at >50 US healthcare institutions[12]

For coverage and access information, visit ymabsconnect.com

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Learn more at danyelzahcp.com

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Y-mAbs Therapeutics, Inc.™