HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TROGARZO safely and effectively. See full prescribing information for TROGARZO.

TROGARZO® (ibalizumab-uiyk) injection, for intravenous use
Initial U.S. Approval: 2018

----------RECENT MAJOR CHANGES ----------
Contraindications (4) 04/2020
Warnings and Precautions, Hypersensitivity Including Infusion-Related and Anaphylactic Reactions (5.1) 04/2020

---------- INDICATIONS AND USAGE ----------
TROGARZO, a CD4-directed post-attachment HIV-1 inhibitor, in combination with other antiretroviral(s), is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen. (1)

---------- DOSAGE AND ADMINISTRATION ----------
TROGARZO is administered intravenously (IV) as a single loading dose of 2,000 mg followed by a maintenance dose of 800 mg every 2 weeks after dilution in 250 mL of 0.9% Sodium Chloride Injection, USP. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------
Injection: 200 mg/1.33 mL (150 mg/mL) in a single-dose vial. (3)

----------CONTRAINDICATIONS ----------
Prior hypersensitivity reaction to TROGARZO or any components of the product. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Hypersensitivity reactions including infusion-related reactions and anaphylactic reactions have been reported following infusion of TROGARZO. (5.1)
- Immune Reconstitution Inflammatory Syndrome (IRIS) has been reported in patients treated with combination antiretroviral therapies. (5.2)

---------- ADVERSE REACTIONS ----------
The most common adverse reactions (incidence ≥ 5%) were diarrhea, dizziness, nausea, and rash. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact THERA patient support™ at 1-833-23THERA (1-833-238-4372) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

---------- USE IN SPECIFIC POPULATIONS ----------
Lactation: Women infected with HIV should be instructed not to breastfeed due to the potential for HIV transmission. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TROGARZO, in combination with other antiretroviral(s), is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

TROGARZO is available in a single-dose, 2 mL vial containing 150 mg/mL of ibalizumab-uiyk. Each vial delivers approximately 1.33 mL containing 200 mg of ibalizumab-uiyk.

TROGARZO is administered intravenously (IV), after diluting the appropriate number of vials in 250 mL of 0.9% Sodium Chloride Injection, USP. Patients should receive a single loading dose of 2,000 mg followed by a maintenance dose of 800 mg every 2 weeks.

Dose modifications of TROGARZO are not required when administered with any other antiretroviral or any other treatments.

2.2 Preparation

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard vial if solution is cloudy, if there is pronounced discoloration or if there is foreign particulate matter.

See Table 1 for the appropriate number of vials required to prepare both the loading dose of 2,000 mg and the maintenance doses of 800 mg.

Table 1. Recommended TROGARZO Dose and Number of Vials Per Administration

TROGARZO Dose	TROGARZO Vials (Total Volume to be Withdrawn)
Loading dose of 2,000 mg	10 vials (13.3 mL)
Maintenance dose of 800 mg	4 vials (5.32 mL)

TROGARZO solution for infusion should be prepared by a trained medical professional using aseptic technique as follows:

- Remove the flip-off cap from the single-dose vial and wipe with an alcohol swab.
- Insert sterile syringe needle into the vial through the center of the stopper and withdraw 1.33 mL from each vial (NOTE: a small residual amount may remain in the vial, discard unused portion) and transfer into a 250

mL intravenous bag of 0.9% Sodium Chloride Injection, USP. Other intravenous diluents must not be used to prepare the TROGARZO solution for infusion.

- Once diluted, the TROGARZO solution should be administered immediately.
- If not administered immediately, store the diluted TROGARZO solution at room temperature (20°C to 25°C, 68°F to 77°F) for up to 4 hours, or refrigerated (2°C to 8°C, 36°F to 46°F) for up to 24 hours. If refrigerated, allow the diluted TROGARZO solution to stand at room temperature (20°C to 25°C, 68°F to 77°F) for at least 30 minutes but no more than 4 hours prior to administration.
- Discard partially used vials or empty vials of TROGARZO and any unused portion of the diluted TROGARZO solution.

2.3 Administration

Diluted TROGARZO solution should be administered by a trained medical professional.

Administer TROGARZO as an IV infusion in the cephalic vein of the patient's right or left arm. If this vein is not accessible, an appropriate vein located elsewhere can be used. Do not administer TROGARZO as an intravenous push or bolus.

The duration of the first infusion (loading dose) should be no less than 30 minutes. If no infusion-associated adverse reactions have occurred, the duration of the subsequent infusions (maintenance doses) can be decreased to no less than 15 minutes.

After the infusion is complete, flush with 30 mL of 0.9% Sodium Chloride Injection, USP.

All patients must be observed for 1 hour after completion of TROGARZO administration for at least the first infusion. If the patient does not experience an infusion-associated adverse reaction, the post-infusion observation time can be reduced to 15 minutes thereafter.

If a maintenance dose (800 mg) of TROGARZO is missed by 3 days or longer beyond the scheduled dosing day, a loading dose (2,000 mg) should be administered as early as possible. Resume maintenance dosing (800 mg) every 14 days thereafter.

3 DOSAGE FORMS AND STRENGTHS

Injection: 200 mg/1.33 mL (150 mg/mL) colorless to slightly yellow and clear to slightly opalescent solution with no visible particles in a single-dose vial.

4 CONTRAINDICATIONS

TROGARZO is contraindicated in patients with a prior hypersensitivity reaction to TROGARZO or any components of the product *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Including Infusion-Related and Anaphylactic Reactions

Hypersensitivity reactions including infusion-related reactions and anaphylactic reactions have been reported following infusion of TROGARZO during post-approval use. Symptoms may include dyspnea, angioedema, wheezing, chest pain, chest tightness, cough, hot flush, nausea, and vomiting. If signs and symptoms of an anaphylactic or other clinically significant hypersensitivity reaction occur, immediately discontinue administration of TROGARZO and initiate appropriate treatment. The use of TROGARZO is contraindicated in patients with known hypersensitivity with TROGARZO *[see Contraindications (4), Adverse Reactions (6.3)]*.

5.2 Immune Reconstitution Inflammatory Syndrome

Immune reconstitution inflammatory syndrome has been reported in one patient treated with TROGARZO in combination with other antiretrovirals. During the initial phase of combination antiretroviral therapies, patients whose immune systems respond may develop an inflammatory response to indolent or residual opportunistic infections, which may necessitate further evaluation and treatment.

6 ADVERSE REACTIONS

The following adverse drug reactions are discussed in other sections of the labeling:

- Immune Reconstitution Inflammatory Syndrome *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

A total of 292 patients with HIV-1 infection have been exposed to TROGARZO IV infusion.

Trial TMB-301

The primary safety assessment of TROGARZO is based on 24 weeks of data from Trial TMB-301. TMB-301 was a single-arm trial of TROGARZO which enrolled 40 heavily treatment-experienced subjects with multidrug resistant HIV-1 on a failing HIV treatment regimen. Subjects received a single 2,000 mg IV loading dose of TROGARZO followed seven days later by the initiation of an optimized background regimen (OBR) including at least one agent to which the subject's virus was susceptible. Two weeks after the TROGARZO loading dose, 800 mg of TROGARZO was administered IV. The IV administration of TROGARZO 800 mg was continued every 2 weeks through Week 25.

The most common adverse reactions (all Grades) reported in at least 5% of subjects were diarrhea, dizziness, nausea, and rash. Table 2 shows the frequency of adverse reactions occurring in 5% or more of subjects.

Table 2. Adverse Reactions (All Grades) Reported in ≥ 5% of Subjects Receiving TROGARZO and Optimized Background Regimen for 23 Weeks in Trial TMB-301

	% Subjects N=40
Diarrhea	8%
Dizziness	8%
Nausea	5%
Rash*	5%

*Includes pooled terms “rash”, “rash erythematous”, “rash generalized”, “rash macular”, “rash maculopapular”, and “rash papular”

Most (90%) of the adverse reactions reported were mild or moderate in severity. Two subjects experienced severe adverse reactions: one subject had a severe rash and one subject developed immune reconstitution inflammatory syndrome manifested as an exacerbation of progressive multifocal leukoencephalopathy.

Laboratory Abnormalities

Table 3 shows the frequency of laboratory abnormalities (≥ Grade 3) in Trial TMB-301.

Table 3. Selected Laboratory Abnormalities (≥ Grade 3) in Trial TMB-301

	% Subjects N=40
Bilirubin (≥ 2.6 x ULN)	5%
Direct Bilirubin (> ULN)	3%
Creatinine (> 1.8 x ULN or 1.5 x baseline)	10%
Blood Glucose (> 250 mg/dL)	3%
Lipase (> 3.0 x ULN)	5%
Uric Acid (> 12 mg/dL)	3%
Hemoglobin (< 8.5 g/dL)	3%
Platelets (< 50,000/mm^3)	3%
Leukocytes (< 1.5 x 10^9 cells/L)	5%
Neutrophils (< 0.6 x 10^9 cells/L)	5%

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to ibalizumab-uiyk in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

All subjects enrolled in clinical trial TMB-301 and trial TMB-202 (a Phase 2b clinical trial that studied TROGARZO administered intravenously as 2,000 mg every 4 weeks or 800 mg every 2 weeks; the safety and effectiveness of this dosing regimen has not been established), were tested for the presence of anti-ibalizumab antibodies throughout their participation. One sample tested positive with low titer anti-ibalizumab antibodies. No adverse reaction or reduced efficacy was attributed to the positive sample reported in this subject.

6.3 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of TROGARZO. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Immune system disorders: hypersensitivity reactions including infusion-related reactions and anaphylactic reactions have been reported *[see Warnings and Precautions (5.1)]*.
- Skin and subcutaneous tissue disorders: pruritus

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to TROGARZO during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1–800–258–4263.

Risk Summary

No adequate human data are available to establish whether or not TROGARZO poses a risk to pregnancy outcomes. Animal reproductive toxicology studies with ibalizumab-uiyk have not been conducted. Monoclonal antibodies, such as ibalizumab-uiyk, are transported across the placenta as pregnancy progresses; therefore,

ibalizumab-uiyk has the potential to be transmitted from the mother to the developing fetus. The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Risk Summary

The Centers for Disease Control and Prevention recommend that HIV-1-infected mothers in the United States not breastfeed their infants to avoid the risk of postnatal transmission of HIV-1 infection.

No data are available regarding the presence of TROGARZO in human milk, the effects on the breastfed child, or the effects on milk production. Human IgG is present in human milk, although published data indicate that antibodies in breast milk do not enter the neonatal or infant circulation system in substantial amounts. Because of the potential for HIV-1 transmission, instruct mothers not to breastfeed if they are receiving TROGARZO.

8.4 Pediatric Use

The safety and effectiveness of TROGARZO in pediatric patients have not been established.

8.5 Geriatric Use

No studies have been conducted with TROGARZO in geriatric patients.

11 DESCRIPTION

TROGARZO is a CD4-directed post-attachment HIV-1 inhibitor.

Ibalizumab-uiyk is a CD4 domain 2-directed humanized monoclonal antibody of immunoglobulin G (IgG) isotype 4 with a molecular weight of approximately 150 kDa. Ibalizumab-uiyk is produced by recombinant DNA technology in murine myeloma non-secreting 0 (NS0) cells.

TROGARZO Injection is a sterile, colorless to slightly yellow and clear to slightly opalescent solution with no visible particles in a single-dose vial for intravenous infusion. Each single-dose vial delivers approximately 1.33 mL containing 200 mg of ibalizumab-uiyk, and contains the following inactive ingredients: 10 mM L-histidine (2.06 mg), 0.045% polysorbate 80 (0.60 mg), 52 mM sodium chloride (4.04 mg) and 5.2% sucrose (69.2 mg). TROGARZO solution has a pH of 6.0 and contains no preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ibalizumab-uiyk is an HIV-1 antiretroviral drug *[see Microbiology (12.4)]*.

12.2 Pharmacodynamics

A clear trend was identified between exposure and response rate for the Phase 2b trial (TMB-202) which studied two different intravenous doses given at two different dosing intervals (every 4 weeks vs. every 2 weeks). The recommended intravenous dosing regimen consisting of a 2,000 mg loading dose followed by a maintenance dose of 800 mg every 2 weeks was selected on the basis of these results.

12.3 Pharmacokinetics

Ibalizumab-uiyk administered as a single agent exhibits nonlinear pharmacokinetics. Following single-dose administrations of ibalizumab-uiyk as 0.5 to 1.5-hour infusions, the area under the concentration-time curve increased in a greater than dose-proportional manner, clearance decreased from 9.54 to 0.36 mL/h/kg and elimination half-life increased from 2.7 to 64 hours as the dose increased from 0.3 to 25 mg/kg. The volume of distribution of ibalizumab-uiyk was approximately that of serum volume, at 4.8 L.

Following the recommended dose regimen (a single loading dose of 2,000 mg followed by a maintenance dose of 800 mg every 2 weeks), ibalizumab-uiyk concentrations reached steady-state levels after the first 800 mg maintenance dose with mean concentrations over 30 mcg/mL throughout the dosing interval.

Specific Populations

A population pharmacokinetic analysis was performed to explore the potential effects of selected covariates (age, body weight, sex, baseline $CD4^+$ cell count) on ibalizumab-uiyk pharmacokinetics. The result suggests that ibalizumab-uiyk concentration decreases as body weight increases; however, the effect is unlikely to impact virologic outcome and does not warrant a dose adjustment.

Pediatric/Geriatric Patients: Ibalizumab-uiyk pharmacokinetics have not been evaluated in pediatric or geriatric patients [*see Use in Specific Populations (8.4, 8.5)*]

Renal/Hepatic Impairment: No formal studies were conducted to examine the effects of either renal or hepatic impairment on the pharmacokinetics of ibalizumab-uiyk. Renal impairment is not anticipated to impact the pharmacokinetics of ibalizumab-uiyk.

Drug Interaction studies

No drug interaction studies have been conducted with ibalizumab-uiyk. Based on ibalizumab-uiyk's mechanism of action and target-mediated drug disposition, drug-drug interactions are not expected.

12.4 Microbiology

Mechanism of Action

Ibalizumab-uiyk, a recombinant humanized monoclonal antibody, blocks HIV-1 from infecting $CD4^+$ T cells by binding to domain 2 of CD4 and interfering with post-attachment steps required for the entry of HIV-1 virus particles into host cells and preventing the viral transmission that occurs via cell-cell fusion.

Ibalizumab-uiyk Does Not Impact CD4 Function

The binding specificity of ibalizumab-uiyk to domain 2 of CD4 allows ibalizumab-uiyk to block viral entry into host cells without causing immunosuppression. Epitope mapping studies indicate that ibalizumab-uiyk binds to a conformational epitope located primarily in domain 2 of the extracellular portion of the CD4 receptor. This epitope is positioned on the surface of CD4 opposite to the site in domain 1 that is required for CD4 binding of the MHC class II molecules and therefore does not interfere with CD4-mediated immune functions. Additionally, ibalizumab-uiyk does not interfere with gp120 attachment to CD4.

Antiviral Activity

Ibalizumab-uiyk inhibits the replication of CCR5- and CXCR4-tropic laboratory strains and primary isolates of HIV-1 in phytohemagglutinin stimulated peripheral blood lymphocytes. The median EC_{50} value (50% effective concentration) for ibalizumab-uiyk against HIV-1 group M isolates (subtypes A, B, C, D, E, or O) was 8 ng/mL (n = 15, range of 0.4 to 600 ng/mL) in cell culture, with lower susceptibility observed in macrophage-tropic HIV-1 strains (BaL, JR-CSF, YU2, and ADA-M). In a single-cycle infection assay, ibalizumab-uiyk inhibited 17 clinical isolates of subtype B with a median EC_{50} value of 12 ng/mL (range of 8.8 to 16.9 ng/mL; mean 12 ± 3 ng/mL) and a median maximum percentage inhibition (MPI) of 97% (range of 89 to 99%; mean 97 ± 3%). Three CCR5-tropic clinical isolates from subtypes B, C, and D, were inhibited with EC_{50} values ranging from 59-66 ng/mL and 3 CXCR4-tropic clinical isolates from subtypes B, C, and D, with EC_{50} values ranging from 44-59 ng/mL.

Antiviral Activity in Combination with Other Antiviral Agents

No antagonism was observed when PBMCs or MAGI-CCR5 cells infected with the subtype B Ba-L or ADA variants of HIV-1 were incubated with ibalizumab-uiyk in combination with the CCR5 co-receptor antagonist maraviroc or when PBMCs infected with the subtype B HT/92/599 variant of HIV-1 were incubated with ibalizumab-uiyk in combination with the gp41 fusion inhibitor enfuvirtide; a nonnucleoside reverse transcriptase inhibitor (efavirenz); nucleoside analog reverse transcriptase inhibitors (abacavir, didanosine, emtricitabine, tenofovir, or zidovudine); or a protease inhibitor (atazanavir).

Antiviral Activity in Antiretroviral-Resistant Virus

Subjects enrolled in TMB-301 were heavily treatment-experienced subjects infected with multidrug resistant HIV-1. Ibalizumab-uiyk inhibited 38 baseline isolates at a median EC_{50} value of 31 ng/mL (range of 13 to 212 ng/mL; mean 39 ± 35 ng/mL) with a median MPI of 97% (range of 41-100%; mean 91 ± 14%). For 10 subjects in TMB-301 who failed treatment, at the time of failure the median ibalizumab-uiyk EC_{50} value was 566 ng/mL

(range of 148 to >54,900 ng/mL; mean 11,768 ± 21,650 ng/mL) representing an EC_{50} value shift of >18-fold. For the HIV-1 derived from the same subjects, the median MPI was 55% (range of 43-72%; mean 56 ± 8%) representing a 42 percentage point reduction.

Decreased Susceptibility

Decreased susceptibility to ibalizumab-uiyk, as defined by a decrease in MPI, has been observed in some subjects experiencing virologic failure and may be associated with genotypic changes in the HIV-1 envelope coding sequence that results in the loss of potential N-linked glycosylation sites (PNGS) in the V5 loop of gp120. The clinical significance of decreased susceptibility to ibalizumab-uiyk has not been established.

Cross-Resistance

Phenotypic and genotypic test results revealed no evidence of cross-resistance between ibalizumab-uiyk and any of the approved classes of anti-retroviral drugs (CCR5 co-receptor antagonists, gp41 fusion inhibitors, integrase strand transfer inhibitors [INSTIs], non-nucleos(t)ide reverse transcriptase inhibitors [NNRTIs], nucleos(t)ide reverse transcriptase inhibitors [NRTIs], or protease inhibitors [PIs]). Ibalizumab-uiyk is active against HIV-1 resistant to all approved antiretroviral agents and exhibits antiretroviral activity against R5-tropic, X4-tropic, and dual-tropic HIV-1.

Decreased susceptibility to ibalizumab-uiyk following multiple dose administrations of ibalizumab-uiyk has been observed in some subjects. Cell culture studies performed with HIV-1 variants with reduced susceptibility to ibalizumab-uiyk indicate that phenotypic changes associated with resistance to ibalizumab-uiyk do not alter susceptibility to other approved agents and do not result in the selection of CD4-independent viral isolates.

CD4 Polymorphisms and Ibalizumab-uiyk Activity

CD4 polymorphisms reported in public databases were analyzed to determine if any naturally occurring amino acid substitutions in the CD4 molecule from different human populations would potentially impact the antiviral activity of ibalizumab-uiyk. None of the known CD4 polymorphisms are likely to have an impact on ibalizumab-uiyk binding to CD4.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis, mutagenesis, and reproductive toxicology studies with ibalizumab-uiyk have not been conducted.

14 CLINICAL STUDIES

Trial TMB-301:

Trial TMB-301 was a single arm, multicenter clinical trial conducted in 40 heavily treatment-experienced HIV-

infected subjects with multidrug resistant HIV-1. Subjects were required to have a viral load greater than 1,000 copies/mL and documented resistance to at least one antiretroviral medication from each of three classes of antiretroviral medications as measured by resistance testing. Subjects must have been treated with antiretrovirals for at least 6 months and be failing or had recently failed (i.e., in the last 8 weeks) therapy.

The trial was composed of three discrete periods:

- Control period (Day 0 to Day 6): Subjects were either monitored on their current failing therapy or received no therapy if they had failed and discontinued treatment within the 8 weeks preceding screening. This was an observational period to establish baseline HIV viral load.
- Functional monotherapy period (Day 7 to Day 13): All subjects received a 2,000 mg loading dose of TROGARZO on Day 7. Subjects on a failing ART regimen continued to receive their failing regimen in addition to the loading dose of TROGARZO. This period was to establish the virologic activity of TROGARZO.
- Maintenance period (Day 14 to Week 25): On Day 14 of the treatment period, viral load was assessed for the primary endpoint, and thereafter the background regimen was optimized to include at least one drug to which the subject's virus was susceptible. The use of an investigational drug(s) as a component of the optimized background regimen was allowed. Beginning at Day 21, an 800 mg maintenance dose of TROGARZO was administered every two weeks through Week 25. This period was to establish the safety and durability of virologic suppression of TROGARZO when used in combination with an optimized background regimen.

The majority of subjects in Trial TMB-301 were male (85%), white (55%) and between 23 and 65 years of age (mean [SD] age: 50.5 [11.0] years). At Baseline, median viral load and $CD4^+$ T cell counts were 35,350 copies/mL and 73 cells/mm^3, respectively. The subjects were heavily treatment-experienced: 53% of participants had been treated with 10 or more antiretroviral drugs prior to trial enrollment; 98% percent had been treated with NRTIs, 98% with PIs, 80% with NNRTIs, 78% with INSTIs, 30% with gp41 fusion inhibitors, and 20% with CCR5 co-receptor antagonists.

The primary efficacy endpoint was the proportion of subjects achieving a ≥ 0.5 $\log_{10}$ decrease in viral load from the beginning to the end of the "Functional monotherapy period" as compared to the proportion of subjects achieving a ≥ 0.5 $\log_{10}$ decrease from the beginning to the end of the "Control period", as defined above. The results of the primary endpoint analysis are shown in Table 4 below.

Table 4. Proportion of Subjects Achieving a ≥ 0.5 log_{10} Decrease in Viral Load at the End of the Control and Functional Monotherapy Periods

	Proportion of Subjects Achieving a ≥ 0.5 log_{10} Decrease in Viral Load N=40	**95% CI***
End of Control Period	3%	(0.06%, 13%)
End of Functional Monotherapy Period	83%	(67%, 93%)

*exact 95% confidence interval

$p < 0.0001$ based on McNemar's test comparing the proportion of subjects achieving ≥ 0.5 log_{10} decrease in viral load at the end of the control and functional monotherapy periods.

At Week 25, viral load <50 and <200 HIV-1 RNA copies/mL was achieved in 43% and 50% of subjects, respectively. Fifty-five percent of subjects had a ≥ 1 log_{10} reduction in viral load, and 48% of subjects had a ≥ 2 log_{10} reduction in viral load at Week 25. An increase in the mean and median number of CD4+ T-cells (44 cells/mm^3 and 17 cells/mm^3, respectively) was observed from Baseline to Week 25. Week 25 outcomes are shown in Table 5 and Table 6.

Table 5. Trial TMB 301 Virologic Outcomes (Snapshot Algorithm) at Week 25

	TROGARZO (N=40)
HIV RNA < 50 copies/mL at Week 25	43%
HIV RNA ⩾ 50 copies/mL at Week 25*	45%
HIV RNA < 200 copies/mL at Week 25	50%
HIV RNA ⩾ 200 copies/mL at Week 25**	38%
No virologic data at Week 25	
Discontinued due to AE or death	13%

*included subjects who had ≥ 50 copies/mL in the Week 25 window, subjects who discontinued study drug due to lack of efficacy, and subjects who discontinued study drug for reasons other than an AE, death and at the time of discontinuation had a viral value ≥ 50 copies/mL

**included subjects who had ≥ 200 copies/mL in the Week 25 window, subjects who discontinued study drug due to lack of efficacy, and subjects who discontinued study drug for reasons other than an AE, death and at the time of discontinuation had a viral value ≥ 200 copies/mL

Table 6. Virologic Response at Week 25 by Baseline CD4 Cell count, Viral Load, Integrase Inhibitor Resistance and OSS*

	Subjects achieving <50 HIV-1 RNA copies/mL (%)	Subjects achieving <200 HIV-1 RNA copies/mL (%)
CD4 Cell Counts		
<50 (n=17)	18	24
50-200 (n=10)	60	70
>200 (n=13)	62	69
Viral Load		
≤100,000 (n=33)	49	58
>100,000 (n=7)	14	14
Resistance		
With INSTI Resistance (n=27)	41	44
Without INSTI Resistance (n=13)	46	62
OSS		
0 (n=5)	20	20
1 (n=12)	42	50
2 (n=18)	50	61
3 (n=3)	33	33
4 (n=2)	50	50

*OSS – Overall Susceptibility Score. The OSS indicates the number of fully active drugs in a subject's OBR based on both current and available historical resistance test results. Demonstrating drug susceptibility by both genotypic and phenotypic testing was required, when testing by both methods was technically feasible. As an example, an OSS of 2 would indicate that the HIV-1 isolate tested was fully susceptible to two drugs in the OBR.

16 HOW SUPPLIED/STORAGE AND HANDLING

TROGARZO (ibalizumab-uiyk) injection is a sterile colorless to slightly yellow and clear to slightly opalescent solution with no visible particles for intravenous infusion. It is packaged in a single-dose 2 mL clear glass vial containing 200 mg/1.33 mL (150 mg/mL) of ibalizumab-uiyk.

TROGARZO is available in a carton containing two single-dose vials (NDC 62064-122-02).

Store vials under refrigeration at 2 to 8ºC (36-46 ºF). Do not freeze and protect from light.

Once diluted, the TROGARZO solution should be administered immediately *[see Dosage and Administration (2.2)]*.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Hypersensitivity

Advise patients of the risk of hypersensitivity reactions including anaphylaxis. Instruct patients to seek immediate medical attention if signs or symptoms of hypersensitivity occur or are suspected. Advise patients who have had clinically significant hypersensitivity reactions to TROGARZO that they should not receive TROGARZO *[see Contraindications (4), Warnings and Precautions (5.1)]*.

Immune Reconstitution Syndrome

Immune Reconstitution Inflammatory Syndrome: Advise patients that immune reconstitution syndrome has been reported in a patient receiving TROGARZO and to inform their health care provider immediately of any symptoms of infection *[see Warnings and Precautions (5.2)]*.

Important Administration Information

Advise the patient it is important to receive TROGARZO injections every two weeks as recommended by their healthcare professional and not to change the dosing schedule of TROGARZO or any antiretroviral medication without consulting their healthcare provider. Advise the patient to contact their healthcare provider immediately if they stop taking TROGARZO or any other drug in their antiretroviral regimen [*see Dosage and Administration (2)]*.

Pregnancy Exposure Registry

Inform patients that there is an antiretroviral pregnancy registry that monitors fetal outcomes of pregnant women exposed to TROGARZO *[see Use in Specific Populations (8.1)]*.

Lactation

Instruct women with HIV-1 infection not to breastfeed because HIV-1 can be passed to the baby in breast milk *[see Use in Specific Populations (8.2)]*.

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PATIENT INFORMATION
TROGARZO® (tro-gar-zo)
(ibalizumab-uiyk)
injection

What is TROGARZO?

TROGARZO is a prescription medicine that is used with other antiretroviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) infection in adults who:

- have received several anti-HIV-1 regimens in the past, **and**
- have HIV-1 virus that is resistant to many antiretroviral medicines, **and**
- who are failing their current antiretroviral therapy

HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).

It is not known if TROGARZO is safe and effective in children.

Do not receive TROGARZO if you have had an allergic reaction to TROGARZO or any of the ingredients in TROGARZO. See the end of this leaflet for a complete list of ingredients in TROGARZO.

Before you receive TROGARZO, tell your healthcare provider about all of your medical conditions, including if you:

- are pregnant or plan to become pregnant. It is not known if TROGARZO may harm your unborn baby. Tell your healthcare provider if you become pregnant during treatment with TROGARZO.

  Pregnancy Registry: There is a pregnancy registry for women who take antiretroviral medicines, including TROGARZO during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk with your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. Do not breastfeed if you are receiving TROGARZO.
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
  - It is not known if TROGARZO passes into breast milk.

  Talk with your healthcare provider about the best way to feed your baby during treatment with TROGARZO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive TROGARZO?

- You will receive TROGARZO by your healthcare provider as an infusion given into your vein over 15 to 30 minutes. A healthcare provider will monitor you during the TROGARZO infusion and for a period of time after your infusion.
- You will receive TROGARZO every two weeks.
- It is important that you receive TROGARZO every two weeks as instructed by your healthcare provider. Do not change the schedule of your TROGARZO infusions or any of your antiretroviral medicines without talking to your healthcare provider first.
- **Tell your healthcare provider right away if you stop receiving TROGARZO infusions or stop taking any other antiretroviral medicines.**

What are the possible side effects of TROGARZO?

TROGARZO can cause serious side effects, including:

- **Allergic reactions.** TROGARZO can cause allergic reactions, including serious reactions, during and after infusion. Tell your healthcare provider or nurse, or get medical help right away if you get any of the following symptoms of an allergic reaction:
  - trouble breathing
  - swelling in your throat
  - wheezing
  - chest pain
  - chest tightness
  - cough
  - hot flush
  - nausea
  - vomiting

- **Changes in your immune system (Immune Reconstitution Inflammatory Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system might get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your health care provider right away if you start having new symptoms after receiving TROGARZO.

The most common side effects of TROGARZO include:

- o diarrhea
- o dizziness
- o nausea
- o rash

These are not all the possible side effects of TROGARZO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

You may also report side effects to THERA patient support™ at 1-833-23THERA (1-833-238-4372).

General information about the safe and effective use of TROGARZO.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your healthcare provider for information about TROGARZO that is written for health professionals.

What are the ingredients in TROGARZO?

Active ingredient: ibalizumab-uiyk

Inactive ingredients: L-histidine, polysorbate 80, sodium chloride, and sucrose.

TROGARZO does not contain any preservative.

Manufactured by: Theratechnologies Inc., 2015 Peel Street, 5th Floor, Montréal, Québec Canada H3A 1T8

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For more information, call THERA patient support™ 1-833-23THERA (1-833-238-4372) or go to www.TROGARZO.com.

THERA technologies

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 04/2020