# Storage, Handling, and Administration Guidance

# Investigational Medicinal Product: FT576

**For Intravenous (IV) Infusion**

**Version:** 1.0

**Version Date:** 18 December 2020

## Protocol FT576-101:

A Phase I Study of FT576 as Monotherapy and in Combination with Daratumumab in Subjects with Relapsed/Refractory Multiple Myeloma

**IND Sponsor:**
Fate Therapeutics, Inc.
3535 General Atomics Court, Suite 200
San Diego, CA 92121

## Signature Approval Page

| Name and Title | Signature and Date |
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# 1. CONTACT INFORMATION

| Name | Email Address |
|---|---|
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| Fate Clinical Trial Manager: Monica Roy | monica.roy@fatetherapeutics.com |
| Fate Manufacturing | manufacturing@fatetherapeutics.com |

# 2. OVERVIEW

| | |
|---|---|
| **Caution:** | FT576 investigational medicinal product (IMP) is for clinical trial use only and to be administered under the oversight of the Principal Investigator (PI) or qualified designee. FT576 may only be used for subjects consented to the FT576-101 protocol. |
| **Description of Drug Product:** | FT576 drug product comprises allogeneic natural killer (NK) cells, derived from a clonal, CD38-knockout, human-induced pluripotent stem cell (iPSC) line that expresses anti-B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR), high-affinity, non-cleavable CD16 (hnCD16), and interleukin (IL)-15/IL-15 receptor fusion protein (IL-15RF). FT576 cells are suspended in infusion medium containing albumin (human) and DMSO. Dosing is based on BCMA CAR expression, where ≥80.0% of administered FT576 viable cells express BCMA CAR. FT576 will be provided by the Sponsor in a cryopreserved bag and thawed at the site of administration. FT576 must be administered using an IV administration set with an in-line filter. |
| **Storage:** | FT576 must be stored in the vapor phase of liquid nitrogen ($VPLN_2$) at ≤-150°C, in a continuously temperature-monitored and alarmed $VPLN_2$ freezer in a controlled-access room with limited personnel access. Temperature excursions up to -135°C for 10 minutes due to normal equipment use (e.g., opening and closing of the storage unit) are allowed. If the temperature warms to >-150°C up to -135°C for >10 minutes or >-135°C for any amount of time, Fate Therapeutics (FATE) must be notified (see Section 12.2 for further details). $VPLN_2$ temperature logs and calibration records must be available to Site Monitors for inspection. |

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| **Product Labeling:** | FT576 labeling will include product name, volume, manufacturer, date of manufacture, Product Lot #, Bag ID #, and number of viable cells (VC). The label will also contain the following statement: "Caution: New Drug – Limited by United States Law to Investigational Use." See Appendix 1 for an example of FT576 labeling. |
| **Product Appearance:** | Upon thaw, FT576 should be a colorless to yellow suspension of cells. |
| **Dose and Schedule:** | FT576 will be administered in a 28-day treatment cycle as follows:<br>• Regimen A: As a single dose on Day 1<br>• Regimen A1: As a fractionated dose on Days 1 and 15<br>• Regimen B: As a single dose on Day 1 in combination with daratumumab<br>• Regimen B1: As a fractionated dose on Days 1 and 15 in combination with daratumumab<br><br>For Regimens A and B, the planned single dose levels (DL) of FT576 on Day 1, based on VC, considered for this study are as follows:<br>• DL0: $5 \times 10^7$ FT576 VC/dose (1 bag at $5 \times 10^7$ FT576 VC/bag)<br>• DL1: $1 \times 10^8$ FT576 VC/dose (2 bags at $5 \times 10^7$ FT576 VC/bag)<br>• DL2: $3 \times 10^8$ FT576 VC/dose (1 bag at $3 \times 10^8$ FT576 VC/bag)<br>• DL3: $6 \times 10^8$ FT576 VC/dose (2 bags at $3 \times 10^8$ FT576 VC/bag)<br>• DL4: $1.5 \times 10^9$ FT576 VC/dose (3 bags at $5 \times 10^8$ FT576 VC/bag)<br>• DL4A: $1 \times 10^9$ FT576 VC/dose (2 bags at $5 \times 10^8$ FT576 VC/bag)<br>• DL5: Not applicable<br>• DL5A: Not applicable<br><br>For Regimens A1 and B1, the planned fractionated dose levels of FT576 on Day 1 and Day 15, based on VCs, considered for this study are as follows:<br>• DL0: Not applicable<br>• DL1: Day 1 = $5 \times 10^7$; Day 15 = $5 \times 10^7$ FT576 VC/dose (1 bag at $5 \times 10^7$ FT576 VC/bag) |

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|---|---|
| | • DL2: Day 1 = $1.5 \times 10^8$; Day 15 = $1.5 \times 10^8$ FT576 VC/dose (3 bags at $5 \times 10^7$ FT576 VC/bag)<br>• DL3: Day 1 = $3 \times 10^8$; Day 15 = $3 \times 10^8$ FT576 VC/dose (1 bag at $3 \times 10^8$ FT576 VC/bag)<br>• DL4: Day 1 = $6 \times 10^8$; Day 15 = $6 \times 10^8$ FT576 VC/dose (2 bags at $3 \times 10^8$ FT576 VC/bag)<br>• DL4A: Not applicable<br>• DL5: Day 1 = $1.5 \times 10^9$; Day 15 = $1.5 \times 10^9$ FT576 VC/dose (3 bags at $5 \times 10^8$ FT576 VC/bag)<br>• DL5A: Day 1 = $1 \times 10^9$; Day 15 = $1 \times 10^9$ FT576 VC/dose (2 bags at $5 \times 10^8$ FT576 VC/bag)<br><br>Retreatment may be given per the study protocol. Dosing is based on BCMA CAR expression, where ≥80.0% of administered FT576 viable cells express BCMA CAR. |
| **Route of Administration:** | FT576 is thawed and administered as an IV infusion via gravity. The following are acceptable forms of IV access in order of preference:<br>1. Central venous catheter (CVC; e.g., Hickman)<br>– **Do not use implanted ports.**<br>2. Non-valved peripherally inserted central catheter (PICC)<br>3. Large-bore (18-gauge) straight IV needle<br>– Use of this form of IV administration should be considered as a last resort if IV administration by CVC or non-valved PICC is not possible.<br><br>FT576 must be administered using an intravenous administration set with an in-line filter. The B. Braun SafeLine® Y-Type Blood Set (REF NF5140), Baxter CLEARLINK System (2C8750), or FATE-approved equivalent, should be used for FT576 administration (see Section 10, Appendix 2, and Appendix 3 for additional details). |

# 3. SUPPLIES

## 3.1. Items Supplied by Fate Therapeutics (FATE)

- FT576 drug product
- Barkey Plasmatherm warming device
  - A water bath and/or use of alternate equipment and procedures approved by FATE is acceptable.
- Optional cart for Plasmatherm storage and transport

## 3.2. Items Supplied by the Clinical Study Site

- Pre-filled sterile IV bag of 0.9% sodium chloride for injection (USP)
- $VPLN_2$ freezer and racks for storing FT576 (racks may be supplied by FATE upon site request)
- Validated puncture-proof transport container that maintains temperature at ≤-150°C
- Cryogenic personal protective equipment such as gloves, apron, lab coat, face shield, and eye protection
- Sterile overwrap bag for thawing cells
- Alcohol wipes and non-sterile gloves
- B. Braun SafeLine® Y-Type Blood Set (REF NF5140), Baxter CLEARLINK System (2C8750), or FATE-approved equivalent

# 4. FT576 PRECAUTIONS

- Do not irradiate FT576.
- Each FT576 bag is single use only.
- Do not administer FT576 using an IV pump.
- Do not use FT576 after expiration date (if applicable).
- Administration of FT576 must be within 40-84 hours after the last dose of fludarabine.
- Do not use FT576 if held for more than 60 minutes following completion of thaw.
- Contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1) immediately if:
  - upon visual inspection of thawed FT576, the bag is found to have visible defects, leaks, or is compromised in any manner;
  - upon visual inspection of thawed FT576, product does not match “Product Appearance” as described in Section 2;

- upon visual inspection of thawed FT576, visible foreign particulate matter (i.e., non-cellular material) is observed; or
- FT576 is thawed and not administered.

Refer to the Study FT576-101 protocol for study conduct information. Refer to the FT576 Investigator's Brochure for product profile, including safety information.

# 5. DRUG SHIPMENT, SUPPLY, AND RESUPPLY

## 5.1. Shipment

- FT576 drug product is only for use in FATE-sponsored clinical trial(s) and will be shipped to clinical study sites by a FATE-approved storage and distribution vendor(s).
- Prior to FT576 shipment, clinical sites will receive an e-mail notification containing courier tracking information from Cryoport or other approved cold chain logistics vendor(s).
- FT576 bags are cryopreserved within cassettes for storage in VPLN$_2$ at clinical study sites. See Appendix 1 for a sample image of the cassette.
- FT576 shipments will arrive at clinical study sites in a VPLN$_2$ shipper.
- Any issues related to shipping or resupply should be directed to the Fate Clinical Trial Manager (see Section 1) and the Site Monitor.

## 5.2. Supply of FT576

- FT576 may be provided in a single shipper or in multiple shipments, depending on expected enrollment projections and clinical site storage capabilities.
- The Fate Clinical Trial Manager, or designee, will complete the Notification of Subject Enrollment form (see Appendix 4) at the beginning of each treatment cycle and provide to Fate Manufacturing and the study site.
- Bags are not subject-specific.

## 5.3. Resupply of FT576

- The supply of FT576 will be closely monitored by FATE. Resupply will be triggered when ≤4 bags of FT576 remain on site. Supply may be replenished sooner if site storage capacity allows.
- Sites are not required to take any action for resupply; however, contact the Site Monitor with resupply questions.
- Contact both the Fate Clinical Trial Manager (see Section 1) and the Site Monitor should you require an expedited shipment or if there are problems or questions regarding the shipment.

# 6. RECEIPT AND STORAGE OF FT576

Details regarding receipt and storage of FT576 are provided below. For information on managing potential drug product quality complaints upon receipt and during storage, please refer to Section 12.

## 6.1. Receipt

- Upon receipt of the $VPLN_2$ shipper, open the outer lid and remove the packing slip.
- Check the contents of the shipper against the packing slip. The shipping documentation should remain on file with other IMP documentation at the clinical study site.
- Carefully open cassettes and confirm the product label against the packing slip. Visually inspect each FT576 bag to ensure it is not compromised in any manner and that there are no visible defects or leaks. Use care to conduct this inspection under temperature control to avoid temperature excursions.
- Confirm that the contents arrived frozen.
- Once the temperature monitoring data has been received, file it with the Fate Investigational Medicinal Product Accountability Log (see Appendix 5).
- Document the **Product Lot #**, **Bag ID #**, **Date Product Received**, and the **Product Received By (**name) on the Fate Investigational Medicinal Product Accountability Log (see Appendix 5). See Appendix 1 for samples of FT576 labeling.

## 6.2. Storage

- FT576 is stored in $VPLN_2$ at ≤-150ºC.
- To avoid temperature excursions, quickly transfer FT576 from its shipping container to the $VPLN_2$ storage unit; this should take no more than 1-3 minutes.

# 7. TRANSPORT OF FT576 TO CLINICAL UNIT

Transport FT576 to the clinical unit (e.g., bedside for subject administration) in a site-validated, puncture-proof transport container. Follow institutional guidelines and/or site Standard Operating Procedures (SOPs).

# 8. DIRECTIONS FOR PREPARATION

All dose preparation is to be performed by qualified and trained personnel using aseptic technique.

## 8.1. Thawing Using the Barkey Plasmatherm Warming Device

### 8.1.1. Set-up

- The Barkey Plasmatherm warming device may be used for thawing of cryopreserved drug products for FATE clinical trials.
- Follow institutional guidelines and/or SOPs for electrical safety, inventory control, and installation requirements of new equipment.
- Initial Set-up: Follow the manufacturer's instructions for using the Barkey Plasmatherm.
- Performance Check: Although the device will arrive calibrated, it is recommended that a simple check of calibration is conducted after initial set-up following institutional guidelines and/or SOPs.
  - Place a thermometer between the water cushions during operation at 37ºC. The thermometer should read 37ºC ± 1.0ºC when the device is properly calibrated.
  - If the calibration check does not pass, contact Fate Manufacturing (see Section 1).

### 8.1.2. Thawing

When multiple FT576 bags will be administered, sequentially thaw and administer bags.

1. The Plasmatherm should be cleaned and disinfected following manufacturer's and/or institutional SOPs prior to thawing and after administering product to each subject.
2. Once on the infusion floor, turn on the Barkey Plasmatherm warming device using the device "On/Off" button at the 12 o'clock position on the operating panel.
   - Refer to the manufacturer's instructions for opening the heating chamber and proper placement of products.
3. Select the Plasma program by pressing the button next to Plasma on the UPPER RIGHT CORNER of the operating panel's display. Refer to the manufacturer's instructions for a description of program selection.
   - The program will start automatically by filling the heating cushions with warmed water.
   - The default automated shutdown time for the Plasma program is 15 minutes.

The automated shutdown time can be extended by pressing the button below the clock icon with a plus (+) sign on the BOTTOM RIGHT CORNER of the display.

- The paddle will begin to operate 2 minutes into the program and create gentle agitation.

4. Once the temperature has reached 37ºC, place the frozen FT576 bag in a sterile overwrap bag for thawing.

5. Place the overwrapped FT576 bag between the water-filled cushions in the Plasmatherm and close the lid.
6. After 3-5 minutes of thawing, open the device lid and inspect the product to confirm that there is no visible ice in the infusion bag and the infusion bag is cool to the touch.
   - If the product cells are still slightly frozen, place the cells back in the Plasmatherm between the cushions and continue to thaw for an additional 1-2 minutes until there is no visible ice in the infusion bag and the infusion bag is cool to the touch.
7. Remove the bag from the device.
8. Visually inspect the contents of the thawed FT576 bag for presence or absence of visible foreign particulate matter (i.e., non-cellular material) or visible cellular clumps. Document the results of visual inspection on the Fate Investigational Medicinal Product Administration Record (Appendix 6).
   - **If visible foreign particulate matter is seen**, do not use that FT576 bag for infusion. Immediately quarantine the FT576 bag and contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1).
   - **If visible cellular clumps are seen**, gently massage the product to dissipate and continue with infusion. Small clumps of cellular material should disperse with gentle massaging. Do not infuse FT576 if clumps are not dispersed.
9. If leakage is noted during the thaw process, do not use that FT576 bag for infusion. Immediately quarantine the FT576 bag and contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1).
10. If no issues, proceed with administering FT576 (Section 10).
11. Document the thaw start and end time of each FT576 bag and the visual inspection on the Fate Investigational Medicinal Product Administration Record (Appendix 6).

### 8.2. Thawing Using a FATE-Approved Water Bath

When multiple FT576 bags will be administered, sequentially thaw and administer bags.

1. The water bath should be cleaned and disinfected following institutional SOPs prior to thawing and after administering product to each subject.
2. For sites using a 37°C water bath, place product bag in an overwrap, remove as much air as possible, and seal bag.
3. Gently massage the bag while thawing.
4. After 3-5 minutes of thawing, inspect the product to confirm that there is no visible ice in the infusion bag and the infusion bag is cool to the touch.
   - If the product cells are still slightly frozen, place the cells back in the water bath and continue to thaw for an additional 1-2 minutes until there is no visible ice in the infusion bag and the infusion bag is cool to the touch.

5. Remove the bag from the water bath.
6. Visually inspect the contents of the FT576 bag for presence or absence of visible cellular clumps or visible foreign particles. Document the results of visual inspection on the Fate Investigational Medicinal Product Administration Record (Appendix 6).
   - Inspect the thawed product for visible foreign particulate matter (i.e., non-cellular material).
   - If any visible cellular clumps are noted after product thaw, gently massage the product to dissipate. Small clumps of cellular material should disperse with gentle massaging. Do not infuse FT576 if clumps are not dispersed.
7. If leakage is noted during the thaw process, do not use that FT576 bag for infusion. Immediately quarantine the FT576 bag and contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1).
8. If no issues, proceed with administering FT576 (Section 10).
9. Document the thaw start and end time and visual inspection of each FT576 bag on the Fate Investigational Medicinal Product Administration Record (Appendix 6).

# 9. STABILITY OF THAWED FT576

**FT576 should be administered as soon as practicable after thawing, preferably within 20 minutes. Do not use the drug product contents if held for more than 60 minutes following completion of thaw.**

Contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1) if administration cannot be initiated within 60 minutes following completion of thaw.

# 10. ADMINISTRATION OF FT576

## 10.1. IV Access

The following are acceptable forms of IV access in order of preference:

1. CVC (e.g., Hickman)
   - **Do not use implanted ports.**
2. Non-valved PICC
3. Large-bore (18-gauge) straight IV needle
   - Use of this form of IV administration should be considered a last resort if IV administration by CVC or non-valved PICC is not possible.

**NOTE: Do not use an IV pump during FT576 administration.**

## 10.2. Administration

Administer pre- and post-study medications relative to FT576 administration in accordance with the Study FT576-101 protocol.

- FT576 should be administered under the supervision of a qualified healthcare professional.
- FT576 must be administered using an intravenous administration set with an in-line filter.
  - The B. Braun SafeLine® Y-Type Blood Set (REF NF5140; see Appendix 2) or Baxter CLEARLINK System (2C8750; see Appendix 3) should be used for FT576 administration. The Blood Set should be primed with normal saline (0.9% sodium chloride in water) prior to spiking the bag containing FT576.
  - An equivalent in-line filter of comparable composition and filter pore size may be used with prior written authorization from FATE.

**NOTE: Do not administer FT576 in the same IV tubing concurrently with products or solutions other than 0.9% sodium chloride for injection (USP).**

Depending on the type of Y-type blood set used, follow the directions for priming and set up per the applicable package instructions (refer to Appendix 2 for B. Braun SafeLine® Y-Type Blood Set instructions; refer to Appendix 3 for Baxter CLEARLINK System instructions).

Instructions for FT576 administration (after priming and set up have been performed) are as follows:

1. Close all roller clamps on the infusion set.
2. Fully spike saline source container and prime the infusion set following the applicable package instructions.
3. Connect set to recipient.
4. Fully spike an inverted FT576 bag with the unused Y-lead. Do not spike FT576 bag while it is hanging.
5. Slowly open the roller clamp below FT576 bag and adjust for desired flow rate.
6. When FT576 bag is empty, close all clamps.
7. To rinse the empty FT576 bag, open clamp below saline solution container. Open clamp below FT576 bag.
8. Allow approximately 50 mL of saline solution to flow into FT576 bag. Close all clamps, invert FT576 bag 2-3 times to ensure thorough rinsing. Use a total of 50 mL 0.9% sodium chloride to flush each bag. This may require multiple flushes.
9. Open the roller clamp that is nearest to the subject and then slowly open the roller clamp below FT576 bag and adjust for desired flow rate.
10. When FT576 product container is empty, close the clamp below the FT576 bag.

11. If additional FT576 bags are to be infused, slowly open the clamp below the 0.9% sodium chloride and allow the saline solution to continue to flush the remaining cells in the tubing while the next FT576 bag is being thawed.
12. Once the new FT576 bag is thawed, remove the empty FT576 bag and spike the new FT576 bag. Repeat Steps 1-11 for each additional bag.
13. Once the last bag of FT576 is rinsed and administered, close the clamp below the FT576 bag. Open the clamp below the 0.9% sodium chloride and allow the saline to flush the remaining cells in the tubing until the fluid in the tubing is clear confirming all cells have been infused.

Issuance, thawing, and administration of bags should be documented on the Fate Investigational Medicinal Product Administration Record (Appendix 6) and available for review by the Site Monitor.

The end of administration time should be recorded after the rinse step has been completed.

When the study drug administration has been completed, discard the empty study drug bag/tubing in accordance with local site policy.

# 11. DRUG PRODUCT ACCOUNTABILITY AND DISPOSITION

The study site cell processing facility or pharmacy, as a delegate of the PI, must maintain accurate records by documenting the following information for each FT576 bag on the Fate Investigational Medicinal Product Accountability Log (Appendix 5):

- **Product Lot #**, **Bag ID #**, **Date Product Received**, and **Product Received By** (name)
- Confirmation of **Visual Inspection Passed**
- **Date Product Issued to Subject** (if not issued, accounting for FT576 not otherwise administered to subjects, e.g., bag leakage, compromised bag integrity, accidentally or deliberately destroyed product); **Study-Assigned Subject ID #**; and **Product Issued By** (name)
- **Site Monitor Verification**

All FT576 bags must be accounted for. A written explanation is required for any discrepancies on the Fate Investigational Medicinal Product Accountability Log (Appendix 5). Documentation must be made available for review upon request from the Sponsor.

If any unused study drug supplies are to be destroyed at the site, the institution/PI must obtain prior written approval from FATE. FATE must approve the site's drug destruction policy in advance of any study drug's destruction. After such destruction, the institution/PI must notify FATE, in writing, what was destroyed (including lot numbers), the method of destruction, the date of destruction, and the location of destruction.

# 12. DRUG PRODUCT COMPLAINTS

## 12.1. Overview

All clinical drug product complaints must be reported immediately to Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1 for contact information). Any FT576 bags that are the subject of a complaint must be placed in quarantined storage until instructed otherwise by FATE. Examples of product complaints include, but are not limited to:

- Product shipments that experience temperature excursions (see Section 12.2 below)
- Damaged shipping container
- Illegible product label
- Visibly compromised drug product container closure
- Visible particulate matter in the drug product
- Receipt of wrong drug product for a given study

If applicable, you will be sent form QA-016-F01 (Complaint Report; see Appendix 7) to document the complaint and to return to Fate Quality Assurance for review.

## 12.2. Temperature Excursions

FT576 must be stored in $VPLN_2$ at ≤-150ºC in a continuously temperature-monitored and alarmed $VPLN_2$ freezer in a controlled-access room with limited personnel access.

$VPLN_2$ temperature logs and calibration records must be available to Site Monitors for inspection. Fate Quality Assurance, the Fate Clinical Trial Manager, and the Site Monitor should be notified when:

- The shipping temperature monitoring data indicates that the temperature warmed to >-150°C up to -135°C for >10 minutes or >-135°C at any point during shipment;
- The storage temperature at the clinical site warms to >-150°C up to -135°C for >10 minutes or >-135°C for any amount of time; or
- A thawed bag is not administered for any reason (e.g., if FT576 is held for more than 60 minutes following completion of thaw, does not pass visual inspection).

The following steps must occur for every temperature excursion:

1. As soon as the temperature excursion is discovered, send an email notification including temperature recordings (as applicable) to Fate Quality Assurance and the Fate Clinical Trial Manager at the email addresses indicated in Section 1. Also include the Site Monitor at the applicable email address. You will be sent form QA-016-F01 (Complaint Report; see Appendix 7) to document the temperature excursion and then return the completed form to Fate Quality Assurance.

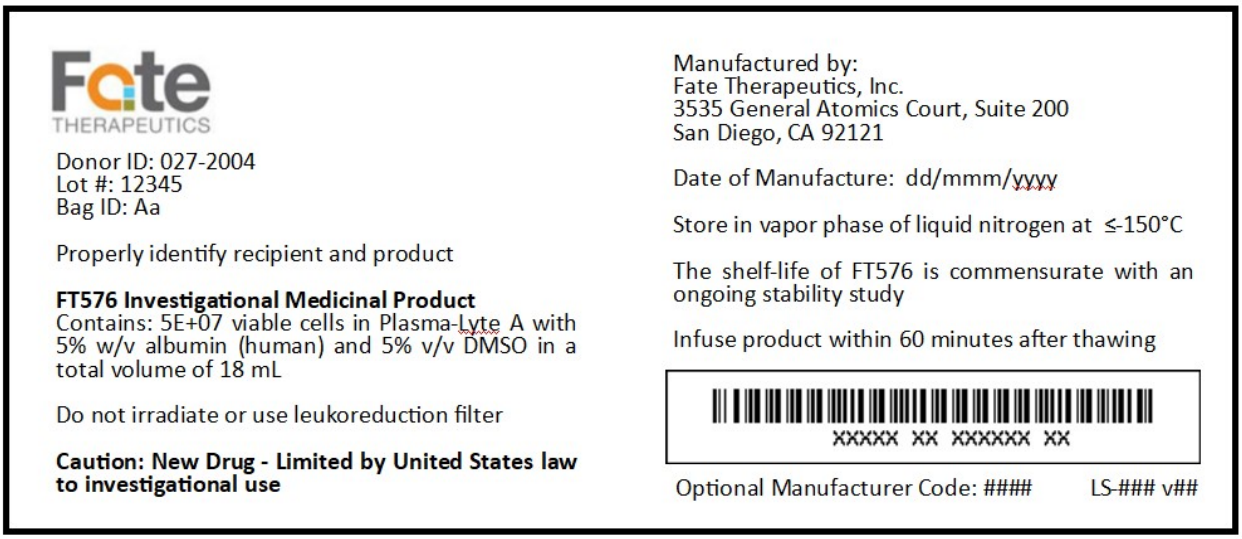
2. FATE will review the available documentation and will notify the site in writing if the product is cleared for use or should be returned/destroyed.

# 13. REVISION HISTORY

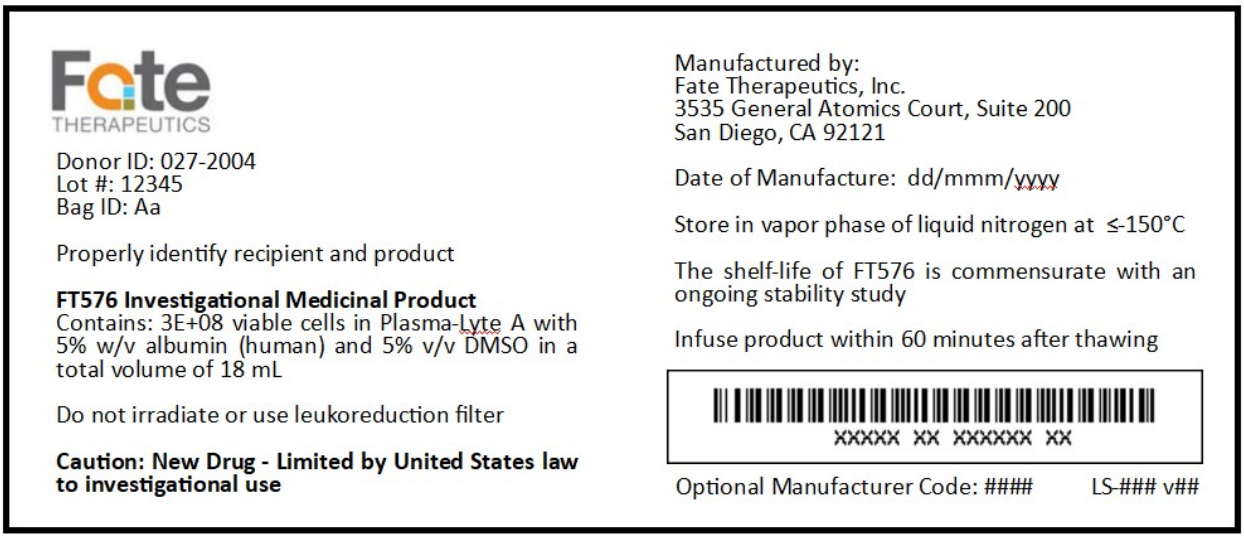
| Version | Change Summary |
|---|---|
| 1.0 | Original document |

# Appendix 1 Sample Images of FT576 Labeling and Cassette

## (A) Representative Label: 5E+07 viable cells in 18 mL




## (B) Representative Label: 3E+08 viable cells in 18 mL



**(C) Representative Label: 5E+08 viable cells in 18 mL**

Fate THERAPEUTICS

Donor ID: 027-2004
Lot #: 12345
Bag ID: Aa

Properly identify recipient and product

**FT576 Investigational Medicinal Product**
Contains: 5E+08 viable cells in Plasma-Lyte A with 5% w/v albumin (human) and 5% v/v DMSO in a total volume of 18 mL

Do not irradiate or use leukoreduction filter

**Caution: New Drug - Limited by United States law to investigational use**

Manufactured by:
Fate Therapeutics, Inc.
3535 General Atomics Court, Suite 200
San Diego, CA 92121

Date of Manufacture: dd/mmm/yyyy

Store in vapor phase of liquid nitrogen at ≤-150°C

The shelf-life of FT576 is commensurate with an ongoing stability study

Infuse product within 60 minutes after thawing

XXXXX XX XXXXXX XX

Optional Manufacturer Code: #### LS-### v##

**(D) Cassette**

# Appendix 2 B. Braun SafeLine® Y-Type Blood Set (REF NF5140) Package Instructions

REF NF5140

**SafeLine®**
**Y-Type Blood Set**

with two Non-Vented Spikes, 170 µm Blood Filter, SafeLine Injection Site, and Spin-Lock® Connector

LENGTH 84 in. (213 cm) (approx.)

PRIMING VOLUME 34 mL (approx.)

10 Drops/mL

GTIN: 04046964187476

Fluid path and areas under end protectors are: STERILE EO NONPYROGENIC

PHT DEHP Contains DEHP

Not made with natural rubber latex.

Pictorial is for reference only. P-4850-6 REV. 11/15 Rx only

For single use only. Do not resterilize.

**CAUTION:** Simultaneous administration from two containers requires constant vigilance.

**WARNING:** Administer blood only with compatible IV solutions.

**Instructions for Use:** Use Aseptic Technique.

- **To access SafeLine Injection Site:** Swab injection site vigorously for 15 seconds and allow to air dry prior to use per institutional protocol. Insert SafeLine Cannula attached to appropriate device through center of septum. Engage locking features if applicable. See Directions for Use accompanying cannula. Flush after each use according to institutional protocol.

  **CAUTION:** Medication additions requiring a conventional needle should be used in emergency situations only.
- Replace set after 4 hours or per AABB guidelines and/or institutional protocol.

1. Close all roller clamps. Fully spike solution container.
2. Slowly open clamp below solution container. Partially open clamp on unused spike lead to prime lead. Close clamp. Gently squeeze and release drip chamber until filter is completely covered. Maintain fluid level above filter.
3. Slowly open lower roller clamp and allow fluid to fill tubing. Invert and tap components while fluid is flowing. Close lower roller clamp. Ensure air is expelled. Repeat prime if necessary. Attach to infusion device.
4. Close all clamps. Fully spike blood container with unused spike lead.
5. To establish blood flow, open roller clamp below blood container. Slowly open lower roller clamp and adjust for desired flow rate.

B BRAUN

B. Braun Medical Inc.
Bethlehem, PA 18018-3524 USA
1-800-227-2862
Assembled in Dominican Republic.

# Appendix 3 Baxter CLEARLINK System (2C8750) Package Instructions

**CLEARLINK** System **2C8750 s**

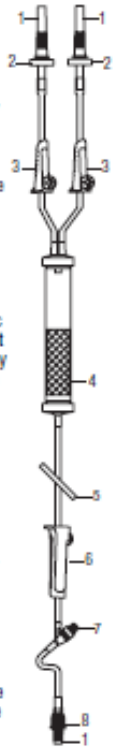
**Y-Type Blood/Solution Set with Standard Blood Filter**
112" (2.8 m)
170 to 260 Micron Filter
Luer Activated Valve
Male Luer Lock Adapter
with Retractable Collar

**10**
**10 drops/mL Approx.**

**Fluid path is sterile, nonpyrogenic.**
**Cautions: Do not use if tip protectors (1) are not in place. Do not place on sterile field.**

**Indications for Use:** For the administration of blood, blood components or solutions from a container into the patient's vascular system through a vascular access device.

**Directions: Use aseptic technique.**
Close On-Off clamps (3) and regulating clamp (6). Insert one spike (2) into solution container. **Invert** filter chamber (4). Open On-Off clamp (3) under solution container. Partially open regulating clamp (6). Allow approximately 1/2 of chamber to fill with solution. Close regulating clamp (6). Partially open On-Off clamp (3) on unused lead, prime and close On-Off clamp (3). Return filter chamber (4) to upright position. Open regulating clamp (6) to prime, purge air. Close regulating clamp (6) until roller meets bottom of frame. Attach male Luer adapter (8) to vascular access device, using a firm push and twist motion and then engage the Luer lock collar to prevent accidental disconnection. Ensure downstream clamp is open. **Swab** Luer activated surface with preferred antiseptic prior to **first use and before every subsequent connection.** Access Luer activated valve (7) by firmly pushing male Luer of connecting device directly against Luer activated surface and rotate until connection is secure.




*To properly set flow always close regulating clamp (6) until roller meets bottom of frame, then reopen to establish flow rate. Repeat procedure if adjusting clamp from fully open position.*

To administer blood, attach blood container to unused lead. Close On-Off clamp (3) under solution container. Open On-Off clamp under blood container.

**Cautions:**
Do not allow air to be trapped in set. Puncturing set components may cause air embolism. Do not swab Luer activated surface (7) when downstream clamp is closed or valve is recessed. Ineffective swabbing may result. Replace set if valve remains recessed.
**Do not access Luer activated valve with needles or cannula. Attempting such access will render the product damaged, replace immediately. Use of Luer lock connection is recommended. If Luer slip connection is used, insert into valve using a firm push and twist motion. Do not leave Luer slip unattended.**
Trace lines before connection. Do not connect any compressed gas device to intravenous injection sites. Rx Only. Single use only. Do not resterilize.

**Notes:**
This product is not made with natural rubber latex.
This product contains DEHP.
Drop size varies with blood and blood products depending on hematocrit and temperature.
**For pressure administration, apply pressure cuff and completely open regulating clamp.**
To stop flow without disturbing regulating device (6), close slide clamp (5). Flush Luer activated valve (7) after injection to prevent inadvertent mixing of incompatible medications/fluids. Flush Luer activated valve after blood infusion. If valve cannot be cleared of blood, replace immediately.
If intermittently disconnecting set from Luer activated valve, immediately cover male Luer of connecting device with a sterile replacement protector.
Replace set per AABB/CDC guidelines.
Lengths are approximate.
For Product Information 1-800-933-0303

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Made in the Dominican Republic
07-36-75-436 Rev 2016-03-01

# Appendix 4 Notification of Subject Enrollment Form

| *Directions: Completed by Fate Clinical and provided to Fate Manufacturing and Study site once confirmed.* | | | |
|---|---|---|---|
| **Date of Enrollment:** (*DD/MMM/YYYY*) *Date consent signed* | /__/__ | | |
| **Site Name/ Site ID #:** | /__ | | |
| **EDC Assigned ID # (xxx-09-zzzz):** | __ – 09 – __ | | |
| **Regimen:** | ☐ Regimen A: Monotherapy FT576 (D1)<br>☐ Regimen A1: Monotherapy FT576 (D1, D15)<br>☐ Regimen B: Combination FT576 + Daratumumab (D1)<br>☐ Regimen B1: Combination FT576 + Daratumumab (D1, D15) | | |
| **Product Volume per Unit:** | 18 mL | | |
| **Expansion cohort?** | ☐ Yes | | ☐ No |
| **Assigned FT576 Dose Level:** | Dose Level | Regimen A or B (D1) | Regimen A1 or B1 (D1,15) |
| | 0 | ☐ 5 x $10^7$ cells | ☐ N/A |
| | 1 | ☐ 1 x $10^8$ cells | ☐ 5 x $10^7$ cells (D1, D15) |
| | 2 | ☐ 3 x $10^8$ cells | ☐ 1.5 x $10^8$ cells (D1, D15) |
| | 3 | ☐ 6 x $10^8$ cells | ☐ 3 x $10^8$ cells (D1, D15) |
| | 4 | ☐ 1.5 x $10^9$ cells | ☐ 6 x $10^8$ cells (D1, D15) |
| | 4A | ☐ 1 x $10^9$ cells | ☐ N/A |
| | 5 | ☐ NA | ☐ 1.5 x $10^9$ cells (D1, D15) |
| | 5A | ☐ NA | ☐ 1 x $10^9$ cells (D1, D15) |
| **Treatment #:** | ☐ Treatment (Cycle 1) | | ☐ Re-Treatment (Cycle 2) |
| **Planned FT576 Infusion Dates:** (*DD/MMM/YYYY*) | **D1:** __/__/__ | | **D1:** __/__/__<br>**D15:** __/__/__ |
| **Signature/Date** | | | **Title** |
| | | | __ |



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# Appendix 5 Fate Investigational Medicinal Product Accountability Log

Fate THERAPEUTICS

## FATE INVESTIGATIONAL MEDICINAL PRODUCT ACCOUNTABILITY LOG

**Product:** _____ **Protocol No.:** _____ **Principal Investigator:** _____

**Site Name:** _____ **Site No.:** _____

| Product Lot # | Bag ID # | Date Product Received | Visual Inspection Passed (Yes/No) [a] | Product Received By | Product Issued (Yes/No) [b] | Date Product Issued to Subject | Study-Assigned Subject ID # | Product Issued By | Site Monitor Verification (initial and date) |
|---|---|---|---|---|---|---|---|---|---|
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[a] If the bag integrity is compromised, contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1 of the Storage, Handling, and Administration Guidance).

[b] If product has not been issued to subject, a written explanation is required (record below).

| | | |
|---|---|---|
| Product Lot #: | Bag ID #: | Reason Product Not Issued: |
| Product Lot #: | Bag ID #: | Reason Product Not Issued: |
| Product Lot #: | Bag ID #: | Reason Product Not Issued: |

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# Appendix 6 Fate Investigational Medicinal Product Administration Record

FATE INVESTIGATIONAL MEDICINAL PRODUCT ADMINISTRATION RECORD

**Subject Information:**

| Name | MRN |
|---|---|
| Subject ID | Date of Infusion (dd/mmm/yyyy) |

Subject Label (if applicable)

**Product Information:**

| Fate IMP ("Product") | Protocol No. |
|---|---|

BAG _____ of _____

**ISSUED PRODUCT:**

Assigned dosage on Subject Enrollment Form: _____ No. of bags required to meet dose: _____

Confirm number of bag(s) × dosage of bag(s) issued equals the total assigned dosage on Subject Enrollment Form.

| Product Lot # | Bag ID # | Bag Volume (mL) | Dose (cells per bag) |
|---|---|---|---|
| | | | |

Issued by *(signature)*: _____ Date: _____

Verified by *(signature)*: _____ Date: _____

**PRODUCT THAW:**

Confirm subject and product identity prior to thawing of product.

| Time into 37°C Thawing Device (24-hr. clock) | Time out of 37°C Thawing Device (24-hr. clock) | Visual Inspection Passed (Yes/No) [a] | Performed By (Initials/Date) |
|---|---|---|---|
| | | | |

[a] If thawed and not administered or otherwise compromised, record observations in notes/comments section below. Contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1 of the Storage, Handling, and Administration Guidance).

Thaw Notes/Comments:

_____

_____

Performed by *(signature)*: _____ Date: _____

Verified by *(signature)*: _____ Date: _____

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# FATE INVESTIGATIONAL MEDICINAL PRODUCT ADMINISTRATION RECORD

**Subject Information:**

| Name | MRN |
|---|---|
| Subject ID | Date of Infusion (dd/mmm/yyyy) |

Subject Label (if applicable)

**Product Information:**

| Fate IMP ("Product") | Protocol No. |
|---|---|

**BAG _____ of _____**

**PRODUCT ADMINISTRATION:**

| Start Time of Administration (24-hr. clock) | Stop Time of Administration (24-hr. clock) [a] | Infusion Interrupted (Yes/No) [b] | Full Bag Infused (Yes/No) [c] | Administration and Rinse Performed By (Initials/Date) |
|---|---|---|---|---|
| | | | | |

[a] The end of administration time (Stop Time) should be recorded after the rinse step has been completed.
[b] If Yes, record reason infusion was interrupted in notes/comments section below.
[c] If No, record volume infused, total nucleated cells (TNC) administered, volume discarded, and reason in notes/comments section below.

Administration Notes/Comments:

_____

_____

Performed by *(signature)*: _____ Date: _____

Verified by *(signature)*: _____ Date: _____

**BAG LABEL RECORDING:**

- For the infused bag, affix label below.
- For bag not infused, quarantine per institutional guidelines and contact Fate Quality Assurance and the Fate Clinical Trial Manager (see Section 1 of the Storage, Handling, and Administration Guidance).

Affix Bag Label for Administered Product Here

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# Appendix 7 Complaint Report (QA-016-F01)

| Fate THERAPEUTICS | Complaint Report | QA-016-F01 |
|---|---|---|

**COMPLAINT NUMBER (ASSIGNED BY QA):**

**SECTION 1:**

Complaint Received From (name, address, email, & phone #):

Complaint Received By/Date/Time:

How was complaint received?

Product and Lot #:

Patient ID # (N/A ☐):

Clinical Trial (IND, CTA) and Protocol #:

Detailed summary of the nature of the complaint, including the complaint's potential impact:

Suggested Actions/Follow Up:

| Fate THERAPEUTICS | Complaint Report | QA-016-F01 |
|---|---|---|

**SECTION 2 - TO BE COMPLETED BY QA:**

Is a MRB necessary? ☐ NO ☐ YES (attach additional documentation)

Is notification of a regulatory authority necessary? (provide justification) ☐ NO ☐ YES

Name: Date:

If yes: Agency to be notified:

Agency contact:

Justification:

Is a recall necessary? ☐ NO ☐ YES, explain:

Initiate Deviation report? (if yes, record DR Number) ☐ NO ☐ YES, explain:

Was the complaint adequately resolved? ☐ YES ☐ NO, explain:

| Approval of Complaint Report | Signature | Date |
|---|---|---|
| Author of Section 1 | | |
| Quality Assurance | | |

# Appendix 8 Abbreviations

| Abbreviation | Term |
|---|---|
| BCMA | B-cell maturation antigen |
| C | Centigrade |
| CAR | Chimeric antigen receptor |
| CVC | Central venous catheter |
| DL | Dose level |
| hnCD16 | High-affinity, non-cleavable CD16 |
| IL | Interleukin |
| IL-15RF | IL-15 receptor fusion protein |
| IMP | Investigational Medicinal Product |
| IND | Investigational New Drug |
| iPSC | Induced pluripotent stem cell |
| IV | Intravenous |
| mL | Milliliter |
| NK | Natural killer |
| PI | Principal Investigator |
| PICC | Peripherally inserted central catheter |
| SOP | Standard Operating Procedure |
| USP | United States Pharmacopeia |
| VC | Viable cells |
| $VPLN_2$ | Vapor phase of liquid nitrogen |