

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13D

Under the Securities Exchange Act of 1934
(Amendment No. 1)*

Mast Therapeutics, Inc.
(Name of Issuer)

Common Stock, par value \$0.001 per share
(Title of Class of Securities)

576314108
(CUSIP Number)

Andrew Langham
Icahn Capital LP
767 Fifth Avenue, 47th Floor
New York, New York 10153
(212) 702-4300
(Name, Address and Telephone Number of Person Authorized to
Receive Notices and Communications)

December 29, 2015
(Date of Event which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of Section 240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box / /.

NOTE: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See Rule 13d-7 for other parties to whom copies are to be sent.

*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

SCHEDULE 13D

CUSIP No. 576314108

1 NAME OF REPORTING PERSON

High River Limited Partnership

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

(a) //

(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS

WC

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER

0

8 SHARED VOTING POWER

0

9 SOLE DISPOSITIVE POWER

0

10 SHARED DISPOSITIVE POWER

0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)

0%

14 TYPE OF REPORTING PERSON

PN

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
Hopper Investments LLC

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
OO

SCHEDULE 13D

CUSIP No. 576314108

1 NAME OF REPORTING PERSON

Barberry Corp.

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

(a) //

(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS

OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER

0

8 SHARED VOTING POWER

0

9 SOLE DISPOSITIVE POWER

0

10 SHARED DISPOSITIVE POWER

0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)

0%

14 TYPE OF REPORTING PERSON

CO

SCHEDULE 13D

CUSIP No. 576314108

- 1 NAME OF REPORTING PERSON
Icahn Partners Master Fund LP
 - 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //
 - 3 SEC USE ONLY
 - 4 SOURCE OF FUNDS
WC
 - 5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /
 - 6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware
- NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:
- 7 SOLE VOTING POWER
0
 - 8 SHARED VOTING POWER
0
 - 9 SOLE DISPOSITIVE POWER
0
 - 10 SHARED DISPOSITIVE POWER
0
 - 11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0
 - 12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /
 - 13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%
 - 14 TYPE OF REPORTING PERSON
PN

SCHEDULE 13D

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
Icahn Offshore LP

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES / /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
PN

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
Icahn Partners LP

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
WC

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
PN

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
Icahn Onshore LP

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
PN

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
Icahn Capital LP

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
PN

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
IPH GP LLC

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
OO

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
Icahn Enterprises Holdings L.P.

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
PN

CUSIP No. 576314108

1 NAME OF REPORTING PERSON
Icahn Enterprises G.P. Inc.

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(a) //
(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS
OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER
0

8 SHARED VOTING POWER
0

9 SOLE DISPOSITIVE POWER
0

10 SHARED DISPOSITIVE POWER
0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)
0%

14 TYPE OF REPORTING PERSON
CO

CUSIP No. 576314108

1 NAME OF REPORTING PERSON

Beckton Corp.

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

(a) //

(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS

OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER

0

8 SHARED VOTING POWER

0

9 SOLE DISPOSITIVE POWER

0

10 SHARED DISPOSITIVE POWER

0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)

0%

14 TYPE OF REPORTING PERSON

CO

CUSIP No. 576314108

1 NAME OF REPORTING PERSON

Carl C. Icahn

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

(a) //

(b) //

3 SEC USE ONLY

4 SOURCE OF FUNDS

OO

5 CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) / /

6 CITIZENSHIP OR PLACE OF ORGANIZATION

United States of America

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

7 SOLE VOTING POWER

0

8 SHARED VOTING POWER

0

9 SOLE DISPOSITIVE POWER

0

10 SHARED DISPOSITIVE POWER

0

11 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

0

12 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES/ /

13 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)

0%

14 TYPE OF REPORTING PERSON

IN

Item 1. Security and Issuer

The Schedule 13D filed with the Securities and Exchange Commission on August 5, 2005 by the Reporting Persons (the "Schedule 13D") with respect to the shares of Common Stock, par value \$0.001 (the "Shares") issued by Mast Therapeutics, Inc. (f/k/a Adventrx Pharmaceuticals Inc.) (the "Issuer") is hereby amended to furnish the additional information set forth herein. All capitalized terms contained herein but not otherwise defined shall have the meanings ascribed to such terms in the Schedule 13D.

This Amendment No. 1 to the Schedule 13D reports that the Reporting Persons ceased to be the beneficial owner of more than five percent (5%) of the Shares.

SIGNATURE

After reasonable inquiry and to the best of each of the undersigned knowledge and belief, each of the undersigned certifies that the information set forth in this statement is true, complete and correct.

Dated: December 30, 2015

ICAHN PARTNERS MASTER FUND LP

ICAHN OFFSHORE LP

ICAHN PARTNERS LP

ICAHN ONSHORE LP

BECKTON CORP.

HOPPER INVESTMENTS LLC

BARBERRY CORP.

HIGH RIVER LIMITED PARTNERSHIP

By: Hopper Investments LLC, general partner

By: Barberry Corp.

By: /s/ Edward E. Mattner

Name: Edward E. Mattner

Title: Authorized Signatory

ICAHN CAPITAL LP

By: IPH GP LLC, its general partner

By: Icahn Enterprises Holdings L.P., its sole member

By: Icahn Enterprises G.P. Inc., its general partner

IPH GP LLC

By: Icahn Enterprises Holdings L.P., its sole member

By: Icahn Enterprises G.P. Inc., its general partner

ICAHN ENTERPRISES HOLDINGS L.P.

By: Icahn Enterprises G.P. Inc., its general partner

ICAHN ENTERPRISES G.P. INC.

By: /s/ SungHwan Cho

Name: SungHwan Cho

Title: Chief Financial Officer

/s/ Carl C. Icahn

CARL C. ICAHN

[Signature Page of Schedule 13D Amendment No. 1 – Mast Therapeutics, Inc.]