Section 1: 8-K (FORM 8-K)

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15 (d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **February 3, 2020**

United Therapeutics Corporation
(Exact Name of Registrant as Specified in its Charter)

Delaware	**000-26301**	**52-1984749**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

1040 Spring Street **Silver Spring, MD** (Address of Principal Executive Offices)	**20910** (Zip Code)

Registrant's telephone number, including area code: **(301) 608-9292**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.01 per share	UTHR	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

On February 3, 2020, United Therapeutics Corporation ("UT") issued a press release announcing the results of its *DISTINCT* clinical study of Unitixin® in patients with small cell lung cancer. The press release is attached as Exhibit 99.1 and are incorporated herein by reference.

UNITUXIN is a registered trademark of United Therapeutics Corporation.

Item 9.01. Exhibits

(d) Exhibits

Exhibit No.	Description of Exhibit
99.1	Press Release dated February 3, 2020, related to the *DISTINCT* Study
104	The cover page from this Current Report on Form 8-K, formatted in Inline XBRL.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

UNITED THERAPEUTICS CORPORATION

Dated: February 3, 2020

By: /s/ Paul A. Mahon
Name: Paul A. Mahon
Title: General Counsel

(Back To Top)

Section 2: EX-99.1 (EXHIBIT 99.1)

Exhibit 99.1

Contact: Dewey Steadman
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E-mail: ir@unither.com

UNITED THERAPEUTICS ANNOUNCES STUDY OF UNITUXIN® (DINUTUXIMAB) FOR SMALL CELL LUNG CANCER DID NOT MEET PRIMARY ENDPOINT

Silver Spring, MD and Research Triangle Park, NC, February 3, 2020: United Therapeutics Corporation (Nasdaq: UTHR) today announced topline results from the phase 2/3 *DISTINCT* clinical study evaluating Unituxin® (dinutuximab) Injection added to irinotecan compared to irinotecan or topotecan alone in patients with relapsed or refractory small cell lung cancer (SCLC). The *DISTINCT* trial did not meet its primary efficacy objective of extending the overall survival with Unituxin and irinotecan versus using irinotecan alone. The safety profile of dinutuximab in *DISTINCT* was consistent with prior studies and the current Unituxin product label.

Full data from the *DISTINCT* study will be made available through scientific disclosure at upcoming conferences and in peer-reviewed publications.

“We thank the principal investigators, patients and their families for participating in the *DISTINCT* study” said Gil Golden, M.D., Ph.D., Chief Medical Officer of United Therapeutics. “We’re clearly disappointed with the *DISTINCT* results but we’ll continue to seek out underappreciated avenues in our core therapeutic areas addressing rare diseases in oncology and pulmonary hypertension. In addition, we look forward to announcing the results of our *INCREASE* study by the end of the first quarter or shortly thereafter.”

United Therapeutics is also pursuing a label expansion for Unituxin in combination with irinotecan and temozolomide for the treatment of pediatric patients with relapsed or refractory neuroblastoma, based on results from the ANBL1221 study conducted by the Children’s Oncology Group. United Therapeutics plans to meet with the FDA to discuss the proposed label expansion in the first half of 2020 and file a supplemental BLA shortly thereafter.

About *DISTINCT*

DISTINCT was a phase 2/3, two-part, open-label, randomized, international, multi-center study of dinutuximab and irinotecan versus irinotecan for second line treatment of patients with relapsed or refractory small cell lung cancer. The phase 2 portion of the study of 12 patients was completed in October 2017. Global enrollment in the phase 3 portion of the study was completed in October 2018 with a total of 471 patients. Patients were randomized 2:2:1 into three arms: irinotecan (190 patients); irinotecan and dinutuximab (187 patients); or topotecan (94 patients). This event-driven study was conducted in 198 centers from 22 countries in North America, Europe, and Asia-Pacific, with 312 observed deaths in the dinutuximab plus irinotecan and irinotecan alone groups as of the data extract used for analysis. The primary objective of this study was to compare overall survival (OS) in patients treated with dinutuximab and irinotecan versus patients treated with irinotecan alone as a second-line treatment for relapsed or refractory small cell lung cancer (SCLC).

The secondary objectives of the study were:

- To compare progression-free survival (PFS), objective response rate (ORR) (complete response [CR] + partial response [PR]), and clinical benefit rate (CR + PR + stable disease [SD]) in patients treated with dinutuximab and irinotecan to patients treated with irinotecan alone.
- To compare the safety of patients treated with dinutuximab and irinotecan to patients treated with irinotecan alone.
- To evaluate the pharmacokinetics (PK) of patients treated with dinutuximab.
- To compare OS, PFS, ORR, and clinical benefit rate (CBR) in patients treated with dinutuximab and irinotecan to patients treated with topotecan alone.

The exploratory objective of the study was to assess the relationship between selected biomarkers and survival of patients treated with dinutuximab.

About Unituxin

Indication

Unituxin is a GD2-binding monoclonal antibody indicated, in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy.

Important Safety Information for Unituxin

CONTRAINDICATIONS

Unituxin is contraindicated in patients with a history of anaphylaxis to dinutuximab.

WARNINGS AND PRECAUTIONS

BOXED WARNING

Serious Infusion Reactions

- **Serious and potentially life-threatening infusion reactions (facial and upper airway edema, dyspnea, bronchospasm, stridor, urticaria, and hypotension) occurred in 26% of patients treated with Unituxin.**
- **Administer required prehydration and premedication including antihistamines prior to each Unituxin infusion.**
- **Monitor patients closely for signs and symptoms of an infusion reaction during and for at least four hours following completion of each Unituxin infusion.**
- **Immediately interrupt Unituxin for severe infusion reactions and permanently discontinue Unituxin for anaphylaxis.**

Neurotoxicity

- **Unituxin causes serious neurologic adverse reactions including severe neuropathic pain and peripheral neuropathy.**
- **Severe neuropathic pain occurs in the majority of patients.**
- **Administer intravenous opioid prior to, during, and for 2 hours following completion of the Unituxin infusion.**
- **In clinical studies of patients with high-risk neuroblastoma, severe (Grade 3) peripheral sensory neuropathy ranged from 2% to 9%.**
- **In clinical studies of Unituxin and related GD2-binding antibodies, severe motor neuropathy has occurred. Resolution of motor neuropathy did not occur in all cases.**
- **Discontinue Unituxin for severe unresponsive pain, severe sensory neuropathy, and moderate to severe peripheral motor neuropathy.**

Serious Infusion Reactions

- Serious infusion reactions requiring urgent intervention including blood pressure support, bronchodilator therapy, corticosteroids, infusion rate reduction, infusion interruption, or permanent discontinuation of Unituxin included facial and upper airway edema, dyspnea, bronchospasm, stridor, urticaria, and hypotension. Infusion reactions generally occurred during or within 24 hours of completing the Unituxin infusion. Due to overlapping signs and symptoms, it was not possible to distinguish between infusion reactions and hypersensitivity reactions in some cases.

- Severe (Grade 3 or 4) infusion reactions occurred in 35 (26%) patients in the Unituxin/13-cis-retinoic acid (RA) group compared to 1 (1%) patient receiving RA alone. Severe urticaria occurred in 17 (13%) patients in the Unituxin/RA group but did not occur in the RA group. Serious adverse reactions consistent with anaphylaxis and resulting in permanent discontinuation of Unituxin occurred in 2 (1%) patients in the Unituxin/RA group. Additionally, 1 (0.1%) patient had multiple cardiac arrests and died within 24 hours after having received Unituxin in Study 2.

Neurotoxicity

- *Pain:* 114 (85%) patients treated in the Unituxin/RA group experienced pain despite pretreatment with analgesics including morphine sulfate infusion. Severe (Grade 3) pain occurred in 68 (51%) patients in the Unituxin/RA group compared to 5 (5%) patients in the RA group. For severe pain, decrease the Unituxin infusion rate to 0.875 mg/m2/hour. Discontinue Unituxin if pain is not adequately controlled despite infusion rate reduction and institution of maximum supportive measures.

- *Peripheral Neuropathy:* Severe (Grade 3) peripheral sensory neuropathy occurred in 2 (1%) patients and severe peripheral motor neuropathy occurred in 2 (1%) patients in the Unituxin/RA group. Permanently discontinue Unituxin in patients with peripheral motor neuropathy of Grade 2 or greater severity, Grade 3 sensory neuropathy that interferes with daily activities for more than 2 weeks, or Grade 4 sensory neuropathy.

- *Neurological Disorders of the Eye:*

    - Neurological disorders of the eye experienced by two or more patients treated with Unituxin included blurred vision, photophobia, mydriasis, fixed or unequal pupils, optic nerve disorder, eyelid ptosis, and papilledema. In Study 1, 3 (2%) patients in the Unituxin/RA group experienced blurred vision, compared to no patients in the RA group. Diplopia, mydriasis, and unequal pupillary size occurred in 1 patient each in the Unituxin/RA group, compared to no patients in the RA group. The duration of eye disorders occurring in Study 1 was not documented. In Study 3, eye disorders occurred in 16 (15%) patients, and in 3 (3%) patients resolution of the eye disorder was not documented. Among the cases with documented resolution, the median duration of eye disorders was 4 days (range: 0, 221 days).

    - Interrupt Unituxin in patients experiencing dilated pupil with sluggish light reflex or other visual disturbances that do not cause visual loss.

    - Upon resolution and if continued treatment with Unituxin is warranted, decrease the Unituxin dose by 50%.

    - Permanently discontinue Unituxin in patients who experience loss of vision and in patients with recurrent eye disorder following dose reduction.

- *Prolonged Urinary Retention:* Urinary retention that persists for weeks to months following discontinuation of opioids has occurred in patients treated with Unituxin. Permanently discontinue Unituxin in patients with prolonged urinary retention that does not resolve with discontinuation of opioids.

- *Transverse Myelitis:* Transverse myelitis has occurred in patients treated with Unituxin. Promptly evaluate any patient with signs or symptoms such as weakness, paresthesia, sensory loss, or incontinence. Permanently discontinue Unituxin in patients who develop transverse myelitis.

- *Reversible Posterior Leukoencephalopathy Syndrome (RPLS):* RPLS has occurred in patients treated with Unituxin. Institute appropriate medical treatment and permanently discontinue Unituxin in patients with signs and symptoms of RPLS (e.g., severe headache, hypertension, visual changes, lethargy, or seizures).

Capillary Leak Syndrome

- Severe (Grade 3 to 5) capillary leak syndrome occurred in 31 (23%) patients in the Unituxin/RA group and in no patients treated with RA alone.

- Depending on severity, manage by immediate interruption, infusion rate reduction or permanent discontinuation of Unituxin and institute supportive management in patients with symptomatic or severe capillary leak syndrome.

Hypotension

- Severe (Grade 3 or 4) hypotension occurred in 22 (16%) patients in the Unituxin/RA group compared to no patients in the RA group.

- Prior to each Unituxin infusion, administer required intravenous hydration.

- Closely monitor blood pressure during Unituxin treatment.

- Depending on severity, manage by immediate interruption, infusion rate reduction or permanent discontinuation of Unituxin and institute supportive management in patients with symptomatic hypotension.

Infection

- Severe (Grade 3 or 4) bacteremia requiring intravenous antibiotics or other urgent intervention occurred in 17 (13%) patients in the Unituxin/RA group compared to 5 (5%) patients treated with RA alone. Sepsis occurred in 24 (18%) of patients in the Unituxin/RA group and in 10 (9%) patients in the RA group.

- Monitor patients closely for signs and symptoms of systemic infection and temporarily discontinue Unituxin in patients who develop systemic infection until resolution of the infection.

Bone Marrow Suppression

- Severe (Grade 3 or 4) thrombocytopenia (39% vs. 25%), anemia (34% vs. 16%), neutropenia (34% vs. 13%), and febrile neutropenia (4% vs. 0 patients) occurred more commonly in patients in the Unituxin/RA group compared to patients treated with RA alone.

- Monitor peripheral blood counts closely during Unituxin therapy.

Electrolyte Abnormalities

- Electrolyte abnormalities occurring in at least 25% of patients who received Unituxin/RA in Study 1 included hyponatremia, hypokalemia, and hypocalcemia. Severe (Grade 3 or 4) hypokalemia and hyponatremia occurred in 37% and 23% of patients in the Unituxin/RA group, respectively, compared to 2% and 4% of patients in the RA group.

- Monitor serum electrolytes daily during therapy with Unituxin.

Atypical Hemolytic Uremic Syndrome

- Hemolytic uremic syndrome in the absence of documented infection and resulting in renal insufficiency, electrolyte abnormalities, anemia, and hypertension occurred in two patients following receipt of the first cycle of Unituxin.

- Permanently discontinue Unituxin and institute supportive management.

Embryo-Fetal Toxicity

- Unituxin may cause fetal harm.

- Advise pregnant women of the potential risk to a fetus.

- Advise females of reproductive potential to use effective contraception during treatment, and for two months after the last dose of Unituxin.

ADVERSE REACTIONS

The most common serious adverse reactions (≥ 5%) are infections, infusion reactions, hypokalemia, hypotension, pain, fever, and capillary leak syndrome.

The most common adverse drug reactions (≥ 25%) in Unituxin/RA compared with RA alone are pain (85% vs. 16%), pyrexia (72% vs. 27%), thrombocytopenia (66% vs. 43%), lymphopenia (62% vs. 36%), infusion reactions (60% vs. 9%), hypotension (60% vs. 3%), hyponatremia (58% vs. 12%), increased alanine aminotransferase (56% vs. 31%), anemia (51% vs. 22%), vomiting (46% vs. 19%), diarrhea (43% vs. 15%), hypokalemia (43% vs. 4%), capillary leak syndrome (40% vs. 1%), neutropenia (39% vs. 16%), urticaria (37% vs. 3%), hypoalbuminemia (33% vs. 3%), increased aspartate aminotransferase (28% vs. 7%), and hypocalcemia (27% vs. 0%). In post-approval use of Unituxin, the adverse reactions of prolonged urinary retention, transverse myelitis, and reversible posterior leukoencephalopathy syndrome were observed. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency.

Please see Full Prescribing Information, including Boxed WARNING, for Unituxin at www.unituxin.com or call 1-877-UNITHER (1-877-864-8437).

About United Therapeutics

United Therapeutics Corporation focuses on the strength of a balanced, value-creating biotechnology model. We are confident in our future thanks to our fundamental attributes, namely our obsession with quality and innovation, the power of our brands, our entrepreneurial culture and our bioinformatics leadership. We also believe that our determination to be responsible citizens – having a positive impact on patients, the environment and society – will sustain our success in the long term.

Through our wholly-owned subsidiary, Lung Biotechnology PBC, we are focused on addressing the acute national shortage of transplantable lungs and other organs with a variety of technologies that either delay the need for such organs or expand the supply. Lung Biotechnology is the first public benefit corporation subsidiary of a public biotechnology or pharmaceutical company.

Forward-looking Statements

Statements included in this press release that are not historical in nature are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, among others, statements regarding our plans to announce the results of the *INCREASE* study, our plans to expand Unituxin's label based on the ANBL1221 results, the ability of our business model to create value, our ability to sustain long-term success, and our organ transplantation research and development programs. These forward-looking statements are subject to certain risks and uncertainties, such as those described in our periodic and other reports filed with the Securities and Exchange Commission that could cause actual results to differ materially from anticipated results. In particular, we note that analysis of the full *DISTINCT* study results is ongoing, including analysis of secondary endpoints. These further analyses could have a material impact on how useful the full results will be to healthcare providers and payers, and how they will be viewed by the FDA and other regulators. All of these factors could have a material impact on how useful the final results will be to healthcare providers, and how they will be viewed by the FDA and other regulators. In addition, the forward-looking statements in this press release are qualified by the cautionary statements, cautionary language and risk factors set forth in our periodic reports and documents filed with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. We claim the protection of the safe harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. We are providing this information as of February 3, 2020 and assume no obligation to update or revise the information contained in this press release whether as a result of new information, future events or any other reason.

(Back To Top)