Filed pursuant to Rule 433
Free Writing Prospectus dated June 19, 2018
Registration No. 333-225178

MAGENTA THERAPEUTICS, INC.

This free writing prospectus updates the preliminary prospectus dated June 8, 2018 included in Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-225178) relating to the initial public offering of the common stock of Magenta Therapeutics, Inc. On June 18, 2018, the issuer filed Amendment No. 2 to the Registration Statement on Form S-1. This free writing prospectus updates and supplements the preliminary prospectus dated June 8, 2018 with information that is reflected in the preliminary prospectus dated June 19, 2018 included in Amendment No. 3 to the Registration Statement.

To review the preliminary prospectus included in Amendment No. 3 to the Registration Statement, click the following link (or if such address has changed, by reviewing the issuer's filings for the relevant date on the SEC web site): http://www.sec.gov/Archives/edgar/data/1690585/000119312518196227/d549494ds1a.htm . The issuer's Central Index Key, or CIK, on the SEC website is 0001690585.

This free writing prospectus reflects the following supplements and updates that were made in the preliminary prospectus:

Risk Factors

The following additional risk factor was added to the section entitled "Risk Factors—Risks Related to Product Development and Regulatory Approval."

Bone marrow transplant is a high-risk procedure with curative potential that may result in complications or adverse events for patients in our clinical trials or for patients that use any of our product candidates, if approved.

Bone marrow transplant can cure patients across multiple diseases, but its use carries with it risks of toxicity, serious adverse events and death. Because many of our therapies are used to prepare or treat patients undergoing bone marrow transplant, patients in our clinical trials or patients that use any of our product candidates may be subject to many of the risks that are currently inherent to the bone marrow transplant process. In particular, bone marrow transplant involves certain known potential post-procedure complications that may manifest several weeks or months after a transplant and which may be more common in certain patient populations. For example, up to 20% of patients with inherited metabolic diseases treated with transplant experience primary engraftment failure, resulting in severe complications, including death. The first patient dosed in our ongoing Phase II clinical trial of MGTA-456 in patients with inherited metabolic diseases successfully engrafted, and subsequently developed autoimmune cytopenia, a known potential complication of bone marrow transplant in this patient population, which includes severe side effects and the possibility of death. This has been deemed by the principal investigator overseeing the Phase II study and the chair of our data safety monitoring committee to be unrelated to the use of MGTA-456 specifically but instead is deemed to be related to complications common to transplant. If these or other serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any of our product candidates, we may need to limit, delay or abandon our further clinical development of those product candidates, even if such events, effects or characteristics were the result of bone marrow transplant or related procedures generally, and not directly or specifically caused or exacerbated by our product candidates. All serious adverse events or unexpected side effects are continually monitored per the clinical study's approved protocol. If serious adverse events are determined to be directly or specifically caused or exacerbated by our product candidates, we would follow the study protocol's requirements, which call for our data safety monitoring committee to review all available clinical data in making a recommendation regarding the study's continuation.

Business

The following disclosure was added to the third paragraph in the section entitled "Business—Background On Our Current Programs—Stem cell expansion program: cord blood—Clinical development plan."

This patient successfully met the primary engraftment endpoint and all of the secondary endpoints within the first 100 days post-transplant. However, on June 14, 2018 (day 122 following transplant), this patient was admitted to the hospital for autoimmune cytopenia, a known potential complication of bone marrow transplant in this patient

population, which includes severe side effects and the possibility of death. This patient was subsequently transferred to the intensive care unit in critical condition due to these autoimmune cytopenia side effects. The occurrence of autoimmune cytopenia has been considered by the principal investigator overseeing the Phase II study and the chair of our data safety monitoring committee to be unrelated to the use of MGTA-456 specifically.

Magenta Therapeutics, Inc. has filed a registration statement (including a prospectus, which is preliminary and subject to completion) with the Securities and Exchange Commission (the "SEC") for the offering to which this communication relates. Before you invest, you are encouraged to read the prospectus in that registration statement and other documents the issuer has filed with the SEC for more complete information about the issuer and this offering. You may get these documents for free by visiting EDGAR on the SEC Website at www.sec.gov. Alternatively, copies of the preliminary prospectus related to the offering may be obtained from J.P. Morgan Securities LLC, c/o Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717, telephone: 866-803-9204; Goldman Sachs & Co. LLC, Prospectus Department, 200 West Street, New York, NY 10282, telephone: 1-866-471-2526, facsimile: 212-902-9316 or by emailing Prospectus-ny@ny.email.gs.com; or Cowen and Company, LLC, c/o Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717, Attn: Prospectus Department, telephone: 631-274-2806.

This communication shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of, these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of any such state or jurisdiction.