As filed with the Securities and Exchange Commission on November 6, 2025
Registration Statement No. 333-287536

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 1
TO

FORM S-3

REGISTRATION STATEMENT
UNDER THE
SECURITIES ACT OF 1933

REPLIMUNE GROUP, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**82-2082553**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification Number)

500 Unicorn Park Drive
Suite 303
Woburn MA 01801
(781) 222-9600

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Sushil Patel
Chief Executive Officer
Replimune Group, Inc.
500 Unicorn Park Drive
Suite 303
Woburn MA 01801
(781) 222-9600

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

With copies to:
Timothy J. Corbett
Thurston J. Hamlette
Morgan, Lewis & Bockius LLP
101 Park Ave.
New York, NY 10178
(212) 309-6000

Approximate date of commencement of proposed sale to the public: **From time to time after this registration statement becomes effective**.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☐

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☐
Non- accelerated filer ☒	Smaller reporting company ☒
	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 7(a)(2)(B) of Securities Act. ☐

This Registration Statement shall hereafter become effective in accordance with the provisions of Section 8(a) of the Securities Act of 1933. If the Securities and Exchange Commission resumes full operation before the Registration Statement becomes effective, we may file an amendment to this Registration Statement requesting a delay or change in the effectiveness of the Registration Statement.

EXPLANATORY NOTE

This Amendment No. 1 ("Amendment No. 1") to the Registration Statement on Form S-3 (File No. 333-287536) of Replimune Group, Inc. (the "Registration Statement") is being filed for the purpose of (a) including on the facing page language provided by Rule 473(b) of the Securities Act for the automatic effectiveness of the Registration Statement 20 days following the filing of this Amendment No. 1; (b) updating the sections entitled "Prospectus Summary," "Legal Matters," and "Incorporation of Certain Information by Reference," in each of the base prospectus and sales agreement prospectus; (c) updating the sections entitled "The Offering," "Dilution," and "Risk Factors" in the sales agreement prospectus, and (d) filing an updated consent of the Company's independent registered public accounting firm as Exhibit 23.2, and an updated opinion and consent of the Company's legal counsel as Exhibit 5.1 and Exhibit 23.1, respectively. The remainder of the Registration Statement remains unchanged.

This Registration Statement contains:

- a base prospectus which covers the offering, issuance and sale by us of up to $250 million of the securities identified therein from time to time in one or more offerings; and
- a sales agreement prospectus covering the offering, issuance and sale by us of up to a maximum aggregate offering price of $100 million of our common stock that may be issued and sold from time to time under a sales agreement with Leerink Partners LLC, as amended, or the Sales Agreement.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered by us pursuant to the base prospectus, other than the shares of common stock under the Sales Agreement, will be specified in a prospectus supplement to the base prospectus. The specific terms of the shares of common stock to be issued and sold under the Sales Agreement are specified in the sales agreement prospectus that immediately follows the base prospectus. The $100 million of shares of common stock that may be offered, issued and sold under the sales agreement prospectus is included in the $250 million of securities that may be offered, issued and sold by us under the base prospectus. Upon termination of the Sales Agreement, any portion of the $100 million of shares of common stock included in the sales agreement prospectus that is not sold pursuant to the Sales Agreement will be available for sale in other offerings pursuant to the base prospectus and a corresponding prospectus supplement, and if no shares of common stock are sold under the Sales Agreement, the full $100 million of securities may be sold in other offerings by the Company pursuant to the base prospectus and a corresponding prospectus supplement.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

Subject to completion, dated November 6, 2025

Prospectus

Replimune®

$250,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

We may offer and sell from time to time up to $250 million in the aggregate of shares of our common stock, shares of preferred stock, warrants and debt securities, as well as units that include any combination of the foregoing securities. We may sell any combination of these securities in one or more offerings.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities pursuant to this prospectus, we will provide a prospectus supplement containing specific terms of the particular offering together with this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities that we may offer. The prospectus supplement also may add, update or change information contained in this prospectus. **This prospectus may not be used to offer and sell securities unless accompanied by the applicable prospectus supplement.**

Our common stock is listed on the Nasdaq Global Select Market under the symbol "REPL." On November 5, 2025, the last reported sale price of our common stock on the Nasdaq Global Select Market was $8.58.

Investing in our securities involves significant risks. We strongly recommend that you read carefully the risks we describe in this prospectus and in any accompanying prospectus supplement, as well as the risk factors that are incorporated by reference into this prospectus from our filings made with the Securities and Exchange Commission. See "Risk Factors" on page 7 of this prospectus.

We may sell the securities directly or to or through underwriters or dealers, and also to other purchasers or through agents. The names of any underwriters or agents that are included in a sale of securities to you, and any applicable commissions or discounts, will be stated in an accompanying prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2025.

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ABOUT THIS PROSPECTUS

This prospectus is part of a shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, under the Securities Act of 1933, as amended. Under this shelf registration statement, we may sell common stock, preferred stock, warrants and debt securities, as well as units that include any combination of the foregoing securities, in one or more offerings from time to time for an aggregate offering amount of up to $250 million. This prospectus provides you with a general description of the securities we may offer.

Each time we sell any type or series of securities under this prospectus, we will provide a prospectus supplement that will include more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference into this prospectus. This prospectus, together with the applicable prospectus supplement, any related free writing prospectus and the documents incorporated by reference into this prospectus and the applicable prospectus supplement, will include all material information relating to the applicable offering. Before buying any of the securities being offered, we urge you to carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectuses we have authorized for use in connection with a specific offering, together with the additional information incorporated herein by reference as described under the heading "Incorporation of Certain Information by Reference."

This prospectus may not be used to consummate a sale of securities unless it is accompanied by an additional prospectus or prospectus supplement.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information appearing in this prospectus, any applicable prospectus supplement and any related free writing prospectus is accurate only as of the date on the front of the document and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, the prospectus supplement or any related free writing prospectus, or the time of any sale of a security.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus includes summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or are incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described under the heading "Where You Can Find More Information."

Unless the context otherwise requires, references in this prospectus to (i) "Replimune," the "Company," "we," "us" and "our" refer to Replimune Group, Inc. and its consolidated subsidiaries and (ii) a year are references to the applicable calendar year and not our fiscal year.

MARKET DATA

This prospectus and the documents incorporated by reference herein include market and industry data and forecasts concerning our business and the markets for certain cancers, including data regarding the estimated size of those markets and the incidence and prevalence of certain medical conditions, that we have derived from independent consultant reports, publicly available information, various industry, medical and general publications, other published industry sources, government data and our internal data and estimates. Independent consultant reports, industry publications and other published industry sources generally indicate that the information contained therein was obtained from sources believed to be reliable. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the markets in which we operate and our management's understanding of industry conditions.

PROSPECTUS SUMMARY

The following summary highlights selected information contained or incorporated by reference elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our securities, you should carefully read this entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the information under the caption "Risk Factors" herein and the applicable prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus, including our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q on file with the SEC and any amendments thereto. You should also carefully read the other information incorporated by reference into this prospectus, including our financial statements and the related notes, and the exhibits to the registration statement of which this prospectus is a part.

Our Company

We are a clinical-stage biotechnology company committed to applying our leading expertise in the field of oncolytic immunotherapy to transform the lives of cancer patients through our novel oncolytic immunotherapies. Our proprietary oncolytic immunotherapy product candidates are intended to maximally activate the immune system against cancer.

Oncolytic immunotherapy is an emerging drug class, which we intend to establish as the second cornerstone of immune-based cancer treatments, alongside checkpoint blockade. Oncolytic immunotherapy exploits the ability of certain viruses to selectively replicate in and directly kill tumors, as well as induce a potent, patient-specific, anti-tumor immune response. Our product candidates incorporate multiple mechanisms of action into a practical "off-the-shelf" approach that is intended to maximize the immune response against a patient's cancer and to offer significant advantages over other approaches to inducing anti-tumor immunity, including personalized vaccine approaches. We believe that the bundling of multiple approaches for the treatment of cancer into single therapies will increase clinical efficacy and simplify the development path of our product candidates, while also improving patient outcomes.

Our proprietary RPx platform is based on a novel, engineered strain of herpes simplex virus 1, or HSV-1, backbone with added payloads intended to maximize immunogenic cell death and induce a systemic anti-tumor immune response. The RPx platform is intended to ignite local activity consisting of direct selective virus-mediated killing of the tumor resulting in the release of tumor-derived antigens and altering of the tumor microenvironment to then activate a strong and durable systemic response. Our product candidates are expected to be synergistic with most established and experimental cancer treatment modalities, and with an attractive safety profile, the RPx platform is expected to have the versatility to be developed alone or combined with a variety of other treatment options. We currently have three RPx product candidates in our development pipeline, RP1 (vusolimogene oderparepvec), our lead product candidate, RP2 and RP3. Although our fiscal year ends March 31st, our programs and program updates are reported on a calendar year basis.

We are conducting a number of clinical trials of RP1, both as a monotherapy and in combination with anti-PD-1 therapy, with a focus on establishing a major skin cancer franchise, assuming approval of our product candidates by the U.S. Food and Drug Administration, or the FDA, and similar applicable foreign regulatory agencies.

Our leading clinical trial of RP1 is referred to as the IGNYTE trial, which is a multi-cohort clinical trial being conducted in collaboration with Bristol Myers Squibb Company, or BMS, under which BMS has granted us a non-exclusive, royalty-free license to, and is supplying at no cost, its anti-PD-1 therapy, nivolumab, for use in combination with RP1.

The leading tumor specific cohort in the IGNYTE trial is our registration directed Phase 2 expansion cohort in anti-PD-1 failed cutaneous melanoma. The anti-PD-1 failed melanoma cohort from the IGNYTE trial includes 140 patients who received RP1 in combination with nivolumab. The primary analysis by independent central review was triggered once all patients had been followed for at least 12 months. As reported in the Journal of Clinical Oncology, July 8, 2025, of the 140 patients enrolled, 48.6% had stage IVM1b/c/d disease, 65.7% had primary anti-PD-1 resistance, 56.4% were PD-L1 negative, and 46.4% received prior anti-PD-1 and anti-cytotoxic T-lymphocyte antigen-4, or anti-CTLA-4, therapy. The confirmed ORR was 32.9% (15.0% complete response) and the responses occurred with similar frequency, depth,

duration, and kinetics for injected and non-injected lesions, including visceral lesions. The median duration of response was 33.7 months and overall survival rates at 1 and 2 years were 75.3% and 63.3%, respectively. RP1 combined with nivolumab continues to be well-tolerated, with mainly Grade 1-2 “on target” side effects, observed.

In November 2024, we announced submission of a biologics license application, or BLA, to the FDA for RP1 (vusolimogene oderparepvec) in combination with nivolumab for the treatment of adult patients with advanced melanoma who have previously received an anti-PD-1 containing regimen, and that the FDA has granted Breakthrough Therapy designation for RP1 in combination with nivolumab in the same setting. The submission was made under the accelerated approval pathway. The FDA accepted our BLA and granted priority review with a Prescription Drug User Fee Act, or PDUFA, goal date of July 22, 2025. On July 21, 2025 the FDA issued a complete response letter, or CRL, for the RP1 BLA for the treatment of advanced melanoma. The FDA stated in the CRL that it was unable to approve the application in its present form and that the IGNYTE trial was not considered to be an adequate and well-controlled clinical investigation that provided substantial evidence of effectiveness, including contribution of components. Furthermore, the FDA said the trial could not be adequately interpreted due to the heterogeneity of the patient population. On September 2, 2025 we announced a type A meeting with the FDA had been scheduled to discuss the CRL following our submission of a briefing book addressing the points raised in the CRL, highlighting prior agreements related to the patient population, criteria for PD-1 resistance, and use of literature to support contribution of components. The briefing book also included an additional analysis of data from the BLA and addressed comments about the phase 3 confirmatory trial design raised by the FDA in the CRL. On September 18, 2025 we announced that, following the type A meeting with the FDA to discuss the CRL, which was conducted on September 16, 2025, we were evaluating feedback received during the meeting to determine our next steps and that, at that time, a path forward under the accelerated approval pathway had not been determined. Following the evaluation of FDA feedback and minutes from the type A meeting, we resubmitted the BLA on October 9, 2025. On October 20, 2025 we announced that the FDA had accepted the resubmission of the BLA for RP1 in combination with nivolumab for the treatment of advanced melanoma in patients who progress on an anti-PD-1 containing regimen. The resubmission included additional information, data and analyses that will be part of the BLA review. The FDA indicated that the resubmission is considered to be a complete response to the CRL and set a PDUFA date of April 10, 2026 based on a Class II resubmission timeline.

We plan to interact with the FDA during the review of the resubmitted BLA and, if approved, intend to bring RP1 to adult patients with advanced melanoma who have previously received an anti-PD-1 containing regimen who otherwise have limited treatment options. Without an approval of RP1 from this resubmitted BLA we might not be able to continue the development of RP1 for this indication, if at all, and we may be required to implement a restructuring plan and review our priorities across the RPx portfolio.

In August 2024, we announced the dosing of the first patient in the IGNYTE-3 trial, or the I-3 trial, a confirmatory study design concept consisting of a 2-arm randomized Phase 3 clinical trial with physician’s choice of treatment as a comparator arm in anti-PD-1 failed melanoma patients. With over 100 sites planned globally and an expectation to enroll 400 patients, the I-3 trial will assess RP1 in combination with nivolumab in patients with advanced melanoma who have progressed on anti-PD-1 and anti-CTLA-4 therapies or are ineligible for anti-CTLA-4 treatment. In the type A meeting minutes following the CRL, the FDA stated a control arm of nivolumab in combination with relatlimab (Opdualag™) may be an acceptable comparator for the I-3 randomized controlled trial. We continue to enroll patients in the I-3 trial.

On October 19, 2025 we announced data from a new ad hoc analysis from the IGNYTE phase 2 cohort of RP1 plus nivolumab, which was released at the European Society for Medical Oncology (ESMO) Congress 2025 held in Berlin. This ad hoc analysis focused on acral melanoma data from patients in the IGNYTE anti-PD-1 failed melanoma cohort and showed treatment with RP1 combined with nivolumab resulted in an objective response rate of 44% (8/18) with a median duration of response of 11.9 months. The safety profile was favorable with generally transient grade 1 and 2 treatment related adverse events, similar to those of the full IGNYTE patient population previously reported. Acral melanoma is a rare and aggressive type of cutaneous melanoma (2 – 3% of all melanoma cases) that frequently occurs on the palms of the hands, soles of the feet, and nailbeds, and often has poor outcomes with many patients presenting with in-transit metastases. Acral melanoma does not typically respond well to available therapies, such as immune

checkpoint inhibitors. Following progression on first-line therapy, aside from targeted therapy for a subset of patients with BRAF mutation-positive tumors, few viable treatment options exist for these patients.

In our non-melanoma skin cancer, or NMSC, cohort of the IGNYTE trial, we provided a data update in December 2023 from the first 30 patients with at least 6 months of follow up including patients with cutaneous squamous cell carcinoma, or CSCC, Merkel cell carcinoma, or MCC, basal cell carcinoma, or BCC, and angiosarcoma in this cohort. The data showed that treatment with RP1 in combination with nivolumab led to an ORR of 30% which is consistent with data from the anti-PD-1 failed melanoma cohort with approximately one-third of patients responding and 60% demonstrating clinical benefit. The combination of RP1 and nivolumab was well tolerated in this patient population with a safety profile consistent with the overall experience seen with this treatment regimen to date. We provided updated data from the NMSC cohort in our June 2025 Investor Day and in October 2025 at ESMO. Responses to RP1 plus nivolumab occurred across the NMSC tumor types enrolled, with confirmed responses seen in patients with both anti-PD-1 naïve and anti-PD-1 failed disease, as well as both in locally advanced and metastatic disease. The ORR by NMSC tumor type for anti-PD-1 naïve patients was 100.0% (n=4) in MCC, 33.3% (n=3) in BCC, 66.7% (n=6) in angiosarcoma, and 56.3% (n=16) in CSCC. The ORR by NMSC tumor type for anti-PD-1 failed patients was 26.3% (n=19) in MCC, 30.0% (n=10) in BCC, 37.5% (n=8) in angiosarcoma, and 15.2% (n=33) in CSCC. We are planning on closing enrollment in this cohort in the fourth quarter of 2025.

Furthering development of RP1, we have open for enrollment a Phase 1b/2 clinical trial of single agent RP1 in solid organ transplant recipients with skin cancers, including CSCC, which we refer to as the ARTACUS trial. We believe that the ARTACUS trial may be potentially registrational (in its own right or, subject to discussion with regulatory authorities, following enrollment of additional patients, including as a potential label expansion after an initial approval of RP1 in a different indication). We are currently planning to enroll up to 65 patients in the ARTACUS trial to assess the safety and efficacy of RP1 in liver, kidney, heart, lung, and hematopoietic cell transplant patients with skin cancers. In November 2023 we presented initial data from the ARTACUS trial of RP1 monotherapy in solid organ transplant recipients with skin cancers at the Society for Immunotherapy of Cancer's, or SITC, 38th Annual Meeting. The data included 23 evaluable patients with CSCC (n=20) and MCC (n=3), demonstrating an ORR of 34.5% and a complete response, or CR, of 21%. RP1 monotherapy was well tolerated in these patients and the safety profile was similar to that observed in our other RP1 clinical trials in patients who are not immune suppressed. No immune-mediated adverse events or evidence of allograft rejection were observed to result from RP1. This data was also presented during oral presentation at the American Association of Cancer Research 2024 Annual Meeting in April 2024. More recently, Dr. Michael R. Migden presented updated data from the ARTACUS trial at the Society for Melanoma Research 22nd International Congress in October 2025. We continue to enroll patients into the ARTACUS trial and are planning a publication of the ARTACUS data in 2026.

As previously reported, our clinical trial of RP1 in patients with CSCC, which we refer to as the CERPASS trial, continues as planned to follow patients that were dosed in the trial.

We are also developing or are continuing to develop additional product candidates, RP2 and RP3, that have been further engineered to enhance anti-tumor immune responses and are intended to address additional tumor types, including traditionally less immune responsive tumor types. In addition to the expression of GALV-GP R(-) and human GM-CSF as in RP1, RP2 has been engineered to express an antibody-like molecule intended to block the activity of CTLA-4, a protein that inhibits the full activation of an immune response, including to tumors. RP3 has been engineered with the intent to further stimulate an anti-tumor immune response through activation of immune co-stimulatory pathways through the additional expression of the ligands for CD40 and 4-1BBL, as well as anti-CTLA-4 and GALV-GP R(-), but without the expression of GM-CSF.

We continue the development of our product candidate RP2 with the goal of moving beyond skin cancers and aiming to treat the more prevalent tumor types commonly found in liver and lung metastasis and including those involving primary liver cancer. Notably, as previously reported, from our Phase-1 clinical trial of RP2 alone and in combination with nivolumab, we have seen durable responses from a monotherapy cohort in a variety of difficult to treat tumors as well as in combination with anti-PD-1 and in particular in patients with metastatic uveal melanoma, or mUM. In November 2023, we presented updated data from a cohort of mUM patients during a Plenary Session at the 20th Annual International Society for Melanoma

Research Congress. The updated data showed RP2 led to an ORR of 29.4% (5 of 17 patients; one of the responding patients was treated with RP2 monotherapy and four of the responding patients were treated with RP2 combined with nivolumab), including responses in patients with liver, lung, and bone metastases. The median DOR at the data cutoff was 11.47 months (range of 2.78 to 21.22 with responses ongoing). Nearly all patients (15 of 17, 88.2%) in the study had progressed on or after immunotherapy with 12 of 17 patients (70.6%) having previously received both anti-PD-1 and anti-CTLA-4 therapies, including four of the responding patients. RP2 was generally well tolerated both as monotherapy and in combination with nivolumab with no additive adverse events observed. The most common grade 1 or 2 treatment related adverse events, or TRAEs, overall in both cohorts were pyrexia, chills, fatigue, hypotension and pruritis. Six patients had grade 3 TRAEs, including two cases of hypotension. There were no grade 4 or 5 TRAEs. In June 2024, we presented that the disease control rate for this cohort of mUM patients was 58.8%.

We have initiated and are enrolling patients in a registration-directed study, or the REVEAL study, of RP2 in mUM patients who are immune checkpoints inhibitor-naïve. The REVEAL study is a randomized, phase 2/3 open label study expected to enroll approximately 280 patients to investigate the efficacy and safety of RP2 in combination with nivolumab vs. ipilimumab in combination with nivolumab in immune checkpoint inhibitor naïve adult patients with metastatic uveal melanoma. The primary endpoints of the trial are overall survival and progression free survival, and key secondary endpoints are overall response rate and disease control rate.

We continue our signal finding trial of RP2 in combination with atezolizumab and bevacizumab in the 2L setting of patients with hepatocellular carcinoma, or HCC, in collaboration with Roche. This Phase 2 clinical trial is currently open and enrollment is underway. The protocol is currently being amended to include RP2 as monotherapy and we plan to release preliminary HCC data by the end of 2026.

We are also planning to open a cohort in our RP2 study to enroll patients with biliary tract cancer, or BTC, and dose RP2 in combination with durvalumab. This cohort is expected to enroll the first patient in the fourth quarter of 2025.

RP1, RP2 and RP3 are administered by direct injection into solid tumors, guided either visually or by ultrasound, computerized tomography or other imaging methods. We believe that direct injection maximizes virus-mediated tumor cell death, provides the most efficient delivery of virus-encoded immune activating proteins into the tumor with the goal of activating systemic immunity, and limits the systemic toxicities that could be associated with intravenous administration. Activation of systemic immunity through local administration is intended to lead to the induction of anti-tumor immune responses leading to clinical response of tumors that have not themselves been injected.

Corporate Information

We are a Delaware corporation formed in July 2017. Our principal executive offices are located at 500 Unicorn Park Drive, Suite 303, Woburn, MA 01801, and our telephone number is (781) 222-9600. Our website is www.replimune.com. Information that is contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. Our fiscal year end is March 31.

Implications of Being a Smaller Reporting Company

We are a “smaller reporting company,” as defined in Regulation S-K. As a result, we may take advantage of certain of the scaled disclosures available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation. We will remain a smaller reporting company if we have (i) less than $250 million in market value of our shares of common stock held by non-affiliates as of the last business day of our second fiscal quarter, or (ii) less than $100 million of annual revenues in our most recent fiscal year completed before the last business day of our second fiscal quarter and less than $700 million in market value of our shares of common stock held by non-affiliates as of the last business day of our second fiscal quarter.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risks described in the documents incorporated by reference in this prospectus and any applicable prospectus supplement and any related free writing prospectus, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to the occurrence of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward- looking statements as a result of certain factors, including the risks described above and in our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q on file with the SEC and any amendments thereto, and in our subsequent reports and filings made with the SEC which are incorporated by reference into this prospectus, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with a specific offering.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the information incorporated by reference into this prospectus, contains, and any applicable prospectus supplement may contain, "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities and Exchange Act of 1934, as amended, or the Exchange Act, including statements regarding our expectations about our cash runway, the design and advancement of our clinical trials, the timing and sufficiency of our clinical trial outcomes to support potential approval of any of our product candidates, our goals to develop and commercialize our product candidates, patient enrollments in our existing and planned clinical trials and the timing thereof, and other statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements that are not statements of historical facts contained in this prospectus, any applicable prospectus supplement and any information incorporated by reference herein and therein may be deemed to be forward-looking statements. In some cases, you can identify these forward-looking statements by the use of words such as "outlook," "believes," "expects," "potential," "continues," "may," "will," "should," "seeks," "approximately," "predicts," "intends," "plans," "estimates," "anticipates" or the negative version of these words or other comparable words. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include, among other things:

- the timing, progress, and results of preclinical studies and clinical trials for our product candidates, including the timing of initiation and completion of studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our ability to obtain additional funding as necessary;
- the timing, scope or likelihood of regulatory filings and approvals, including timing of approval by the U.S. Food and Drug Administration, or the FDA, of, RP1 or any of our other product candidates;
- the timing, scope, or likelihood of foreign regulatory filings and approvals;
- our ability to develop our product candidates for use in combination with other checkpoint blockade therapies, including anti-PD-1;
- our ability to develop and advance any future product candidates into, and successfully complete, clinical trials;
- our expectations regarding the size of the patient populations for RP1, RP2 and/or RP3 or any other product candidates from our RPx platform if approved for commercial use;
- our ability to successfully qualify, obtain approval for, and maintain successful operation, approval and qualification of our in-house manufacturing operations;
- our ability to obtain and maintain sufficient quantities of raw material supplies or access single or limited sources of goods or services needed to build or maintain our product candidate supplies or otherwise operate our in-house manufacturing facility;
- the costs of operating our in-house manufacturing facility;
- our estimates regarding expenses and capital requirements;
- the implementation of our business model and our strategic plans for our business, RP1 and our other product candidates;
- the rate and degree of market acceptance and clinical utility of RP1 and our other product candidates;
- the potential benefits of and our ability to establish or maintain future collaborations or strategic relationships;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering RP1 and our other product candidates, claims

others may make regarding rights in our intellectual property, and any potential infringement, misappropriation or other violation of any third-party intellectual property rights;

- our competitive position, and developments and projections relating to our competitors and our industry;
- negative developments in the fields of immuno-oncology or oncolytic immunotherapy;
- the impact of laws and regulations; and
- the other risks and uncertainties described under "Risk factors" of our Annual Report on Form 10-K for the year ended March 31, 2025 and our subsequent filings which are incorporated by reference into this prospectus.

The forward-looking statements made in this prospectus, any applicable prospectus supplement and the documents that we incorporate by reference herein and therein relate only to events as of the date on which the statements are made. These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this prospectus, any applicable prospectus supplement and the documents that we incorporate by reference herein and therein. Moreover, we operate in a competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this prospectus, any applicable prospectus supplement and the documents that we incorporate by reference herein and therein. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise, except to the extent required by applicable law. You should not rely on forward-looking statements as predictions of future events. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any related free writing prospectuses we may authorize for use in connection with a specific offering, we currently expect to use the net proceeds from the securities offered hereunder, if any, together with our existing cash and cash equivalents, short-term investments and proceeds from our available term loan facility, to fund the continued development of our RPx platform including indication expansion with RP1 in skin cancer and broadening the RP2 clinical development plan as well as for general corporate purposes, including working capital requirements and operating expenses. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the securities offered by us hereunder. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus.

THE SECURITIES WE MAY OFFER

We may sell common stock, preferred stock, warrants and debt securities, as well as units that include any combination of the foregoing securities, in one or more offerings from time to time under this prospectus at prices and on terms to be determined at the time of any offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement or free writing prospectus, or both, that will describe the specific amounts, prices and other important terms of the securities being offered.

DESCRIPTION OF CAPITAL STOCK

The following is a description of certain provisions of our certificate of incorporation and bylaws, and certain provisions of the Delaware General Corporation Law, or DGCL. The following description does not purport to be complete and is subject to, and qualified in its entirety by reference to, our certificate of incorporation and bylaws, each filed as exhibits to the registration statement of which this prospectus forms a part, and the terms and provisions of the DGCL. For more complete information, you should carefully review our certificate of incorporation and bylaws, which have been filed with the SEC as exhibits to our registration statement of which this prospectus forms a part and which may be obtained as described below under "Where You Can Find More Information."

Our authorized capital stock consists of 150 million shares of common stock, par value $0.001 per share, and 10 million shares of undesignated preferred stock, par value $0.001 per share.

Common stock

Subject to any preferential rights that may be applicable to any outstanding shares of preferred stock from time to time, the holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. The holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Preferred stock

Pursuant to our certificate of incorporation, our board of directors has the authority, without further action by our stockholders, to issue up to 10 million shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions, as well as the number of shares constituting and the designation of any series, thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences or sinking fund terms any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. There are currently no shares of preferred stock outstanding, and we have no present plan to issue any shares of preferred stock.

The DGCL provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Pre-funded Warrants

We have outstanding pre-funded warrants to purchase shares of our common stock consisting of pre-funded warrants to purchase an aggregate of:

- 217,391 shares of our common stock at an exercise price of $0.0001 per share, which were issued in June 2020 in an underwritten public offering;
- 125,000 shares of our common stock at an exercise price of $0.0001 per share, which were issued in October 2020 in an underwritten public offering;
- 4,200,000 shares of our common stock at an exercise price of $0.0001 per share, which were issued in December 2022 in an underwritten public offering;

- 5,669,578 shares of our common stock at an exercise price of $0.001 per share, which were issued in June 2024 in a private placement, or the June 2024 Pre-Funded Warrants; and
- 3,846,184 shares of our common stock at an exercise price of $0.0001 per share, which were issued in December 2024 in an underwritten public offering, or the December 2024 Pre-Funded Warrants.

Each pre-funded warrant entitles the holder to purchase one share of our common stock at the applicable per share exercise price. The pre-funded warrants do not expire and may be exercised by the holder at any time after their original issuance. Unless otherwise modified by a holder of a pre-funded warrant, no holder may exercise a pre-funded warrant (i) if such holder, together with its affiliates, would beneficially own more than 9.99% (or, in the case of the December 2024 Pre-Funded Warrants, 4.99%) of the number of shares of our common stock outstanding immediately after giving effect to such exercise, or (ii) if the combined voting power of our securities beneficially owned by such holder, together with its affiliates, would exceed 9.99% (or, in the case of the December 2024 Pre-Funded Warrants, 4.99%) of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise of such pre-funded warrants, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, a holder of a pre-funded warrant may increase or decrease this percentage to any other percentage not in excess of 19.99% or, in the case of the June 2024 Pre-Funded Warrants, 9.99%, by providing us with at least 61 days' prior notice. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants are subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

Anti-takeover effects of provisions of Delaware law and our certificate of incorporation and bylaws

Requirements for advance notification of stockholder meetings, nominations and proposals

Our certificate of incorporation provides that special meetings of the stockholders may be called only by or at the direction of our board of directors. Our bylaws prohibit the conduct of any business at a special meeting other than as specified in the notice for such meeting. These provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control or management of our company.

Our bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of our board of directors or a committee of our board of directors. In order for any matter to be "properly brought" before a meeting, a stockholder will have to comply with advance notice requirements and provide us with certain information. Additionally, vacancies and newly created directorships may be filled only by a vote of a majority of the directors then in office, even if less than a quorum, and not by the stockholders. Our bylaws allow the presiding officer at a meeting of the stockholders to adopt rules and regulations for the conduct of meetings which may have the effect of precluding the conduct of certain business at a meeting if the rules and regulations are not followed. These provisions may also defer, delay or discourage a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Our certificate of incorporation provides that our board of directors is expressly authorized to adopt, amend or repeal our bylaws.

No cumulative voting

The DGCL provides that stockholders are not entitled to cumulate votes in the election of directors unless our certificate of incorporation provides otherwise. Our certificate of incorporation does not expressly provide for cumulative voting.

Amendments to certificate of incorporation and bylaws

The DGCL provides that, unless a corporation's certificate of incorporation provides otherwise, the affirmative vote of holders of shares constituting a majority of the votes of all shares entitled to vote may approve amendments to the certificate of incorporation.

Our certificate of incorporation and bylaws provide that the affirmative vote of holders of at least 75% of the outstanding shares of capital stock, voting together as a single class, and entitled to vote in the election of directors will be required to amend, alter, change or repeal certain provisions of our certificate of incorporation and bylaws. This requirement of a supermajority vote to approve amendments to our certificate of incorporation and bylaws could enable a minority of our stockholders to exercise veto power over such amendments.

Forum selection clause

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers or other employees to us or our stockholders; (iii) any action asserting a claim against us or any director or officer or other employee of ours arising pursuant to any provision of the DGCL or our certificate of incorporation or bylaws; or (iv) any action asserting a claim against us or any director or officer or other employee of ours governed by the internal affairs doctrine. This exclusive forum provision would not apply to suits brought to enforce any liability or duty created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. To the extent that any such claims may be based upon federal law claims, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. Our certificate of incorporation further provides that any person or entity that acquires any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions described above.

Staggered board

Our certificate of incorporation provides that our board of directors is divided into three classes of directors, with the directors in each class serving staggered three-year terms and with the number of directors in each class to be as nearly equal as possible.

Stockholder action by written consent

Pursuant to Section 228 of the DGCL, any action required to be taken at any annual or special meeting of the stockholders may be taken without a meeting, without prior notice and without a vote, if a consent or consents in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares of our stock entitled to vote thereon were present and voted, unless the corporation's certificate of incorporation provides otherwise. Our certificate of incorporation prohibits the taking of any action of our stockholders by written consent without a meeting.

Delaware anti-takeover statute

We have not opted out of, and therefore are subject to, Section 203 of the DGCL. Section 203 provides that, subject to certain exceptions specified in the law, a publicly-held Delaware corporation shall not engage in certain "business combinations" with any "interested stockholder" for a three-year period after the date of the transaction in which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned under employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

- on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 662⁄3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. Since Section 203 will apply to us, we expect that it would have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. In such event, we would also anticipate that Section 203 could discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders. Under certain circumstances, Section 203 makes it more difficult for a person who would be an "interested stockholder" to effect various business combinations with a corporation for a three-year period. The provisions of Section 203 may encourage companies interested in acquiring our company to negotiate in advance with our board of directors because the stockholder approval requirement would be avoided if our board of directors approves either the business combination or the transaction that results in the stockholder becoming an interested stockholder. These provisions also may make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Authorized but unissued capital stock

The DGCL does not require stockholder approval for any issuance of authorized shares. However, the listing requirements of the Nasdaq Global Select Market, which apply so long as our common stock remains listed on the Nasdaq Global Select Market, require stockholder approval of certain issuances equal to or exceeding 20% of the then outstanding voting power or then outstanding number of shares of common stock. These additional shares may be used for a variety of corporate purposes, including future public offerings, to raise additional capital or to facilitate acquisitions.

One of the effects of the existence of unissued and unreserved common stock or preferred stock may be to enable our board of directors to issue shares to persons friendly to current management, which issuance could render more difficult or discourage an attempt to obtain control of our company by means of a merger, tender offer, proxy contest or otherwise, and thereby protect the continuity of our management and possibly deprive our investors of opportunities to sell their shares of common stock at prices higher than prevailing market prices.

Registration rights

Certain of the holders of our common stock, or their transferees, are entitled to registration rights with respect to the registration of the resale of such shares under the Securities Act.

On June 14, 2024, in connection with the closing of a private placement, we entered into a registration rights agreement, or the Registration Rights Agreement, pursuant to which certain holders of our common stock have certain registration rights in respect of the securities acquired in connection with the private placement, subject to customary conditions.

On March 5, 2025, we entered into a registration rights agreement, or the Affiliate Registration Rights Agreement, with 667, L.P. and Baker Brothers Life Sciences, L.P., collectively, the BBA Funds. Pursuant to the Affiliate Registration Rights Agreement, the BBA Funds are entitled to certain resale registration rights with respect to shares of our common stock issued or issuable upon the exercise or conversion of any other securities (whether equity, debt or otherwise) now owned or subsequently acquired by the BBA Funds, subject to certain specified exceptions, conditions and limitations as set forth in the Affiliate Registration Rights Agreement.

Limitations of liability and indemnification

Our certificate of incorporation limits the liability of directors to the fullest extent permitted by Delaware law. The effect of these provisions is to eliminate our rights and the rights of our stockholders,

through stockholders' derivative suits on our behalf, to recover monetary damages from a director for breach of fiduciary duty as a director, including breaches resulting from grossly negligent behavior. However, exculpation does not apply to any director if the director has acted in bad faith, knowingly or intentionally violated the law, authorized illegal dividends or redemptions or derived an improper benefit from his or her actions as a director.

In addition, our certificate of incorporation and bylaws provide that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. We also expect to continue to maintain directors' and officers' liability insurance. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and executive officers.

The limitation of liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders.

In addition to the indemnification required in our certificate of incorporation and bylaws, we enter into indemnification agreements with each of our directors and executive officers. These agreements provide for the indemnification of our directors and executive officers for all reasonable expenses and liabilities incurred in connection with any action or proceeding brought against them by reason of the fact that they are or were our agents. We believe that these provisions and indemnification agreements, as well as maintaining directors' and officers' liability insurance, help to attract and retain qualified persons as directors and officers.

Market listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "REPL."

Transfer agent and registrar

The transfer agent and registrar for our common stock is Computershare Trust Company N.A.

DESCRIPTION OF DEBT SECURITIES

The following is a general description of the terms of debt securities we may issue from time to time unless we provide otherwise in the applicable prospectus supplement. Particular terms of any debt securities we offer will be described in the prospectus supplement relating to such debt securities.

As required by Federal law for all bonds and notes of companies that are publicly offered, any debt securities we issue will be governed by a document called an "indenture." We have summarized the general features of the debt securities to be governed by the indenture. The summary is not complete. An indenture is a contract between us and a financial institution acting as trustee on behalf of the holders of the debt securities, and is subject to and governed by the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. The trustee has two main roles. First, the trustee can enforce holders' rights against us if we default. There are some limitations on the extent to which the trustee acts on holders' behalf, described in the second paragraph under "Description of Debt Securities — Events of Default." Second, the trustee performs certain administrative duties, such as sending interest and principal payments to holders.

Because this section is a summary, it does not describe every aspect of any debt securities we may issue or the indenture governing any such debt securities. Particular terms of any debt securities we offer will be described in the prospectus supplement relating to such debt securities, and we urge you to read the applicable executed indenture, which will be filed with the SEC at the time of any offering of debt securities, because it, and not this description, will define the rights of holders of such debt securities.

A prospectus supplement will describe the particular terms of any series of debt securities we may issue, including some or all of the following:

- the designation or title of the series of debt securities;
- the total principal amount of the series of debt securities, the denominations in which the offered debt securities will be issued and whether the offering may be reopened for additional securities of that series and on what terms;
- the percentage of the principal amount at which the series of debt securities will be offered;
- the date or dates on which principal will be payable;
- the rate or rates (which may be either fixed or variable) and/or the method of determining such rate or rates of interest, if any;
- the date or dates from which any interest will accrue, or the method of determining such date or dates, and the date or dates on which any interest will be payable;
- the terms for redemption, extension or early repayment, if any;
- the currencies in which the series of debt securities are issued and payable;
- whether the amount of payments of principal, interest or premium, if any, on a series of debt securities will be determined with reference to an index, formula or other method and how these amounts will be determined;
- the place or places of payment, transfer, conversion and/or exchange of the debt securities;
- the provision for any sinking fund;
- any restrictive covenants;
- events of default;
- whether the series of debt securities are issuable in certificated form;
- any provisions for legal defeasance or covenant defeasance;
- whether and under what circumstances we will pay additional amounts in respect of any tax, assessment or governmental charge and, if so, whether we will have the option to redeem the debt securities rather than pay the additional amounts (and the terms of this option);

- any provisions for convertibility or exchangeability of the debt securities into or for any other securities;
- whether the debt securities are subject to subordination and the terms of such subordination;
- any listing of the debt securities on any securities exchange;
- whether the issuance of the debt securities may limit the incurrence of additional debt;
- if applicable, a discussion of material United States federal income tax considerations, including those related to original issue discount, if applicable; and
- any other material terms.

The debt securities may be secured or unsecured obligations. Unless the prospectus supplement states otherwise, principal, interest and premium, if any, will be paid by us in immediately available funds.

General

The indenture may provide that any debt securities proposed to be sold under this prospectus and the applicable prospectus supplement relating to such debt securities ("offered debt securities") and any debt securities issuable upon conversion or exchange of other offered securities ("underlying debt securities") may be issued under the indenture in one or more series.

For purposes of this prospectus, any reference to the payment of principal of, or interest or premium, if any, on, debt securities will include additional amounts if required by the terms of the debt securities.

Debt securities issued under an indenture, when a single trustee is acting for all debt securities issued under the indenture, are called the "indenture securities." The indenture may also provide that there may be more than one trustee thereunder, each with respect to one or more different series of securities issued thereunder. See "Description of Debt Securities — Resignation of Trustee" below. At a time when two or more trustees are acting under an indenture, each with respect to only certain series, the term "indenture securities" means the one or more series of debt securities with respect to which each respective trustee is acting. In the event that there is more than one trustee under an indenture, the powers and trust obligations of each trustee described in this prospectus will extend only to the one or more series of indenture securities for which it is trustee. If two or more trustees are acting under an indenture, then the indenture securities for which each trustee is acting would be treated as if issued under separate indentures.

We refer you to the applicable prospectus supplement relating to any debt securities we may issue from time to time for information with respect to any deletions from, modifications of or additions to the Events of Default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection, that will be applicable with respect to such debt securities.

We have the ability to issue indenture securities with terms different from those of indenture securities previously issued and, without the consent of the holders thereof, to reopen a previous issue of a series of indenture securities and issue additional indenture securities of that series unless the reopening was restricted when that series was created.

Conversion and Exchange

If any debt securities are convertible into or exchangeable for other securities, the related prospectus supplement will explain the terms and conditions of the conversion or exchange, including the conversion price or exchange ratio (or the calculation method), the conversion or exchange period (or how the period will be determined), if conversion or exchange will be mandatory or at the option of the holder or us, provisions for adjusting the conversion price or the exchange ratio and provisions affecting conversion or exchange in the event of the redemption of the underlying debt securities. These terms may also include provisions under which the number or amount of other securities to be received by the holders of the debt securities upon conversion or exchange would be calculated according to the market price of the other securities as of a time stated in the prospectus supplement.

Payment and Paying Agents

We will pay interest to the person listed in the applicable trustee's records as the owner of the debt security at the close of business on a particular day in advance of each due date for interest, even if that person no longer owns the debt security on the interest due date. That day, often approximately two weeks in advance of the interest due date, is called the "record date." Because we will pay all the interest for an interest period to the holders on the record date, holders buying and selling debt securities must work out between themselves the appropriate purchase price. The most common manner is to adjust the sales price of the debt securities to prorate interest fairly between buyer and seller based on their respective ownership periods within the particular interest period. This prorated interest amount is called "accrued interest."

Events of Default

Holders of debt securities of any series will have rights if an Event of Default occurs in respect of the debt securities of such series and is not cured, as described later in this subsection. The term "Event of Default" in respect of the debt securities of any series means any of the following:

- we do not pay the principal of, or any premium on, a debt security of the series on its due date;
- we do not pay interest on a debt security of the series within 30 days of its due date;
- we remain in breach of a covenant in respect of debt securities of the series for 60 days after we receive a written notice of default stating we are in breach. The notice must be sent by either the trustee or holders of at least 25% of the principal amount of debt securities of the series;
- we file for bankruptcy or certain other events of bankruptcy, insolvency or reorganization occur;
- any guarantee in respect of a debt security of the series ceases to be in full force and effect or any guarantor denies or disaffirms is obligation under its guarantee; and
- any other Event of Default occurs in respect of debt securities of the series described in the prospectus supplement.

An Event of Default for a particular series of debt securities does not necessarily constitute an Event of Default for any other series of debt securities issued under the same or any other indenture. The trustee may withhold notice to the holders of debt securities of any default, except in the payment of principal, premium or interest, if it considers the withholding of notice to be in the best interests of the holders.

Remedies if an Event of Default Occurs

If an Event of Default has occurred and has not been cured or waived, the trustee or the holders of not less than 25% in principal amount of the debt securities of the affected series may declare the entire principal amount of all the debt securities of that series to be due and immediately payable. This is called a declaration of acceleration of maturity. A declaration of acceleration of maturity may be cancelled by the holders of a majority in principal amount of the debt securities of the affected series if the default is cured or waived and certain other conditions are satisfied.

Except in cases of default, where the trustee has some special duties, the trustee typically is not required to take any action under an indenture at the request of any holders unless the holders offer the trustee reasonable protection from expenses and liability (called an "indemnity"). If reasonable indemnity is provided, the holders of a majority in principal amount of the outstanding debt securities of the relevant series may direct the time, method and place of conducting any lawsuit or other formal legal action seeking any remedy available to the trustee. The trustee may refuse to follow those directions in certain circumstances.

Before a holder is allowed to bypass the trustee and bring its own lawsuit or other formal legal action or take other steps to enforce its rights or protect its interests relating to any debt securities, the following must occur:

- the holder must give the trustee written notice that an Event of Default has occurred and remains uncured;

- the holders of at least 25% in principal amount of all outstanding debt securities of the relevant series must make a written request that the trustee take action because of the default and must offer reasonable indemnity to the trustee against the cost and other liabilities of taking that action;
- the trustee must not have taken action for 60 days after receipt of the above notice and offer of indemnity; and
- the holders of a majority in principal amount of the debt securities must not have given the trustee a direction inconsistent with the above notice during that 60-day period.

However, a holder is entitled at any time to bring a lawsuit for the payment of money due on its debt securities on or after the due date. Each year, we will furnish to each trustee a written statement of certain of our officers certifying that to their knowledge we are in compliance with the indenture and the debt securities, or else specifying any default.

Waiver of Default

The holders of a majority in principal amount of the relevant series of debt securities may waive a default for all such series of debt securities. If this happens, the default will be treated as if it had not occurred. No one can waive a payment default on a holder's debt security, however, without the holder's approval.

Merger or Consolidation

Under the terms of an indenture, we may be permitted to consolidate or merge with another entity. We may also be permitted to sell all or substantially all of our assets to another entity. However, typically we may not take any of these actions unless all the following conditions are met:

- if we do not survive such transaction or we convey, transfer or lease our properties and assets substantially as an entirety, the acquiring company must be a corporation, limited liability company, partnership or trust, or other corporate form, organized under the laws of any state of the United States or the District of Columbia, and such company must agree to be legally responsible for our debt securities, and, if not already subject to the jurisdiction of any state of the United States or the District of Columbia, the new company must submit to such jurisdiction for all purposes with respect to the debt securities and appoint an agent for service of process;
- alternatively, we must be the surviving company;
- immediately after the transaction no Event of Default or event that would become an Event of Default will exist;
- we must deliver certain certificates and documents to the trustee; and
- we must satisfy any other requirements specified in the prospectus supplement relating to a particular series of debt securities.

Modification or Waiver

There are three types of changes we may make to an indenture and the debt securities issued thereunder.

Changes Requiring Approval

First, there are changes that we may not be able to make to debt securities without specific approval of all of the affected holders. The following is a list of the types of changes that may require specific approval:

- change the stated maturity of the principal of or rate of interest on a debt security;
- reduce any amounts due on a debt security;
- reduce the amount of principal payable upon acceleration of the maturity of a security following a default;
- change the place or currency of payment on a debt security (except as otherwise described in the prospectus or prospectus supplement);

- impair the right of holders to sue for payment;
- adversely affect any right to convert or exchange a debt security in accordance with its terms;
- reduce the percentage of holders of debt securities whose consent is needed to modify or amend the indenture;
- reduce the percentage of holders of debt securities whose consent is needed to waive compliance with certain provisions of the indenture or to waive certain defaults;
- modify any other aspect of the provisions of the indenture dealing with supplemental indentures, modification and waiver of past defaults, changes to the quorum or voting requirements or the waiver of certain covenants; and
- change any obligation we or any guarantor may have in respect of the payment of principal, interest or other amounts.

Changes Not Requiring Approval

The second type of change does not require any vote by the holders of the debt securities. This type is limited to clarifications and certain other changes that would not adversely affect holders of the outstanding debt securities in any material respect, including the addition of covenants and guarantees.

Changes Requiring Majority Approval

Any other change to the indenture and the debt securities must be approved by the holders of a majority in aggregate principal amount of all of the series issued under the same supplemental indenture affected by the change, with all affected series voting together as one class for this purpose.

The holders of a majority in principal amount of all of the series of debt securities issued under a supplemental indenture, voting together as one class for this purpose, may waive our compliance obligations with respect to some of our covenants in that supplemental indenture. However, we cannot obtain a waiver of a payment default or of any of the matters covered by the bullet points included above under “Description of Debt Securities — Modification or Waiver — Changes Requiring Approval.”

Further Details Concerning Voting

Debt securities will not be considered outstanding, and therefore not eligible to vote, if we have deposited or set aside in trust money for their payment or redemption. Debt securities will also not be eligible to vote if they have been fully defeased as described later under “Description of Debt Securities — Defeasance — Legal Defeasance.”

We generally will be entitled to set any day as a record date for the purpose of determining the holders of outstanding indenture securities that are entitled to vote or take other action under the indenture not more than 90 calendar days nor less than 20 calendar days prior to the proposed date of such vote or consent.

Book-entry and other indirect holders will need to consult their banks or brokers for information on how approval may be granted or denied if we seek to change the indenture or the debt securities or request a waiver.

Defeasance

The following provisions will be applicable to each series of debt securities unless we state in the applicable prospectus supplement that the provisions of covenant defeasance and legal defeasance will not be applicable to that series.

Covenant Defeasance

We can make the deposit described below and be released from some of the restrictive covenants in the indenture under which the particular series was issued. This is called “covenant defeasance.” In that event, the holders would lose the protection of those restrictive covenants but would gain the protection of having

money and government securities set aside in trust to repay holders' debt securities. If applicable, a holder also would be released from the subordination provisions described under "Description of Debt Securities — Indenture Provisions — Subordination" below. In order to achieve covenant defeasance, we must do the following:

- we must deposit in trust for the benefit of all holders of such debt securities a combination of money and non-callable U.S. government notes or bonds that will be sufficient to pay and discharge all interest, principal and any other payments on the debt securities on their various due dates;
- we may be required to deliver to the trustee a legal opinion of our counsel confirming that, under current U.S. Federal income tax law, we may make the above deposit without causing the holders to be taxed on the debt securities any differently than if we did not make the deposit and just repaid the debt securities ourselves at maturity; and
- we must deliver to the trustee certain documentation stating that all conditions precedent to covenant defeasance have been complied with.

If we accomplish covenant defeasance, holders can still look to us for repayment of the debt securities if there were a shortfall in the trust deposit or the trustee is prevented from making payment. In fact, if one of the remaining Events of Default occurred (such as our bankruptcy) and the debt securities became immediately due and payable, there might be a shortfall. Depending on the event causing the default, holders may not be able to obtain payment of the shortfall.

Legal Defeasance

As described below, we can legally release ourselves from all payment and other obligations on the debt securities of a particular series (called "legal defeasance"), (1) if there is a change in U.S. Federal tax law that allows us to effect the release without causing the holders to be taxed any differently than if the release had not occurred, and (2) if we put in place the following other arrangements for holders to be repaid:

- we must deposit in trust for the benefit of all holders of such debt securities a combination of money and U.S. government notes or bonds that will be sufficient to pay and discharge all interest, principal and any other payments on the debt securities on their various due dates;
- we may be required to deliver to the trustee a legal opinion confirming that there has been a change in current U.S. Federal tax law or an Internal Revenue Service ruling that allows us to make the above deposit without causing the holders to be taxed on the debt securities any differently than if we did not make the deposit and just repaid the debt securities ourselves at maturity; and
- we must deliver to the trustee a legal opinion and officers' certificate stating that all conditions precedent to legal defeasance have been complied with.

If we ever did accomplish legal defeasance, as described above, holders would have to rely solely on the trust deposit for repayment of the debt securities. Holders could not look to us for repayment in the unlikely event of any shortfall. Conversely, the trust deposit would most likely be protected from claims of our lenders and other creditors if we ever became bankrupt or insolvent.

Resignation of Trustee

Each trustee may resign or be removed with respect to one or more series of indenture securities provided that a successor trustee is appointed to act with respect to such series. In the event that two or more persons are acting as trustee with respect to different series of indenture securities under the indenture, each of the trustees will be a trustee of a trust separate and apart from the trust administered by any other trustee.

Trustee

We intend to name the indenture trustee for each series of indenture securities in the related prospectus supplement.

Certain Considerations Relating to Foreign Currencies

Debt securities denominated or payable in foreign currencies may entail significant risks. These risks include the possibility of significant fluctuations in the foreign currency markets, the imposition or modification of foreign exchange controls and potential illiquidity in the secondary market. These risks will vary depending upon the currency or currencies involved and will be more fully described in the applicable prospectus supplement.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock, shares of our preferred stock or debt securities. The following description sets forth certain general terms and provisions of the warrants that we may offer pursuant to this prospectus. The particular terms of the warrants and the extent, if any, to which the general terms and provisions may apply to the warrants so offered will be described in the applicable prospectus supplement.

Warrants may be issued independently or together with other securities and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants.

A copy of the forms of the warrant agreement and the warrant certificate relating to any particular issue of warrants will be filed with the SEC each time we issue warrants, and you should read those documents for provisions that may be important to you. For more information on how you can obtain copies of the forms of the warrant agreement and the related warrant certificate, if applicable, see "Where You Can Find More Information."

Stock Warrants

The prospectus supplement relating to a particular issue of warrants to issue shares of our common stock or shares of our preferred stock will describe the terms of the common share warrants and preferred share warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of the warrants;
- the designation and terms of the shares of common stock or shares of preferred stock that may be purchased upon exercise of the warrants;
- the terms for changes or adjustments to the exercise price of the warrants;
- if applicable, the designation and terms of the securities that the warrants are issued with and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares of common stock or shares of preferred stock that may be purchased upon exercise of a warrant and the price at which the shares may be purchased upon exercise;
- the dates on which the right to exercise the warrants commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material United States federal income tax considerations;
- anti-dilution provisions of the warrants, if any;
- redemption or call provisions, if any, applicable to the warrants;
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants; and
- any other information we think is important about the warrants.

Debt Warrants

The prospectus supplement relating to a particular issue of warrants to issue debt securities will describe the terms of those warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of the warrants;
- the designation and terms of the debt securities purchasable upon exercise of the warrants;
- the terms for changes or adjustments to the exercise price of the warrants;
- if applicable, the designation and terms of the debt securities that the warrants are issued with and the number of warrants issued with each debt security;
- if applicable, the date from and after which the warrants and any debt securities issued with them will be separately transferable;
- the principal amount of debt securities that may be purchased upon exercise of a warrant and the price at which the debt securities may be purchased upon exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- whether the warrants represented by the warrant certificates or debt securities that may be issued upon exercise of the warrants will be issued in registered or bearer form;
- information relating to book-entry procedures, if any;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material United States federal income tax considerations;
- anti-dilution provisions of the warrants, if any;
- redemption or call provisions, if any, applicable to the warrants;
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants; and
- any other information we think is important about the warrants.

Exercise of Warrants

Each warrant will entitle the holder of the warrant to purchase at the exercise price set forth in the applicable prospectus supplement the number of shares of common stock, shares of preferred stock or the principal amount of debt securities being offered. Holders may exercise warrants at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants are void. Holders may exercise warrants as set forth in the prospectus supplement relating to the warrants being offered.

Until a holder exercises the warrants to purchase our shares of common stock, shares of preferred stock or debt securities, the holder will not have any rights as a holder of our shares of common stock, shares of preferred stock or debt securities, as the case may be, by virtue of ownership of warrants.

DESCRIPTION OF UNITS

We may issue, in one or more series, units consisting of common stock, preferred stock, or warrants for the purchase of common stock or preferred stock in any combination. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreement that contains the terms of the units. We will incorporate by reference from reports that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

Units may be issued under a unit agreement that we enter into with a unit agent. We will indicate the name and address of the unit agent, if applicable, in the prospectus supplement relating to the particular series of units being offered.

The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities composing the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities composing the units; and
- whether the units will be issued in fully registered or global form.

FORMS OF SECURITIES

Each debt security, warrant and unit will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, warrants or units represented by these global securities. The depositary maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities of a particular series, depositary shares, subscription right, units and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depositary for the global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a global security, the depositary will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depositary, or its nominee, is the registered owner of a global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture, deposit agreement, subscription rights agreement, warrant agreement or unit agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, purchase unit agreement or warrant agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depositary for that global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, deposit agreement, subscription rights agreement, unit agreement or warrant agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture, unit agreement or warrant agreement, the depositary for the global security would authorize the participants holding the relevant beneficial interests to

give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to warrants, purchase agreements or units, represented by a global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent, unit agent or other agent of ours, or any agent of any trustee, warrant agent or unit agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in "street name," and will be the responsibility of those participants.

If the depositary for any of the securities represented by a global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depositary. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers;
- in an "at the market offering," within the meaning of Rule 415(a)(4) of the Securities Act;
- in negotiated transactions;
- in block trades; or
- through a combination of any of these methods or any other method permitted by law.

In addition, we may issue the securities as a dividend or distribution to our existing security holders. We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers.

In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions. The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- at a fixed price, or prices, which may be changed from time to time;
- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in any accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an "underwriter" as that term is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in

settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in one business day, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the aggregate maximum discount, commission or agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

LEGAL MATTERS

Certain legal matters, including the validity of the issuance of the securities offered, will be passed upon for us by Morgan, Lewis & Bockius LLP, New York, New York. Additional legal matters may be passed upon by us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended March 31, 2025 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information requirements of the Exchange Act, and in accordance with the Exchange Act, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). Our corporate website address is *www.replimune.com*. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information contained in documents that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC before the date of this prospectus, while information that we file later with the SEC will automatically update and supersede prior information. Any information so updated and superseded shall not be deemed, except as so updated and superseded, to constitute a part of this prospectus. We incorporate by reference the documents listed below and any future filings we will make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the filing of the registration statement and prior to the effectiveness of the registration statement, and prior to the termination of the offering:

- our Annual Report on Form 10-K for the fiscal year ended March 31, 2025, filed with the SEC on May 22, 2025;
- our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2025, filed with the SEC on August 7, 2025, and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2025, filed with the SEC on November 6, 2025;
- our Current Reports on Form 8-K filed with the SEC on July 22, 2025, September 4, 2025, September 18, 2025, and October 20, 2025 (provided that any portions of such reports that are deemed furnished and not filed pursuant to instructions to Form 8-K shall not be incorporated by reference into this prospectus); and
- our description of our common stock contained in the registration statement on Form 8-A, filed on July 17, 2018, as the description therein has been updated and superseded by the description of our capital stock contained in Exhibit 4.3 to our Annual Report on Form 10-K for the fiscal year ended March 31, 2025, as filed with the SEC on May 22, 2025, and including any amendments and reports filed for the purpose of updating such description.

Notwithstanding the foregoing, unless specifically stated to the contrary, none of the information that is not deemed "filed" with the SEC, including information furnished under Items 2.02 or 7.01 of any Current Report on Form 8-K, will be incorporated by reference into, or otherwise included in, this prospectus.

We make available, free of charge, through our website at www.replimune.com under "Investor and Media" our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not incorporated by reference into this prospectus and should not be considered part of this prospectus or any applicable prospectus supplement. In addition, the SEC maintains an Internet website that contains reports, proxy and information statements, and other information that we file with the SEC at www.sec.gov. You may also obtain, free of charge, a copy of any of these documents (other than exhibits to these documents unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus) by writing or calling us at the following address and telephone number:

Replimune Group, Inc.
Attention: Investor Relations
500 Unicorn Park, Suite 303
Woburn MA 01801
+1 (781) 222-9600

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

$250,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

PROSPECTUS

, 2025

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

Subject to completion, dated November 6, 2025

PROSPECTUS

$100,000,000

Common Stock

We entered into a sales agreement with Leerink Partners LLC, or the Agent, dated August 3, 2023, relating to the sale of shares of our common stock, $0.001 par value per share, or Common Stock, offered by this prospectus. Pursuant to the sales agreement, we may offer and sell shares of our Common Stock from time to time through the Agent, acting as our sales agent or principal. We and the Agent entered into amendments to the sales agreement, after giving effect to which we and the Agent agreed that we may offer and sell from time to time under the sales agreement an aggregate offering price of up to $100 million of our Common Stock. References in this prospectus to the Sales Agreement refer to the foregoing sales agreement, as amended.

We previously filed a prospectus, dated August 3, 2023, or the Prior Prospectus, for the offer and sale of shares of our Common Stock having an aggregate offering price of up to $250 million from time to time through the Agent pursuant to the Sales Agreement under the shelf registration statement on Form S-3 (File No. 333-273633), as amended by Post-Effective Amendment No. 1 and Post-Effective Amendment No. 2. As of the date of this prospectus, we have not sold any shares of our Common Stock pursuant to the Sales Agreement or the Prior Prospectus. All of the shares of our Common Stock available to be sold under the Sales Agreement as of the date of this prospectus will no longer be offered or sold under the Prior Prospectus. Instead, the $100 million of shares of our Common Stock available to be sold under the Sales Agreement will be offered and sold under this prospectus.

Sales of our Common Stock, if any, under this prospectus may be made in sales deemed to be "at the market offerings" as defined in Rule 415(a) promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through the Nasdaq Global Select Market or any other existing trading market for our Common Stock. The Agent will use commercially reasonable efforts to sell on our behalf all of the shares of our Common Stock requested to be sold by us under the Sales Agreement, consistent with its normal trading and sales practices, on terms mutually agreed between the Agent and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The Agent will be entitled to compensation at a commission rate of 3.0% of the gross sales price per share sold pursuant to the terms of the Sales Agreement. See "Plan of Distribution" beginning on page 17 of this prospectus for additional information regarding the compensation to be paid to the Agent. In connection with the sale of our Common Stock on our behalf, the Agent will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of the Agent will be deemed to be underwriting commissions or discounts. We also have agreed to provide indemnification and contribution to the Agent with respect to certain liabilities, including liabilities under the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Our Common Stock is listed on the Nasdaq Global Select Market under the symbol "REPL." On November 5, 2025, the last reported sale price of our Common Stock on the Nasdaq Global Select Market was $8.58.

Investing in our Common Stock involves significant risks. See "Risk Factors" beginning on page 8 of this prospectus and in the documents incorporated by reference in this prospectus for a discussion of the factors you should consider before deciding to purchase our Common Stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

Leerink Partners

The date of this prospectus is , 2025.

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ABOUT THIS PROSPECTUS

This prospectus is part of a shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, under the Securities Act. Under this shelf registration process, we may from time to time sell the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to $100 million. You should read this prospectus together with the additional information described under the heading "Where You Can Find More Information" beginning on page 19 of this prospectus.

This prospectus describes the terms of this offering of our Common Stock and also adds to and updates information contained in the documents incorporated by reference into this prospectus. To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference into this prospectus that was filed with the SEC before the date of this prospectus, on the other hand, you should rely on the information in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference into this prospectus — the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in or incorporated by reference in this prospectus or in any related free writing prospectus filed by us with the SEC. We have not, and the Agent has not, authorized anyone to provide you with different information. This prospectus and any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus and any related free writing prospectus or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

We take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus or any related free writing prospectus that we may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any related free writing prospectus, or any sale of a security.

For investors outside the United States: neither we, nor the Agent, have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about, and to observe any restrictions relating to, this offering and the distribution of this prospectus.

Unless the context otherwise requires, references in this prospectus to (i) "Replimune," the "Company," "we," "us" and "our" refer to Replimune Group, Inc. and its consolidated subsidiaries and (ii) a year are references to the applicable calendar year and not our fiscal year.

MARKET DATA

This prospectus and the documents incorporated by reference herein include market and industry data and forecasts concerning our business and the markets for certain cancers, including data regarding the estimated size of those markets and the incidence and prevalence of certain medical conditions, that we have derived from independent consultant reports, publicly available information, various industry, medical and general publications, other published industry sources, government data and our internal data and estimates. Independent consultant reports, industry publications and other published industry sources generally indicate that the information contained therein was obtained from sources believed to be reliable. Our internal data and estimates are based upon information obtained from trade and business organizations and other contacts in the markets in which we operate and our management's understanding of industry conditions.

PROSPECTUS SUMMARY

The following summary highlights selected information contained or incorporated by reference elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our securities, you should carefully read this entire prospectus, any applicable prospectus supplement and any related free writing prospectus, including the information under the caption "Risk Factors" herein and any applicable prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus, including our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q on file with the SEC and any amendments thereto. You should also carefully read the other information incorporated by reference into this prospectus, including our financial statements and the related notes, and the exhibits to the registration statement of which this prospectus is a part.

Our Company

We are a clinical-stage biotechnology company committed to applying our leading expertise in the field of oncolytic immunotherapy to transform the lives of cancer patients through our novel oncolytic immunotherapies. Our proprietary oncolytic immunotherapy product candidates are intended to maximally activate the immune system against cancer.

Oncolytic immunotherapy is an emerging drug class, which we intend to establish as the second cornerstone of immune-based cancer treatments, alongside checkpoint blockade. Oncolytic immunotherapy exploits the ability of certain viruses to selectively replicate in and directly kill tumors, as well as induce a potent, patient-specific, anti-tumor immune response. Our product candidates incorporate multiple mechanisms of action into a practical "off-the-shelf" approach that is intended to maximize the immune response against a patient's cancer and to offer significant advantages over other approaches to inducing anti-tumor immunity, including personalized vaccine approaches. We believe that the bundling of multiple approaches for the treatment of cancer into single therapies will increase clinical efficacy and simplify the development path of our product candidates, while also improving patient outcomes.

Our proprietary RPx platform is based on a novel, engineered strain of herpes simplex virus 1, or HSV-1, backbone with added payloads intended to maximize immunogenic cell death and induce a systemic anti-tumor immune response. The RPx platform is intended to ignite local activity consisting of direct selective virus-mediated killing of the tumor resulting in the release of tumor-derived antigens and altering of the tumor microenvironment to then activate a strong and durable systemic response. Our product candidates are expected to be synergistic with most established and experimental cancer treatment modalities, and with an attractive safety profile, the RPx platform is expected to have the versatility to be developed alone or combined with a variety of other treatment options. We currently have three RPx product candidates in our development pipeline, RP1 (vusolimogene oderparepvec), our lead product candidate, RP2 and RP3. Although our fiscal year ends March 31st, our programs and program updates are reported on a calendar year basis.

We are conducting a number of clinical trials of RP1, both as a monotherapy and in combination with anti-PD-1 therapy, with a focus on establishing a major skin cancer franchise, assuming approval of our product candidates by the U.S. Food and Drug Administration, or the FDA, and similar applicable foreign regulatory agencies.

Our leading clinical trial of RP1 is referred to as the IGNYTE trial, which is a multi-cohort clinical trial being conducted in collaboration with Bristol Myers Squibb Company, or BMS, under which BMS has granted us a non-exclusive, royalty-free license to, and is supplying at no cost, its anti-PD-1 therapy, nivolumab, for use in combination with RP1.

The leading tumor specific cohort in the IGNYTE trial is our registration directed Phase 2 expansion cohort in anti-PD-1 failed cutaneous melanoma. The anti-PD-1 failed melanoma cohort from the IGNYTE trial includes 140 patients who received RP1 in combination with nivolumab. The primary analysis by independent central review was triggered once all patients had been followed for at least 12 months. As reported in the Journal of Clinical Oncology, July 8, 2025, of the 140 patients enrolled, 48.6% had stage IVM1b/c/d disease, 65.7% had primary anti-PD-1 resistance, 56.4% were PD-L1 negative, and 46.4% received prior anti-PD-1 and anti-cytotoxic T-lymphocyte antigen-4, or anti-CTLA-4, therapy. The confirmed

ORR was 32.9% (15.0% complete response) and the responses occurred with similar frequency, depth, duration, and kinetics for injected and non-injected lesions, including visceral lesions. The median duration of response was 33.7 months and overall survival rates at 1 and 2 years were 75.3% and 63.3%, respectively. RP1 combined with nivolumab continues to be well-tolerated, with mainly Grade 1-2 "on target" side effects, observed.

In November 2024, we announced submission of a biologics license application, or BLA, to the FDA for RP1 (vusolimogene oderparepvec) in combination with nivolumab for the treatment of adult patients with advanced melanoma who have previously received an anti-PD-1 containing regimen, and that the FDA has granted Breakthrough Therapy designation for RP1 in combination with nivolumab in the same setting. The submission was made under the accelerated approval pathway. The FDA accepted our BLA and granted priority review with a Prescription Drug User Fee Act, or PDUFA, goal date of July 22, 2025. On July 21, 2025 the FDA issued a complete response letter, or CRL, for the RP1 BLA for the treatment of advanced melanoma. The FDA stated in the CRL that it was unable to approve the application in its present form and that the IGNYTE trial was not considered to be an adequate and well-controlled clinical investigation that provided substantial evidence of effectiveness, including contribution of components. Furthermore, the FDA said the trial could not be adequately interpreted due to the heterogeneity of the patient population. On September 2, 2025 we announced a type A meeting with the FDA had been scheduled to discuss the CRL following our submission of a briefing book addressing the points raised in the CRL, highlighting prior agreements related to the patient population, criteria for PD-1 resistance, and use of literature to support contribution of components. The briefing book also included an additional analysis of data from the BLA and addressed comments about the phase 3 confirmatory trial design raised by the FDA in the CRL. On September 18, 2025 we announced that, following the type A meeting with the FDA to discuss the CRL, which was conducted on September 16, 2025, we were evaluating feedback received during the meeting to determine our next steps and that, at that time, a path forward under the accelerated approval pathway had not been determined. Following the evaluation of FDA feedback and minutes from the type A meeting, we resubmitted the BLA on October 9, 2025. On October 20, 2025 we announced that the FDA had accepted the resubmission of the BLA for RP1 in combination with nivolumab for the treatment of advanced melanoma in patients who progress on an anti-PD-1 containing regimen. The resubmission included additional information, data and analyses that will be part of the BLA review. The FDA indicated that the resubmission is considered to be a complete response to the CRL and set a PDUFA date of April 10, 2026 based on a Class II resubmission timeline.

We plan to interact with the FDA during the review of the resubmitted BLA and, if approved, intend to bring RP1 to adult patients with advanced melanoma who have previously received an anti-PD-1 containing regimen who otherwise have limited treatment options. Without an approval of RP1 from this resubmitted BLA we might not be able to continue the development of RP1 for this indication, if at all, and we may be required to implement a restructuring plan and review our priorities across the RPx portfolio.

In August 2024, we announced the dosing of the first patient in the IGNYTE-3 trial, or the I-3 trial, a confirmatory study design concept consisting of a 2-arm randomized Phase 3 clinical trial with physician's choice of treatment as a comparator arm in anti-PD-1 failed melanoma patients. With over 100 sites planned globally and an expectation to enroll 400 patients, the I-3 trial will assess RP1 in combination with nivolumab in patients with advanced melanoma who have progressed on anti-PD-1 and anti-CTLA-4 therapies or are ineligible for anti-CTLA-4 treatment. In the type A meeting minutes following the CRL, the FDA stated a control arm of nivolumab in combination with relatlimab (Opdualag^{TM}) may be an acceptable comparator for the I-3 randomized controlled trial. We continue to enroll patients in the I-3 trial.

On October 19, 2025 we announced data from a new ad hoc analysis from the IGNYTE phase 2 cohort of RP1 plus nivolumab, which was released at the European Society for Medical Oncology (ESMO) Congress 2025 held in Berlin. This ad hoc analysis focused on acral melanoma data from patients in the IGNYTE anti-PD-1 failed melanoma cohort and showed treatment with RP1 combined with nivolumab resulted in an objective response rate of 44% (8/18) with a median duration of response of 11.9 months. The safety profile was favorable with generally transient grade 1 and 2 treatment related adverse events, similar to those of the full IGNYTE patient population previously reported. Acral melanoma is a rare and aggressive type of cutaneous melanoma (2 – 3% of all melanoma cases) that frequently occurs on the palms of the hands, soles of the feet, and nailbeds, and often has poor outcomes with many patients presenting with in-transit metastases. Acral melanoma does not typically respond well to available therapies, such as immune

checkpoint inhibitors. Following progression on first-line therapy, aside from targeted therapy for a subset of patients with BRAF mutation-positive tumors, few viable treatment options exist for these patients.

In our non-melanoma skin cancer, or NMSC, cohort of the IGNYTE trial, we provided a data update in December 2023 from the first 30 patients with at least 6 months of follow up including patients with cutaneous squamous cell carcinoma, or CSCC, Merkel cell carcinoma, or MCC, basal cell carcinoma, or BCC, and angiosarcoma in this cohort. The data showed that treatment with RP1 in combination with nivolumab led to an ORR of 30% which is consistent with data from the anti-PD-1 failed melanoma cohort with approximately one-third of patients responding and 60% demonstrating clinical benefit. The combination of RP1 and nivolumab was well tolerated in this patient population with a safety profile consistent with the overall experience seen with this treatment regimen to date. We provided updated data from the NMSC cohort in our June 2025 Investor Day and in October 2025 at ESMO. Responses to RP1 plus nivolumab occurred across the NMSC tumor types enrolled, with confirmed responses seen in patients with both anti–PD-1 naïve and anti-PD-1 failed disease, as well as both in locally advanced and metastatic disease. The ORR by NMSC tumor type for anti-PD-1 naïve patients was 100.0% (n=4) in MCC, 33.3% (n=3) in BCC, 66.7% (n=6) in angiosarcoma, and 56.3% (n=16) in CSCC. The ORR by NMSC tumor type for anti-PD-1 failed patients was 26.3% (n=19) in MCC, 30.0% (n=10) in BCC, 37.5% (n=8) in angiosarcoma, and 15.2% (n=33) in CSCC. We are planning on closing enrollment in this cohort in the fourth quarter of 2025.

Furthering development of RP1, we have open for enrollment a Phase 1b/2 clinical trial of single agent RP1 in solid organ transplant recipients with skin cancers, including CSCC, which we refer to as the ARTACUS trial. We believe that the ARTACUS trial may be potentially registrational (in its own right or, subject to discussion with regulatory authorities, following enrollment of additional patients, including as a potential label expansion after an initial approval of RP1 in a different indication). We are currently planning to enroll up to 65 patients in the ARTACUS trial to assess the safety and efficacy of RP1 in liver, kidney, heart, lung, and hematopoietic cell transplant patients with skin cancers. In November 2023 we presented initial data from the ARTACUS trial of RP1 monotherapy in solid organ transplant recipients with skin cancers at the Society for Immunotherapy of Cancer's, or SITC, 38th Annual Meeting. The data included 23 evaluable patients with CSCC (n=20) and MCC (n=3), demonstrating an ORR of 34.5% and a complete response, or CR, of 21%. RP1 monotherapy was well tolerated in these patients and the safety profile was similar to that observed in our other RP1 clinical trials in patients who are not immune suppressed. No immune-mediated adverse events or evidence of allograft rejection were observed to result from RP1. This data was also presented during oral presentation at the American Association of Cancer Research 2024 Annual Meeting in April 2024. More recently, Dr. Michael R. Migden presented updated data from the ARTACUS trial at the Society for Melanoma Research 22nd International Congress in October 2025. We continue to enroll patients into the ARTACUS trial and are planning a publication of the ARTACUS data in 2026.

As previously reported, our clinical trial of RP1 in patients with CSCC, which we refer to as the CERPASS trial, continues as planned to follow patients that were dosed in the trial.

We are also developing or are continuing to develop additional product candidates, RP2 and RP3, that have been further engineered to enhance anti-tumor immune responses and are intended to address additional tumor types, including traditionally less immune responsive tumor types. In addition to the expression of GALV-GP R(-) and human GM-CSF as in RP1, RP2 has been engineered to express an antibody-like molecule intended to block the activity of CTLA-4, a protein that inhibits the full activation of an immune response, including to tumors. RP3 has been engineered with the intent to further stimulate an anti-tumor immune response through activation of immune co-stimulatory pathways through the additional expression of the ligands for CD40 and 4-1BBL, as well as anti-CTLA-4 and GALV-GP R(-), but without the expression of GM-CSF.

We continue the development of our product candidate RP2 with the goal of moving beyond skin cancers and aiming to treat the more prevalent tumor types commonly found in liver and lung metastasis and including those involving primary liver cancer. Notably, as previously reported, from our Phase-1 clinical trial of RP2 alone and in combination with nivolumab, we have seen durable responses from a monotherapy cohort in a variety of difficult to treat tumors as well as in combination with anti-PD-1 and in particular in patients with metastatic uveal melanoma, or mUM. In November 2023, we presented updated data from a cohort of mUM patients during a

Plenary Session at the 20th Annual International Society for Melanoma Research Congress. The updated data showed RP2 led to an ORR of 29.4% (5 of 17 patients; one of the responding patients was treated with RP2 monotherapy and four of the responding patients were treated with RP2 combined with nivolumab), including responses in patients with liver, lung, and bone metastases. The median DOR at the data cutoff was 11.47 months (range of 2.78 to 21.22 with responses ongoing). Nearly all patients (15 of 17, 88.2%) in the study had progressed on or after immunotherapy with 12 of 17 patients (70.6%) having previously received both anti-PD-1 and anti-CTLA-4 therapies, including four of the responding patients. RP2 was generally well tolerated both as monotherapy and in combination with nivolumab with no additive adverse events observed. The most common grade 1 or 2 treatment related adverse events, or TRAEs, overall in both cohorts were pyrexia, chills, fatigue, hypotension and pruritis. Six patients had grade 3 TRAEs, including two cases of hypotension. There were no grade 4 or 5 TRAEs. In June 2024, we presented that the disease control rate for this cohort of mUM patients was 58.8%.

We have initiated and are enrolling patients in a registration-directed study, or the REVEAL study, of RP2 in mUM patients who are immune checkpoints inhibitor-naïve. The REVEAL study is a randomized, phase 2/3 open label study expected to enroll approximately 280 patients to investigate the efficacy and safety of RP2 in combination with nivolumab vs. ipilimumab in combination with nivolumab in immune checkpoint inhibitor naïve adult patients with metastatic uveal melanoma. The primary endpoints of the trial are overall survival and progression free survival, and key secondary endpoints are overall response rate and disease control rate.

We continue our signal finding trial of RP2 in combination with atezolizumab and bevacizumab in the 2L setting of patients with hepatocellular carcinoma, or HCC, in collaboration with Roche. This Phase 2 clinical trial is currently open and enrollment is underway. The protocol is currently being amended to include RP2 as monotherapy and we plan to release preliminary HCC data by the end of 2026.

We are also planning to open a cohort in our RP2 study to enroll patients with biliary tract cancer, or BTC, and dose RP2 in combination with durvalumab. This cohort is expected to enroll the first patient in the fourth quarter of 2025.

RP1, RP2 and RP3 are administered by direct injection into solid tumors, guided either visually or by ultrasound, computerized tomography or other imaging methods. We believe that direct injection maximizes virus-mediated tumor cell death, provides the most efficient delivery of virus-encoded immune activating proteins into the tumor with the goal of activating systemic immunity, and limits the systemic toxicities that could be associated with intravenous administration. Activation of systemic immunity through local administration is intended to lead to the induction of anti-tumor immune responses leading to clinical response of tumors that have not themselves been injected.

Corporate Information

We are a Delaware corporation formed in July 2017. Our principal executive offices are located at 500 Unicorn Park Drive, Suite 303, Woburn, MA 01801, and our telephone number is (781) 222-9600. Our website is www.replimune.com. Information that is contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. Our fiscal year end is March 31.

Implications of Being a Smaller Reporting Company

We are a “smaller reporting company,” as defined in Regulation S-K. As a result, we may take advantage of certain of the scaled disclosures available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation. We will remain a smaller reporting company if we have (i) less than $250 million in market value of our shares of our Common Stock held by non-affiliates as of the last business day of our second fiscal quarter or (ii) less than $100 million of annual revenues in our most recent fiscal year completed before the last business day of our second fiscal quarter and less than $700 million in market value of our shares of our Common Stock held by non-affiliates as of the last business day of our second fiscal quarter.

THE OFFERING

Common Stock offered by us:	Shares of our Common Stock having an aggregate offering price of up to $100 million.
Common Stock to be outstanding after this offering:	Up to 90,058,267 shares, assuming sales of 11,655,012 shares of our Common Stock in this offering at an offering price of $8.58 per share, which was the last reported sale price of our Common Stock on the Nasdaq Global Select Market on November 5, 2025. The actual number of shares issued will vary depending on how many shares of our Common Stock we choose to sell and the prices at which such sales occur.
Manner of offering:	"At the market offering" that may be made from time to time through the Agent. See "Plan of Distribution" beginning on page 17 of this prospectus.
Use of proceeds:	Our management will retain broad discretion regarding the allocation and use of the net proceeds from this offering. We currently expect to use the net proceeds from the securities offered hereunder, together with our existing cash and cash equivalents, short-term investments and proceeds from our available term loan facility, to fund the continued development of our RPx platform including indication expansion with RP1 in skin cancer and broadening the RP2 clinical development plan as well as for general corporate purposes, including working capital requirements and operating expenses. See "Use of Proceeds" on page 12 of this prospectus.
Risk factors:	Investing in our Common Stock involves significant risks. See "Risk Factors" beginning on page 8 of this prospectus and the other information included in, or incorporated by reference into, this prospectus for a discussion of certain factors you should carefully consider before deciding to invest in shares of our Common Stock.
Nasdaq Global Select Market symbol:	"REPL"

The number of shares of our Common Stock to be outstanding after this offering, as set forth above, is based on 78,403,255 shares of Common Stock outstanding as of September 30, 2025, which amount excludes:

- 12,232,757 shares of our Common Stock issuable upon the exercise of stock options outstanding as of September 30, 2025, at a weighted average exercise price of $14.04 per share;
- 5,107,447 shares of our Common Stock underlying unvested restricted stock units and performance stock units outstanding as of September 30, 2025 at a weighted average grant date fair value of $9.96 per share;
- 14,058,153 shares of our common stock issuable upon the exercise of existing pre-funded warrants outstanding as of September 30, 2025;
- 1,897,696 shares of our Common Stock reserved, as of September 30, 2025, for future issuance under our 2018 Omnibus Incentive Compensation Plan; and
- 4,102,399 shares of our Common Stock reserved, as of September 30, 2025, for future issuance under our Employee Stock Purchase Plan.

RISK FACTORS

An investment in our Common Stock involves a high degree of risk. Before deciding whether to invest in our Common Stock, you should carefully consider the risks described below and discussed under the sections captioned "Risk Factors" contained in our most recent Annual Report on Form 10-K, as well as in any of our subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference herein in their entirety, together with other information in this prospectus, the information and documents incorporated by reference in this prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our Common Stock to decline, resulting in a loss of all or part of your investment.

Risks Related to this Offering

Management will have broad discretion as to the use of the net proceeds from this offering, and may not use the proceeds effectively.

Our management will have broad discretion as to the application of the net proceeds from this offering and could use them in a manner that does not effectively maximize the potential of our clinical development programs and pipeline. Our management's use of the net proceeds from this offering may not increase the market value of our Common Stock. In fact, our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates, and cause the market value of our Common Stock to decline.

If you purchase shares of our Common Stock in this offering, you may suffer immediate dilution of your investment.

The shares sold in this offering, if any, will be sold from time to time at various prices. It is possible that the offering price of our Common Stock will be substantially higher than the net tangible book value per share of our Common Stock. Therefore, if you purchase shares of our Common Stock in this offering, you may pay a price per share that substantially exceeds our net tangible book value per share after this offering. In such event, you will experience immediate dilution representing the difference between the price you paid in this offering and our as adjusted net tangible book value per share after giving effect to the sales of shares in this offering at the applicable offering prices. To the extent outstanding options, warrants or pre-funded warrants are exercised for shares of our Common Stock at exercise prices that are lower than the price you paid in this offering, you will incur further dilution.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our Common Stock or other securities convertible into or exchangeable for our Common Stock at prices that may not be the same as the prices per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the prices per share paid by investors in this offering, and investors purchasing shares of our Common Stock or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of our Common Stock, or securities convertible or exchangeable into our Common Stock, in future transactions may be higher or lower than the prices per share paid by investors in this offering.

It is not possible to predict the aggregate proceeds resulting from sales of our Common Stock made under the Sales Agreement.

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to the Agent at any time throughout the term of the Sales Agreement. The number of shares of our Common Stock that are sold through the Agent after delivering a placement notice will fluctuate based on a number of factors, including the market price of our Common Stock during the sales period, the limits we set with the Agent in any applicable placement notice, and the demand for our Common Stock during the sales period. Because the price per share of our Common Stock will fluctuate

during the sales period, it is not currently possible to predict the aggregate proceeds to be raised in connection with those sales.

The shares of our Common Stock offered hereby will be sold in "at the market" offerings, and investors who buy shares of our Common Stock at different times will likely pay different prices.

Investors who purchase shares of our Common Stock in this offering at different times will likely pay different prices, and so may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares of our Common Stock sold in this offering. In addition, subject to the final determination by our board of directors or a committee thereof, there is no minimum or maximum sales price for shares of our Common Stock to be sold in this offering. Investors may experience a decline in the value of the shares of our Common Stock they purchase in this offering as a result of sales made at prices lower than the prices they paid.

The price of our Common Stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our Common Stock in this offering.

Our stock price has been and is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your shares of our Common Stock at or above the price at which it was acquired.

The offering could negatively impact our ability to use our net operating losses and other tax attributes.

The ability to fully utilize our net operating loss carryforwards, excess business interest carryforwards, and tax credit carryforwards will be limited under Section 382 of the Internal Revenue Code of 1986, as amended, if we were to undergo a change in ownership of more than 50% of our capital stock over a three-year period as measured under Section 382. The application of these rules is complex and generally focus on ownership changes involving stockholders owning directly or indirectly 5% or more of our Common Stock, subject to complex aggregation, segregation, and constructive ownership rules. The Section 382 limitations could come into play in the event of the sale of the company, significant new stock issuances or other transactions, including secondary market sales of our Common Stock.

As a result of the shutdown of the federal government, we have determined to rely on Section 8(a) of the Securities Act to cause the registration statement of which this prospectus forms a part to become effective automatically. Our reliance on Section 8(a) could result in a number of potential adverse consequences, including the need for us to file a post-effective amendment and distribute an updated prospectus to investors, or a stop order issued preventing use of the registration statement, and a corresponding substantial stock price decline, litigation, reputational harm or other negative results.

The registration statement of which this prospectus forms a part is expected to become automatically effective by operation of law pursuant to Section 8(a) of the Securities Act on the 20th calendar day after the most recent amendment of the registration statement filed with the SEC, in lieu of the SEC declaring the registration statement effective following the completion of its review. Although our reliance on Section 8(a) does not relieve us and other parties from the responsibility for the adequacy and accuracy of the disclosure set forth in the registration statement and for ensuring that the registration statement complies with applicable requirements, use of Section 8(a) poses a risk that, after the date of this prospectus, we may be required to file a post-effective amendment to the registration statement and distribute an updated prospectus to investors, or otherwise abandon this offering, if changes to the information in this prospectus are required, or if a stop order under Section 8(d) of the Securities Act prevents continued use of the registration statement. These or similar events could cause the trading price of our Common Stock to decline substantially, result in securities class action or other litigation, and subject us to significant monetary damages, reputational harm and other negative results.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the information incorporated by reference into this prospectus, contains, and any applicable prospectus supplement may contain, "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities and Exchange Act of 1934, as amended, or the Exchange Act, including statements regarding our expectations about our cash runway, the design and advancement of our clinical trials, the timing and sufficiency of our clinical trial outcomes to support potential approval of any of our product candidates, our goals to develop and commercialize our product candidates, patient enrollments in our existing and planned clinical trials and the timing thereof, and other statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements that are not statements of historical facts contained in this prospectus, any applicable prospectus supplement and any information incorporated by reference herein and therein may be deemed to be forward-looking statements. In some cases, you can identify these forward-looking statements by the use of words such as "outlook," "believes," "expects," "potential," "continues," "may," "will," "should," "seeks," "approximately," "predicts," "intends," "plans," "estimates," "anticipates" or the negative version of these words or other comparable words. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include, among other things:

- the timing, progress, and results of preclinical studies and clinical trials for our product candidates, including the timing of initiation and completion of studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our ability to obtain additional funding as necessary;
- the timing, scope or likelihood of regulatory filings and approvals, including timing of approval by the U.S. Food and Drug Administration, or the FDA, of, RP1 or any of our other product candidates;
- the timing, scope, or likelihood of foreign regulatory filings and approvals;
- our ability to develop our product candidates for use in combination with other checkpoint blockade therapies, including anti-PD-1;
- our ability to develop and advance any future product candidates into, and successfully complete, clinical trials;
- our expectations regarding the size of the patient populations for RP1, RP2 and/or RP3 or any other product candidates from our RPx platform if approved for commercial use;
- our ability to successfully qualify, obtain approval for, and maintain successful operation, approval and qualification of our in-house manufacturing operations;
- our ability to obtain and maintain sufficient quantities of raw material supplies or access single or limited sources of goods or services needed to build or maintain our product candidate supplies or otherwise operate our in-house manufacturing facility;
- the costs of operating our in-house manufacturing facility;
- our estimates regarding expenses and capital requirements;
- the implementation of our business model and our strategic plans for our business, RP1 and our other product candidates;
- the rate and degree of market acceptance and clinical utility of RP1 and our other product candidates;
- the potential benefits of and our ability to establish or maintain future collaborations or strategic relationships;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering RP1 and our other product candidates, claims

others may make regarding rights in our intellectual property, and any potential infringement, misappropriation or other violation of any third-party intellectual property rights;

- our competitive position, and developments and projections relating to our competitors and our industry;
- negative developments in the fields of immuno-oncology or oncolytic immunotherapy;
- the impact of laws and regulations; and
- the other risks and uncertainties described under "Risk factors" of our Annual Report on Form 10-K for the year ended March 31, 2025 and our subsequent filings which are incorporated by reference into this prospectus.

The forward-looking statements made in this prospectus, any applicable prospectus supplement and the documents that we incorporate by reference herein and therein relate only to events as of the date on which the statements are made. These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this prospectus, any applicable prospectus supplement and the documents that we incorporate by reference herein and therein. Moreover, we operate in a competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this prospectus, any applicable prospectus supplement and the documents that we incorporate by reference herein and therein. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise, except to the extent required by applicable law. You should not rely on forward-looking statements as predictions of future events. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements.

USE OF PROCEEDS

We may issue and sell shares of our Common Stock having aggregate sales proceeds of up to $100 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. We currently expect to use the net proceeds from the securities offered hereunder, if any, together with our existing cash and cash equivalents, short-term investments and proceeds from our available term loan facility, to fund the continued development of our RPx platform including indication expansion with RP1 in skin cancer and broadening the RP2 clinical development plan as well as for general corporate purposes, including working capital requirements and operating expenses.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds from this offering or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures will depend on numerous factors, including the progress and results of our research and development efforts, the amount of cash used by our operations, and the other factors described under “Risk Factors” in this prospectus and the information incorporated by reference herein. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending application of the net proceeds, we may invest the net proceeds from this offering in short- and intermediate- term, interest- bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DILUTION

If you invest in our Common Stock, your interest will be diluted to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our Common Stock immediately after this offering. Our net tangible book value of our Common Stock as of September 30, 2025 was approximately $263.3 million, or approximately $3.36 per share of Common Stock based upon 78,403,255 shares outstanding. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of September 30, 2025.

After giving effect to the sale of our Common Stock in the aggregate amount of $100 million at an assumed offering price of $8.58 per share, the last reported sale price of our Common Stock on the Nasdaq Global Select Market on November 5, 2025, and after deducting commissions and estimated offering expenses payable by us of approximately $150,000, our as adjusted net tangible book value as of September 30, 2025 would have been approximately $360.2 million, or $3.99 per share of our Common Stock. This represents an immediate increase in net tangible book value of $0.63 per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of $4.59 per share to new investors in this offering. Dilution per share to new investors participating in this offering is determined by subtracting as adjusted net tangible book value per share after this offering from the $8.58, the assumed offering price. The following table illustrates this calculation on a per share basis. The as adjusted information is illustrative only and will adjust based on the actual prices to the public, the actual number of shares sold and other terms of the offering determined at the times shares of our Common Stock are sold pursuant to this prospectus. The shares sold in this offering, if any, will be sold from time to time at various prices.

Assumed offering price per share		$8.58
Net tangible book value per share as September 30, 2025	$3.36	
Increase in net tangible book value per share attributable to the offering	0.63	
As adjusted net tangible book value per share after giving effect to this offering		3.99
Dilution per share to new investors participating in the offering		$4.59

The number of shares of our Common Stock to be outstanding after this offering, as set forth above, is based on 78,403,255 shares of Common Stock outstanding as of September 30, 2025, which amount excludes:

- 12,232,757 shares of our Common Stock issuable upon the exercise of stock options outstanding as of September 30, 2025, at a weighted average exercise price of $14.04 per share;
- 5,107,447 shares of our Common Stock underlying unvested restricted stock units and performance stock units outstanding as of September 30, 2025 at a weighted average grant date fair value of $9.96 per share;
- 14,058,153 shares of our common stock issuable upon the exercise of existing pre-funded warrants outstanding as of September 30, 2025;
- 1,897,696 shares of our Common Stock reserved, as of September 30, 2025, for future issuance under our 2018 Omnibus Incentive Compensation Plan; and
- 4,102,399 shares of our Common Stock reserved, as of September 30, 2025, for future issuance under our Employee Stock Purchase Plan.

To the extent outstanding warrants or options are exercised at prices per share that are less than the prices paid by investors in this offering, or shares of our Common Stock issued upon the vesting of outstanding restricted stock units, there will be further dilution to investors. In addition, to the extent that we issue additional equity securities in connection with future capital raising activities, our then-existing stockholders may experience dilution.

MATERIAL UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion summarizes certain United States, or U.S., federal income tax considerations relevant to the acquisition, ownership and disposition of our Common Stock by Non-U.S. Holders (as defined below). This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended, or the Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as in effect on the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state, or local jurisdiction or under U.S. federal gift and estate tax laws. In addition, this discussion does not address tax considerations applicable to a Non-U.S. Holder's particular circumstances or to Non-U.S. Holders that may be subject to special tax rules, including, without limitation:

- banks, insurance companies or other financial institutions;
- persons subject to the alternative minimum tax;
- tax-exempt organizations;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities treated as partnerships for U.S. federal income tax purposes;
- dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than 5% of our Common Stock, except to the extent specifically set forth below;
- real estate investment trusts or regulated investment companies;
- certain former citizens or long-term residents of the U.S.;
- persons who hold our Common Stock as part of a straddle, hedge, conversion, constructive sale, or other integrated security transaction;
- accrual method taxpayers subject to special tax accounting rules as a result of their use of financial statements (pursuant to Section 451 of the Code); or
- persons who do not hold our Common Stock as a capital asset (within the meaning of Section 1221 of the Code).

If a partnership or entity classified as a partnership for U.S. federal income tax purposes holds our Common Stock, the tax treatment of a partner or such partnership generally will depend on the status of the partner and upon the activities of the partnership. Accordingly, partnerships that hold our Common Stock, and partners in such partnerships, should consult their tax advisors.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our Common Stock arising under the U.S. federal estate or gift tax rules or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

For purposes of this summary, a "Non-U.S. Holder" means a beneficial owner of shares of our Common Stock (other than a partnership) that, for U.S. federal income tax purposes, is not (i) an individual that is a citizen or resident of the U.S.; (ii) a corporation or other entity treated as a corporation for U.S. federal income tax purposes that is created or organized under the laws of the U.S., any state thereof or the

District of Columbia; (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or (iv) a trust if (A) a court within the U.S. is able to exercise primary control over its administration and one or more "United States persons" (as defined in the Code) have the authority to control all substantial decisions of such trust, or (B) the trust has made an election under the applicable Treasury regulations to be treated as a U.S. person.

Distributions

In general, if we make a distribution to a Non-U.S. Holder with respect to our Common Stock, it will constitute a dividend for U.S. federal income tax purposes to the extent paid out of our current or accumulated earnings and profits as determined under the Code. If the amount of a distribution exceeds our current and accumulated earnings and profits, such excess first will be treated as a tax-free return of capital to the extent of the Non-U.S. Holder's adjusted tax basis in our Common Stock and thereafter will be treated as capital gain subject to the tax treatment described below in "Sale or Other Taxable Disposition of Common Stock." Dividends paid to a Non-U.S. Holder that are not effectively connected with the Non-U.S. Holder's conduct of a trade or business within the U.S. will generally be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends, unless such dividend is eligible for a reduced rate under an applicable income tax treaty. In order to obtain a reduced rate of withholding, a Non-U.S. Holder is generally required to provide to the applicable withholding agent an IRS Form W-8BEN or IRS Form W-8BEN-E (or other applicable form) properly certifying such Non-U.S. Holder's eligibility for the reduced rate. Non-U.S. Holders that do not timely provide the applicable withholding agent with the required certification, but that qualify for a reduced withholding rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under an applicable income tax treaty and the timing and manner of claiming the benefits.

Dividends that are effectively connected with a Non-U.S. Holder's conduct of a trade or business in the U.S. (and, if an applicable income tax treaty so requires, are attributable to a permanent establishment or fixed base maintained by the Non-U.S. Holder in the U.S.) are taxed on a net-income basis at the regular graduated rates and in the manner applicable to United States persons. The Non-U.S. Holder is generally required to provide to the applicable withholding agent a properly executed IRS Form W-8ECI (or a suitable substitute form) in order to claim an exemption from, or reduction in, U.S. federal withholding. In addition, a "branch profits tax" may be imposed at a 30% rate (or a reduced rate under an applicable income tax treaty) on any effectively connected dividends received by a foreign corporation for the taxable year, as adjusted for certain items.

Sale or Other Taxable Disposition of Common Stock

A Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax with respect to gain, if any, recognized on the sale or other taxable disposition of shares of our Common Stock unless (i) the gain is effectively connected with the conduct by such Non-U.S. Holder of a trade or business within the United States (and, if an applicable income tax treaty so requires, is attributable to a permanent establishment or fixed base maintained by the Non-U.S. Holder in the United States), (ii) in the case of an individual, such Non-U.S. Holder is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are satisfied, or (iii) our Common Stock constitutes a U.S. real property interest by reason of our status as a U.S. real property holding corporation, or a USRPHC under the Foreign Investment in Real Property Tax Act, or FIRPTA, for U.S. federal income tax purposes.

In the case described in (i) above, gain or loss recognized on the disposition of shares of our Common Stock generally will be subject to U.S. federal income taxation in the same manner as if such gain or loss were recognized by a U.S. person, and, in the case of a Non-U.S. Holder that is a foreign corporation, may also be subject to the branch profits tax at a rate of 30%, or a lower applicable treaty branch profits tax rate.

In the case described in (ii) above, the Non-U.S. Holder will be subject to a 30% tax on any capital gain recognized on the disposition of shares of our Common Stock, after being offset by certain U.S.-source capital losses.

In the case described in (iii) above, a corporation is a USRPHC if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business (all as determined for U.S. federal income tax purposes). We have not determined whether we are a USRPHC. If we were a USRPHC during the shorter of the five-year period preceding the disposition or the Non-U.S. Holder's holding period, Non-U.S. Holders owning (directly or indirectly) more than 5% of our Common Stock will be subject to different tax consequences and should consult their own tax advisers. FIRPTA will not, however, apply to gain realized on the sale or disposition of our Common Stock by a Non-U.S. Holder that owns, directly or indirectly at any time during the shorter of the five-year period preceding the date of disposition or the Non-U.S. Holder's holding period, 5% or less of our common stock so long as our common stock is "regularly traded on an established securities market" (such as the Nasdaq Global Select Market) as defined under applicable Treasury regulations.

If gain on the sale or other taxable disposition of our Common Stock were subject to taxation under FIRPTA, a Non-U.S. Holder generally would be subject to U.S. federal income tax on the gain realized on a disposition of the common stock at the graduated U.S. federal income tax rates applicable to U.S. persons, generally would be required to file a U.S. federal income tax return, and, if our Common Stock was not then publicly traded, and certain other conditions were met, the purchaser would be required to withhold 15% of the sales proceeds.

Information Reporting and Backup Withholding

Information returns will be filed annually with the IRS in connection with any dividends paid on our Common Stock to a Non-U.S. Holder. Copies of these information returns may also be made available under the provisions of a specific tax treaty or other agreement to the tax authorities of the country in which the Non-U.S. Holder resides. Unless the Non-U.S. Holder complies with certification procedures to establish that it is not a United States person, information returns may be filed with the IRS in connection with the proceeds from a sale or other disposition, and the Non-U.S. Holder may be subject to backup withholding (currently at a rate of 24%) on dividends paid on our Common Stock or on the proceeds from a sale or other disposition of shares of our Common Stock. The certification procedures required to claim a reduction or exemption from withholding tax on payments described above under "Distributions" will satisfy the certification requirements necessary to avoid backup withholding as well. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

Foreign Account Tax Compliance Act

Under the Foreign Account Tax Compliance Act, or FATCA, and additional guidance issued by the IRS, a U.S. federal withholding tax of 30% will generally apply to dividends paid on our Common Stock to (i) a foreign financial institution (as a beneficial owner or as an intermediary), unless such institution is subject to an agreement with the U.S. government (which may be in the form of compliance with an intergovernmental agreement with the U.S. government) to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which would include certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners), or (ii) a foreign entity that is not a financial institution (as a beneficial owner or as an intermediary), unless such entity provides the withholding agent with a certification identifying the substantial U.S. owners of the entity, which generally includes any U.S. person who directly or indirectly owns more than 10% of the entity. While such withholding tax would have applied also to payments of gross proceeds from the sale or other disposition on or after January 1, 2019 of our Common Stock, recently proposed Treasury Regulations eliminate such withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued.

Non-U.S. Holders are encouraged to consult with their tax advisors regarding the possible implications of the FATCA withholding rules on their investment in our Common Stock. If a dividend payment is both subject to withholding under FATCA and subject to the withholding tax discussed above under "— Distributions," the withholding under FATCA may be credited against, and therefore reduce, such other withholding tax.

PLAN OF DISTRIBUTION

On August 3, 2023, we entered into a sales agreement with Leerink Partners LLC, or the Agent, under which we may issue and sell shares of our Common Stock from time to time through the Agent. We and the Agent entered into amendments to the sales agreement on May 16, 2024, November 25, 2024 and May 22, 2025, after giving effect to which we and the Agent agreed that we may offer and sell from time to time under the sales agreement an aggregate offering price of up to $100 million of our Common Stock. The sales agreement and the amendment to the sales agreement have been filed as an exhibit to the shelf registration statement on Form S-3 of which this prospectus forms a part. References in this prospectus to the Sales Agreement refer to the foregoing sales agreement, as amended.

Sales of our Common Stock, if any, will be made by any method that is deemed to be an "at-the-market offering" as defined in Rule 415 under the Securities Act, including sales made directly on or through the Nasdaq Global Select Market, on or through any other existing trading market for our Common Stock or to or through a market maker. If expressly authorized by us, the Agent may also sell our Common Stock in negotiated transactions, block trades or a combination of these methods. The Agent will offer our Common Stock subject to the terms and conditions of the Sales Agreement on a daily basis or as otherwise agreed upon by us and the Agent. We will designate the maximum number or amount of our Common Stock to be sold through the Agent on a daily basis or otherwise determine such maximum number or amount together with the Agent. We may instruct the Agent not to sell our Common Stock if the sales cannot be effected at or above the price designated by us from time to time. We or the Agent may suspend the offering of our Common Stock upon proper notice to the other party.

We will pay the Agent a commission, in cash, for their services in acting as agent in the sale of our Common Stock. The Agent will be entitled to compensation at a fixed commission rate of 3.0% of the gross proceeds from each sale of our Common Stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have agreed to reimburse the Agent for certain specified expenses, including the fees and disbursements of their outside legal counsel in an amount not to exceed $50,000. We have also agreed to reimburse the Agent for fees and disbursements of their outside legal counsel incurred in connection with the amendment to the Sales Agreement executed on May 22, 2025 and other matters in an amount not to exceed $50,000. In accordance with FINRA Rule 5110, these reimbursed fees and expenses are deemed sales compensation to the Agent in connection with this offering. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to the Agent under the terms of the Sales Agreement, will be approximately $125,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory or self-regulatory organization in connection with the sales of our Common Stock, will equal our net proceeds for the sale of such Common Stock. The Agent will provide written confirmation to us no later than the next succeeding trading day on the Nasdaq Global Select Market after each day on which Common Stock is sold through it as sales agent under the Sales Agreement. Each confirmation will include the number or amount of shares sold through it as sales agent on that day, the volume-weighted average price of the shares sold and the net proceeds to us from such sales. We will report at least quarterly the number of shares of Common Stock sold through the Agent under the Sales Agreement, the net proceeds to us and the compensation paid by us to the Agent in connection with the sales of Common Stock during the relevant period.

Settlement for sales of Common Stock will occur on the first trading day following the date on which any sales are made, or on some other date that is agreed upon by us and the Agent in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our Common Stock as contemplated in this prospectus will be settled through the facilities of The Depository Trust Company or by such other means as we and the Agent may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Subject to the terms and conditions of the Sales Agreement, the Agent will use its commercially reasonable efforts, consistent with its normal sales practices and applicable state and federal laws, rules and regulations and the rules of the Nasdaq Global Select Market to sell on our behalf all of the Common Stock requested to be sold by us. In connection with the sale of the Common Stock on our behalf, the Agent will

be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of the Agent will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to the Agent against certain civil liabilities, including liabilities under the Securities Act.

The offering of our Common Stock pursuant to the Sales Agreement will terminate upon the termination of the Sales Agreement as permitted therein. We and the Agent may each terminate the Sales Agreement at any time upon ten days' prior notice in each party's sole discretion. The Agent may terminate the Sales Agreement at any time in certain circumstances, including the occurrence of a material and adverse change in our business or financial condition that makes it impractical or inadvisable to market our Common Stock or to enforce contracts for the sale of our Common Stock.

The Agent and its affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. As sales agent, Leerink Partners LLC will not engage in any transactions that stabilize our Common Stock. Our Common Stock is listed on the Nasdaq Global Select Market and trades under the symbol "REPL." The transfer agent of our Common Stock is Computershare Trust Company N.A.

This prospectus in electronic format may be made available on a website maintained by the Agent and the Agent may distribute this prospectus electronically.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by Morgan, Lewis & Bockius LLP, New York, New York. The Agent is being represented in connection with this offering by Cravath, Swaine & Moore LLP, New York, New York.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended March 31, 2025 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information requirements of the Exchange Act, and in accordance with the Exchange Act, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). Our corporate website address is *www.replimune.com*. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information contained in documents that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC before the date of this prospectus, while information that we file later with the SEC will automatically update and supersede prior information. Any information so updated and superseded shall not be deemed, except as so updated and superseded, to constitute a part of this prospectus. We incorporate by reference the documents listed below and any future filings we will make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the filing of the registration statement and prior to the effectiveness of the registration statement, and prior to the termination of the offering:

- our Annual Report on Form 10-K for the fiscal year ended March 31, 2025, filed with the SEC on May 22, 2025;
- our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2025, filed with the SEC on August 7, 2025, and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2025, filed with the SEC on November 6, 2025;
- our Current Reports on Form 8-K filed with the SEC on July 22, 2025, September 4, 2025, September 18, 2025, and October 20, 2025 (provided that any portions of such reports that are deemed furnished and not filed pursuant to instructions to Form 8-K shall not be incorporated by reference into this prospectus); and
- our description of our common stock contained in the registration statement on Form 8-A, filed on July 17, 2018, as the description therein has been updated and superseded by the description of our capital stock contained in Exhibit 4.3 to our Annual Report on Form 10-K for the fiscal year ended March 31, 2025, as filed with the SEC on May 22, 2025, and including any amendments and reports filed for the purpose of updating such description.

Notwithstanding the foregoing, unless specifically stated to the contrary, none of the information that is not deemed "filed" with the SEC, including information furnished under Items 2.02 or 7.01 of any Current Report on Form 8-K, will be incorporated by reference into, or otherwise included in, this prospectus.

We make available, free of charge, through our website at www.replimune.com under "Investor and Media" our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not incorporated by reference into this prospectus and should not be considered part of this prospectus or any applicable prospectus supplement. In addition, the SEC maintains an Internet website that contains reports, proxy and information statements, and other information that we file with the SEC at www.sec.gov. You may also obtain, free of charge, a copy of any of these documents (other than exhibits to these documents unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus) by writing or calling us at the following address and telephone number:

Replimune Group, Inc.
Attention: Investor Relations
500 Unicorn Park, Suite 303
Woburn MA 01801
+1 (781) 222-9600

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

$100,000,000

Common Stock

PROSPECTUS

Leerink Partners

, 2025

PART II. INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The expenses in connection with the issuance and distribution of the securities being registered will be borne by us and are set forth in the following table. All amounts except the registration fee are estimated.

SEC registration fee	$38,275[1]
Legal fees and expenses	[2]
Accounting fees and expenses	[2]
Printing expenses	[2]
Transfer and registrar fee	[2]
Miscellaneous	[2]
Total	[2]

(1) Previously paid.

(2) These fees will be dependent on the type of securities offered and the number of offerings and, therefore, cannot be estimated at this time. The applicable prospectus supplement will set forth the estimated amount of expenses of any offerings of securities.

Item 15. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors, and other corporate agents.

As permitted by Delaware law, our certificate of incorporation provides that, to the fullest extent permitted by Delaware law, no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director. Pursuant to Delaware law such protection would be not available for liability:

- for any breach of a duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for any transaction from which the director derived an improper benefit; or
- for an act or omission for which the liability of a director is expressly provided by an applicable statute, including unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law.

Our certificate of incorporation also provides that if Delaware law is amended after the approval by our stockholders of the certificate of incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law.

Our bylaws further provide that we must indemnify our directors and officers to the fullest extent permitted by Delaware law. Our bylaws also authorize us to indemnify any of our employees or agents and permit us to secure insurance on behalf of any officer, director, employee or agent for any liability arising out of his or her action in that capacity, whether or not Delaware law would otherwise permit indemnification.

In addition, our bylaws also provide that we are required to advance expenses to our directors and officers as incurred in connection with legal proceedings against them for which they may be indemnified and that the rights conferred in the bylaws are not exclusive.

We have entered into indemnification agreements with each of our directors and executive officers.

These agreements, among other things, require us to indemnify each director and officer to the fullest extent permitted by Delaware law, the certificate of incorporation and bylaws, for expenses such as, among

other things, attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. We also have directors' and officers' liability insurance.

The SEC has taken the position that personal liability of directors for violation of the federal securities laws cannot be limited and that indemnification by us for any such violation is unenforceable. The limitation of liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

Item 16. Exhibits

		Incorporated by Reference		
Exhibit Number	**Exhibit Description**	**Form**	**Date**	**Number**
1.1*	Form of Underwriting Agreement			
1.2	Sales Agreement, dated as of August 3, 2023, by and between Replimune Group, Inc. and Leerink Partners LLC	S-3	August 3, 2023	1.2
1.3	Amendment No. 1 to Sales Agreement, dated as of May 16, 2024, by and between Replimune Group, Inc. and Leerink Partners LLC	S-3	May 16, 2024	1.3
1.4	Amendment No. 2 to Sales Agreement, dated as of November 25, 2024, by and between Replimune Group, Inc. and Leerink Partners LLC	S-3	May 23, 2025	333-287536
1.5	Amendment No. 3 to Sales Agreement, dated as of May 22, 2025, by and between Replimune Group, Inc. and Leerink Partners LLC	S-3	May 23, 2025	333-287536
3.1	Third Amended and Restated Certificate of Incorporation of Replimune Group, Inc. (conformed to include the Certificate of Amendment to the Third Amended and Restated Certificate of Incorporation filed on September 9, 2019)	10-K	June 3, 2020	3.1
3.2	Amended and Restated By-laws of Replimune Group, Inc.	8-K	July 24, 2018	3.2
4.1	Form of Common Stock Certificate of the Registrant	S-1/A	July 10, 2018	4.1
4.2	Form of Pre-Funded Warrant (2019)	8-K	November 18, 2019	4.1
4.3	Form of Pre-Funded Warrant (2020)	8-K	June 10, 2020	4.1
4.4	Form of Pre-Funded Warrant (2022)	8-K	December 12, 2022	4.1
4.5	Form of Pre-Funded Warrant (June 2024)	8-K	June 13, 2024	4.1
4.6	Form of Pre-Funded Warrant (December 2024)	8-K/A	December 4, 2024	4.1
4.7*	Form of certificate of designation with respect to any preferred stock issued hereunder and the related form of preferred stock certificate			

Exhibit Number	Exhibit Description	Incorporated by Reference		
		Form	Date	Number
4.8	Form of Indenture to be entered into between registrant and trustee acceptable to the Replimune Group, Inc.	S-3	May 23, 2025	333-287536
4.9*	Form of debt security			
4.10*	Form of Warrant Agreement and Warrant Certificate			
4.11*	Form of Unit Agreement and Unit Certificate			
5.1	Opinion of Morgan, Lewis & Bockius LLP			
23.1	Consent of Morgan, Lewis & Bockius LLP (included in Exhibit 5.1)			
23.2	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm			
24.1	Power of Attorney	S-3	May 23, 2025	333-287536
25.1**	Form T-1 Statement of Eligibility of Trustee under the Indenture			
107	Filing Fee Table	S-3	May 23, 2025	333-287536

* To be filed by amendment or as an exhibit to a document filed under the Exchange Act and incorporated by reference herein.

** To be filed separately pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939, as amended, and the appropriate rules and regulations thereunder.

Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that the undertakings set forth in paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is therefore unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 1 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the town of Woburn, Commonwealth of Massachusetts on November 6, 2025.

REPLIMUNE GROUP, INC.

By: /s/ Sushil Patel

Sushil Patel
Chief Executive Officer and Director

Pursuant to the requirements of the Securities Act of 1933, as amended, this Amendment No. 1 to the Registration Statement has been signed by the following persons in the capacities and on the date indicated.

Name	Title	Date
/s/ Sushil Patel Sushil Patel	Chief Executive Officer and Director (Principal Executive Officer)	November 6, 2025
/s/ Emily Hill Emily Hill	Chief Financial Officer (Principal Financial Officer)	November 6, 2025
/s/ Andrew Schwendenman Andrew Schwendenman	Chief Accounting Officer (Principal Accounting Officer)	November 6, 2025
* Philip Astley-Sparke	Director	November 6, 2025
* Kapil Dhingra	Director	November 6, 2025
* Madhavan Balachandran	Director	November 6, 2025
* Christy Oliger	Director	November 6, 2025
* Paolo Pucci	Director	November 6, 2025
* Joseph Slattery	Director	November 6, 2025

Name	Title	Date
* Veleka Peeples-Dyer	Director	November 6, 2025
* Dieter Weinand	Director	November 6, 2025
* Michael Goller	Director	November 6, 2025

By: /s/ Shawn Glidden
Shawn Glidden
Attorney-in-Fact

EXHIBIT 5.1

Morgan Lewis

November 6, 2025

Replimune Group, Inc.
500 Unicorn Park Drive
Suite 303
Woburn, MA 01801

Ladies and Gentlemen:

We have acted as counsel to Replimune Group, Inc., a Delaware corporation (the "Company"), in connection with an Amendment No. 1 to the Registration Statement on Form S-3 (File No. 333-287536) (as amended, the "Registration Statement") filed by the Company with the Securities and Exchange Commission under the Securities Act of 1933, as amended (the "Securities Act") on the date hereof. The Company has provided us with two prospectuses that form a part of the Registration Statement: (i) a base prospectus (the "Base Prospectus"), which provides that it may be supplemented in the future by one or more prospectus supplements (each, a "Prospectus Supplement"), and (ii) a sales agreement prospectus (the "ATM Agreement Prospectus"), covering the offering, issuance and sale of up to $100,000,000 of shares of common stock, $0.001 par value per share, of the Company ("Common Stock") that may be issued and sold under the Sales Agreement, dated August 3, 2023, between the Company and Leerink Partners LLC, as amended pursuant to Amendment No. 1 to the Sales Agreement, dated May 16, 2024, Amendment No. 2 to the Sales Agreement, dated November 25, 2024, and Amendment No. 3 to the Sales Agreement, dated May 22, 2025 (such agreement as amended, the "ATM Agreement", and such shares of Common Stock to be sold thereunder, the "Placement Shares").

The Registration Statement, including the Base Prospectus (as supplemented from time to time by one or more Prospectus Supplements) and the ATM Agreement Prospectus, will provide for the registration of the offering and sale by the Company of up to $250,000,000 of an indeterminate amount of (i) shares of Common Stock issuable pursuant to the Base Prospectus (as supplemented from time to time by one or more Prospectus Supplements) or the ATM Agreement Prospectus; (ii) shares of the Company's preferred stock, $0.001 par value per share ("Preferred Stock") issuable pursuant to the Base Prospectus (as supplemented from time to time by one or more Prospectus Supplements); (iii) warrants to purchase shares of Common Stock, shares of Preferred Stock and/or Debt Securities issuable pursuant to the Base Prospectus (as supplemented from time to time by one or more Prospectus Supplements) (the "Warrants"); (iv) one or more series of debt securities of the Company, which may be convertible into or exchangeable for shares of Common Stock and/or Preferred Stock (the "Debt Securities"), which may be issued pursuant to the indenture to be dated on or about the date of the first issuance of Debt Securities thereunder, by and between a trustee to be selected by the Company (the "Trustee") and qualified to act as such under the Trust Indenture Act of 1939, as amended (the "TIA") and the Company, in the form filed as Exhibit 4.8 to the Registration Statement (the "Indenture") issuable pursuant to the Base Prospectus (as supplemented from time to time by one or more Prospectus Supplements); (v) units ("Units") comprised of shares of Common Stock, shares of Preferred Stock, warrants and other securities of the Company in any combination issuable pursuant to the Base Prospectus (as supplemented from time to time by one or more Prospectus Supplements); and (vi) the Placement Shares.

The Common Stock, the Preferred Stock, the Debt Securities, the Warrants, the Units and the Placement Shares are collectively referred to herein as the "Registered Securities." The Registered Securities are being registered for offering and sale from time to time pursuant to Rule 415 of the Securities Act. This opinion letter is furnished to you at your request to enable you to fulfill the requirements of Item 601(b)(5) of Regulation S-K, in connection with the filing of the Registration Statement.

We have reviewed the corporate proceedings taken by the Company with respect to the registration of the Registered Securities. We have examined and relied upon originals or copies of such records, instruments, certificates, memoranda, and other documents as we have deemed necessary or advisable for purposes of this opinion and have assumed, without independent inquiry, the accuracy of those documents. In that examination, we have assumed the genuineness of all signatures, the conformity to the originals of all documents reviewed by us as copies, the authenticity and completeness of all original documents reviewed by us in original or copy form, and the legal competence of each individual executing such documents.

Our opinion is subject to the following assumptions, exceptions and qualifications:

(i) We have assumed that the issuance, sale, amount, and terms of each of the Registered Securities to be offered from time to time by the Company will be duly authorized and established by proper action of the Board of Directors of the Company, and in accordance with the Third Amended and Restated Certificate of Incorporation of the Company, as amended from time to time, the Amended and Restated By-laws of the Company, as amended from time to time, and applicable Delaware law, and that, at the time of each such issuance and sale of such Registered Securities, the Company will continue to be validly existing and in good standing under the laws of the State of Delaware, with the requisite corporate power and authority to issue and sell all such Registered Securities.

(ii) We have assumed that any shares of Common Stock issued by the Company pursuant to the Registration Statement, the Base Prospectus and any related Prospectus Supplement, including the ATM Agreement Prospectus, from time to time will not exceed the maximum authorized number of shares of Common Stock under the Third Amended and Restated Certificate of Incorporation of the Company, as the same may have been amended, minus that number of shares of Common Stock that may have been issued and are outstanding, or are reserved for issuance for other purposes, at such time.

(iii) We have assumed that any shares of Preferred Stock issued pursuant to the Registration Statement, the Base Prospectus and any related Prospectus Supplement, from time to time will not exceed the maximum authorized number of shares of Preferred Stock under the Third Amended and Restated Certificate of Incorporation of the Company, as amended from time to time, minus that number of shares of Preferred Stock that may have been issued and are outstanding, or are reserved for issuance for other purposes, at such time and that an appropriate certificate of designation relating to each such series of Preferred Stock will have been duly authorized and established by proper action of the Board of Directors of the Company and filed with the Secretary of State of the State of Delaware as required under Delaware law, and in accordance with the Third Amended and Restated Certificate of Incorporation of the Company, as amended from time to time, the Amended and Restated By-laws of the Company, as amended from time to time, and applicable Delaware law, and that such certificate of designation will have been filed with the Secretary of State of the State of Delaware.

(iv) We have assumed that any Warrants issued by the Company pursuant to the Registration Statement, the Base Prospectus and any related Prospectus Supplement, from time to time, will be issued under one or more valid, binding, and enforceable warrant agreements (each a "Warrant Agreement"); and that any Warrants offered under the Registration Statement and the related Warrant Agreement, as applicable, will be executed in the forms to be filed as exhibits to the Registration Statement or incorporated by reference therein.

(v) We have assumed that any Debt Securities issued by the Company pursuant to the Registration Statement, the Base Prospectus and any related Prospectus Supplement, from time to time, will be issued under and in conformity with a valid, binding and enforceable Indenture, which shall be delivered by the Trustee, and the Trustee will have all requisite power and authority to effect the transactions contemplated by such Indenture, and the Trustee or an authenticating agent for the Trustee will duly authenticate the Debt Securities pursuant to the applicable Indenture, and the applicable Indenture will be the valid and binding obligation of the Trustee and will be enforceable against the Trustee in accordance with its terms. With respect to any applicable Indenture, we are expressing no opinion herein as to (a) the application of or compliance with any foreign, federal or state law or regulation or (b) the power, authority or competence of any party, other than the Company.

(vi) We have assumed that any Units will be issued by the Company pursuant the Registration Statement, the Base Prospectus and any related Prospectus Supplement, from time to time, will be issued under one or more valid, binding, and enforceable unit agreements to be entered into between the Company and a financial institution as unit agent (the "Unit Agreement"); and that any Units offered under the Registration Statement and the related Unit Agreement, as applicable, will be executed in the forms to be filed as exhibits to the Registration Statement or incorporated by reference therein.

(vii) We have assumed that the Registration Statement and any amendments thereto (including post-effective amendments) will have become effective and such effectiveness shall not have been terminated or rescinded and will comply with all applicable federal and state laws, and all Prospectus Supplement(s) required by applicable laws will have been delivered and filed as required by such laws and the Registered Securities will have been issued and sold in accordance with the terms of such Prospectus Supplement(s), at the time the Registered Securities are offered and issued as contemplated by the Registration Statement, the Base Prospectus and any related Prospectus Supplement, including the ATM Agreement Prospectus.

(viii) The enforcement of any obligations of the Company may be limited by bankruptcy, insolvency, reorganization, moratorium, marshaling or other laws and rules of law affecting the enforcement generally of creditors' rights and remedies, including, without limitation, fraudulent conveyance and fraudulent transfer laws.

(ix) Our opinions are subject to the effects of general principles of equity (whether considered in a proceeding at law or in equity), including but not limited to, principles limiting the availability of specific performance or injunctive relief, and concepts of materiality and reasonableness, and the implied duty of good faith and fair dealing.

(x) We express no opinion as to the enforceability of any particular provision of any of the Registered Securities relating to:

(a) waivers of rights to object to jurisdiction or venue, or consents to jurisdiction or venue;

(b) waivers of rights to (or methods of) service of process, or rights to trial by jury, or other rights or benefits bestowed by operation of law;

(c) waiver of any applicable defenses, setoffs, recoupments, or counterclaims;

(d) the granting of any power of attorney or of any proxy to any person;

(e) exculpation or exoneration clauses, clauses relating to rights of indemnity or contribution, and clauses relating to releases or waivers of unmatured claims or rights;

(f) waivers or variations of legal provisions or rights which are not capable of waiver or variation under application law; and

(g) the imposition or collection of interest on overdue interest or providing for a penalty rate of interest or late charges on overdue or defaulted obligations, or the payment of any premium, liquidated damages, or other amount which may be held by any court to be a "penalty" or a "forfeiture."

We express no opinion as to the effect of events occurring, circumstances arising or changes of law becoming effective or occurring, after the date hereof on the matters addressed in this opinion letter, and we assume no responsibility to inform you of additional or changed facts, or changes in law, of which we may become aware.

Subject to the limitations set forth below, we have made such examination of law as we have deemed necessary for the purposes of expressing the opinions set forth in this letter. Such opinions are limited solely to the Delaware General Corporation Law as applied by courts located in Delaware and, with respect to the applicable Indenture, the internal substantive laws of the State of New York (other than tax, usury, antitrust, insolvency, fraudulent conveyance or fraudulent transfer laws, blue sky and securities laws, as to which we express no opinion) as applied by courts located in New York without regard to choice of law. We express no opinion whatsoever as to the compliance or noncompliance by any person with antifraud or information delivery provisions of any state or federal laws, rules and regulations, and no inference regarding such compliance or noncompliance may be drawn from any opinion herein.

Based upon the foregoing, we are of the opinion that:

1. The Placement Shares, when issued and paid for in accordance with the ATM Agreement and as contemplated in the Registration Statement and in the ATM Agreement Prospectus, will be validly issued, fully paid and nonassessable.

2. The shares of Common Stock registered under the Registration Statement for offer and sale by the Company, when duly authorized and issued against the full payment specified therefor, which must have a value not less than the par value thereof, will be validly issued, fully paid and nonassessable.

3. The shares of Preferred Stock registered under the Registration Statement, when duly authorized and issued against the full payment specified therefor, which must have a value not less than the par value thereof, will be validly issued, fully paid and nonassessable.

4. The Warrants registered under the Registration Statement, when duly authorized, executed and delivered against the payment specified therefor, and pursuant to a Warrant Agreement or agreements duly authorized, executed and delivered by the Company and the holder of the Warrants, will be valid and binding obligations of the Company.

5. The Debt Securities registered under the Registration Statement, when duly authorized, executed and delivered against the payment specified therefor pursuant to the Indenture that has been qualified under the TIA and any underwriting agreement or purchase agreement duly authorized, executed and delivered by the Company and the initial purchasers of the Debt Securities, will be valid and binding obligations of the Company.

6. The Units registered under the Registration Statement, when duly authorized, executed and delivered against the payment specified therefor, and pursuant to a Unit Agreement or agreements duly authorized, executed and delivered by the Company and the holder of the Units, will be valid and binding obligations of the Company.

This opinion letter is given as of the date hereof, and we express no opinion as to the effect of subsequent events or changes in law occurring or becoming effective after the date hereof. We assume no obligation to update this opinion letter or otherwise advise you with respect to any facts or circumstances or changes in law that may hereafter occur or come to our attention.

We hereby consent to the filing of this opinion as Exhibit 5.1 to the Registration Statement and to the reference to this firm under the heading “Legal Matters” in the Base Prospectus and the ATM Agreement Prospectus included in the Registration Statement. In rendering this opinion and giving this consent, we do not admit that we are an “expert” within the meaning of the Securities Act.

Very truly yours,

/s/ Morgan, Lewis & Bockius LLP

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Replimune Group, Inc. of our report dated May 22, 2025 relating to the financial statements, which appears in Replimune Group, Inc.'s Annual Report on Form 10-K for the year ended March 31, 2025. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Florham Park, New Jersey
November 6, 2025