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Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-231577

PROSPECTUS SUPPLEMENT

$100,000,000
Common Stock

We have entered into a certain Sales Agreement, or the sales agreement, with Cowen and Company, LLC, or Cowen, relating to shares of our common stock offered by this prospectus supplement. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $100 million from time to time after the date of this prospectus supplement through Cowen, acting as our agent.

Our common stock is listed on the Nasdaq Global Market, or the Exchange, under the symbol "GLYC." On October 5, 2020 the last reported sale price of our common stock was $3.27 per share.

Sales of our common stock, if any, under this prospectus supplement will be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific number or dollar amount of securities, but will act as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cowen for sales of common stock sold pursuant to the sales agreement will be an amount equal to 3.0% of the gross proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Exchange Act of 1934, as amended.

Our business and an investment in our common stock involve a significant risks. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 8 of this prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus supplement.

Neither the securities and exchange commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus and the accompanying prospectus are truthful or complete. Any representation to the contrary is a criminal offense.

Cowen

October 7, 2020

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Prospectus Supplement

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement relates to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus, together with the information incorporated by reference in this prospectus supplement, and any free writing prospectus supplement or prospectus supplement that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents we have referred you to under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." These documents contain important information that you should consider when making your investment decision.

This prospectus supplement describes the terms of this offering of common stock and also adds to and updates information contained in the documents incorporated by reference into this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference into this prospectus supplement that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. 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 supplement—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 supplement, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering. We have not, and the sales agent has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the sales agent is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted.

You should assume that the information appearing in this prospectus supplement, the documents incorporated by reference in this prospectus supplement, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the documents incorporated by reference in this prospectus supplement, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus supplement to "GlycoMimetics," "company," "we," "us" and "our" or similar references refer to GlycoMimetics, Inc.

This prospectus supplement and the information incorporated by reference herein include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement are the property of their respective owners.

PROSPECTUS SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement, including the information incorporated by reference in this prospectus supplement, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information under the heading "Risk Factors" in this prospectus supplement on page 6 and under similar headings in the documents incorporated by reference into this prospectus supplement.

We are a clinical-stage biotechnology company focused on the discovery and development of novel glycomimetic drugs to address unmet medical needs resulting from diseases in which carbohydrate biology plays a key role. We are developing a pipeline of glycomimetics, which are molecules that mimic the structure of carbohydrates involved in important biological processes, to inhibit disease-related functions of carbohydrates such as the roles they play in inflammation, cancer and infection. We believe this represents an innovative approach to drug discovery to treat a wide range of diseases. We are focusing our efforts on drug candidates for rare diseases that we believe will qualify for orphan drug designation.

Our proprietary glycomimetics platform is based on our expertise in carbohydrate chemistry and our understanding of the role carbohydrates play in key biological processes. Most human proteins are modified by the addition of complex carbohydrate structures to the surface of such proteins, which affects the functions of the proteins and their interactions with other molecules. Our initial research and development efforts have focused on drug candidates targeting selectins, which are proteins that serve as adhesion molecules and bind to carbohydrates that are involved in the inflammatory component and progression of a wide range of diseases, including hematologic disorders, cancer and cardiovascular disease. For example, we believe that members of the selectin family play a key role in tumor metastasis and resistance to chemotherapy. Inhibiting specific carbohydrates from binding to selectins has long been viewed as a potentially attractive approach for therapeutic intervention. The ability to successfully develop drug-like compounds that inhibit binding with selectins, known as selectin antagonists, has historically been limited by the complexities of carbohydrate chemistry. We believe our expertise in carbohydrate chemistry enables us to design selectin antagonists and other glycomimetics that may inhibit the disease-related functions of certain carbohydrates in order to develop novel drug candidates to address orphan diseases with high unmet medical need.

Our lead glycomimetic drug candidate, uproleselan, is a specific E-selectin inhibitor that we are developing to be used in combination with chemotherapy to treat patients with acute myeloid leukemia, or AML, a life-threatening hematologic cancer, and potentially other hematologic cancers. We completed an initial Phase 1 trial in healthy volunteers for uproleselan, and in May 2017 we completed enrollment in a Phase 1/2 clinical trial in patients with either relapsed/refractory or de novo/secondary AML. In December 2018, at the annual meeting of the American Society of Hematology, or ASH, we presented clinical data from this Phase 1/2 clinical trial that showed high remission rates, improved overall survival and improved event-free survival, all compared to historical controls derived from third-party clinical trials evaluating treatment with standard chemotherapy.

In March 2018, we announced our design for a randomized, double-blind, placebo-controlled Phase 3 clinical trial to evaluate uproleselan in individuals with relapsed/refractory AML, which design is aligned with guidance received from the U.S. Food and Drug Administration, or FDA. Based on consultations with the FDA, the single pivotal trial is planned to enroll approximately 380 adult patients with relapsed or refractory AML at centers in the United States, Canada, Europe and Australia. We dosed the first patient in this trial in November 2018. The primary efficacy endpoint will

be overall survival; importantly, the FDA has advised us that data on overall survival will not need to be censored for transplant in the primary efficacy analysis, meaning that patients who proceed to transplant will continue to be included as part of the survival analysis. All patients will be treated with standard chemotherapy of either MEC (mitoxantrone, etoposide and cytarabine) or FAI (fludarabine, cytarabine and idarubicin), with approximately one-half of the patients randomized to receive uproleselan in addition to chemotherapy. Patients receiving uproleselan will be dosed for one day prior to initiation of chemotherapy, twice a day through the chemotherapy regimen, and then for two days after the end of chemotherapy, which was the same regimen as in the Phase 1/2 trial. The dose regimen will be fixed, rather than weight-based, which we believe will simplify administration. We plan to offer up to three cycles of consolidation therapy in both arms of the trial for patients who achieve remission. We believe that multiple cycles of treatment in patients who respond may drive an even deeper response in patients treated with uproleselan. If this is the case, it could lengthen the duration of remission with potential for additional benefit on survival. Key secondary endpoints of the Phase 3 trial will include the incidence of severe mucositis and remission rate, which will be assessed in a hierarchical fashion which may provide supportive data.

Uproleselan received orphan drug designation from the FDA in May 2015 for the treatment of patients with AML. In June 2016, uproleselan received fast track designation from the FDA for the treatment of adult patients with relapsed or refractory AML and elderly patients aged 60 years or older with AML. In May 2017, uproleselan received Breakthrough Therapy designation from the FDA for the treatment of adult patients with relapsed or refractory AML. In May 2017, the European Commission, based on a favorable recommendation from the EMA Committee for Orphan Medicinal Products, granted orphan designation for uproleselan for the treatment of patients with AML. In June 2018, we received a response from the EMA to our request for scientific advice with respect to our Marketing Authorization Application, or MAA, development plan. Based on this guidance, we are conducting the global Phase 3 clinical trial and intend to pursue regulatory approval of uproleselan for the treatment of AML.

In May 2018, we signed a Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute, or NCI, part of the National Institutes of Health. Under the terms of the CRADA, we will collaborate with both the NCI and the Alliance for Clinical Trials in Oncology to conduct a Phase 2/3 randomized, controlled clinical trial testing the addition of uproleselan to a standard cytarabine/daunorubicin chemotherapy regimen (7&3) in older adults with previously untreated AML who are suitable for intensive chemotherapy. The primary endpoint will be overall survival, which is defined as the time from the date of randomization to death from any cause, with a planned interim analysis based on event-free survival after the first 250 patients have been enrolled in the trial. The full trial is expected to enroll approximately 670 patients. Under the terms of the CRADA, the NCI may also fund additional research, including clinical trials involving pediatric patients with AML as well as preclinical experiments and clinical trials evaluating alternative populations and chemotherapy regimens. We will supply uproleselan as well as provide financial support to augment data analysis and monitoring for the Phase 3 program. The trial opened for enrollment in early 2019 and enrolled the first patient in April 2019.

As a potential life-cycle extension to uproleselan, we have rationally designed an innovative antagonist of E-selectin, GMI-1687, that could be suitable for subcutaneous administration. When given by subcutaneous injection in animal models, GMI-1687 has been observed to have equivalent activity to uproleselan, but at an approximately 1,000-fold lower dose. We believe that GMI-1687 could be developed to broaden the clinical usefulness of an E-selectin antagonist to conditions where outpatient treatment is preferred or required. We are currently conducting preclinical studies with GMI-1687 to support our planned submission of an investigational new drug application, or IND, to the FDA.

We are developing an additional drug candidate, GMI-1359, that simultaneously targets both E-selectin and a chemokine receptor known as CXCR4. Since E-selectin and CXCR4 are implicated in

the retention of cancer cells in the bone and bone marrow, we believe that targeting both E-selectin and CXCR4 with a single compound could improve efficacy in the treatment of cancers that affect the bone and bone marrow, particularly solid tumors that have a propensity to metastasize to bone, such as breast and prostate cancer. We completed a Phase 1 randomized, double-blind, placebo-controlled, single-dose escalation trial of GMI-1359 in healthy volunteers. In this trial, volunteer participants received a single injection of either GMI-1359 or placebo, after which they were evaluated for safety, tolerability and pharmacokinetics, or PK. This trial was conducted at a single site in the United States. GMI-1359 was generally well tolerated in this trial, with no participants experiencing serious adverse events. In the fourth quarter of 2019, we initiated a Phase 1b trial of GMI-1359 in hormone receptor positive breast cancer patients whose tumors have spread to bone, and the first patient was dosed in January 2020. The trial is being conducted at Duke University and will evaluate dose escalation as well as safety, PK and pharmacodynamics markers of biologic activity in these patients. In January 2020, the FDA granted GMI-1359 orphan drug designation and rare pediatric disease designation for the treatment of osteosarcoma, a rare cancer affecting approximately 900 adolescents each year in the United States. These designations are expected to make GMI-1359 eligible for priority review by the FDA.

In addition to our programs described above, we are also advancing other preclinical-stage programs. These programs include small-molecule glycomimetic compounds that inhibit the protein galectin-3, which we believe may have potential to be used for the treatment of fibrosis, cancer and cardiovascular disease.

We previously developed another glycomimetic drug candidate, rivipansel, a pan-selectin antagonist for the potential treatment of vaso-occlusive crisis, or VOC, a debilitating and painful condition that occurs periodically throughout the life of a person with sickle cell disease, or SCD. Rivipansel received fast track designation from the FDA as well as orphan drug designation from the FDA in the United States and from the European Medicines Agency, or EMA, in the European Union. We entered into an exclusive license agreement with Pfizer Inc., or the Pfizer Agreement, for Pfizer to further develop, obtain regulatory approval and potentially commercialize rivipansel worldwide. Pfizer conducted a pivotal Phase 3 clinical trial to evaluate the efficacy and safety of rivipansel in patients aged six and older with SCD who were hospitalized for VOC and required treatment with intravenous opioids. The clinical trial did not meet its primary or key secondary efficacy endpoints. Pfizer terminated the Pfizer Agreement effective as of April 2020, resulting in the transfer of development and commercialization rights, including the investigational new drug (IND) application for rivipansel, back to us.

In June 2020, the Foundation for Sickle Cell Disease Research, or FSCDR, released an abstract that presented new data from a post hoc analysis of the Phase 3 clinical trial data set. The abstract showed that patients experiencing acute VOC requiring hospitalization who were treated with rivipansel within approximately 26 hours of the onset of pain in their crisis experienced a statistically significant improvement in the primary efficacy endpoint of time to readiness for discharge. Specifically, the analysis showed a median improvement in time to readiness for discharge compared to placebo of 56.3 hours (p=0.03, 0.58 HR). The abstract has been accepted for a poster presentation at the September 2020 meeting of the FSCDR. We intend to discuss this and other data with the FDA to determine possible next steps, if any, for this program in acute VOC.

Our Collaboration and License Agreements

Apollomics

In January 2020, we entered into an exclusive collaboration and license agreement with Apollomics (Hong Kong) Limited, or Apollomics, for the development and commercialization of uproleselan and GMI-1687 in Mainland China, Hong Kong, Macau and Taiwan, also known as Greater China. Under the terms of the agreement, Apollomics will be responsible for clinical development and

commercialization in Greater China. We will also collaborate with Apollomics to advance the preclinical and clinical development of GMI-1687. We received an upfront cash payment of $9.0 million and, subject to the terms of the agreement, will be eligible to receive potential milestone payments totaling approximately $180.0 million, as well as tiered royalties ranging from the high single digits to 15%, as a percentage of net sales. Apollomics will be responsible for all costs related to development, regulatory approvals, and commercialization activities for uproleselan and GMI-1687 in Greater China, and we and Apollomics expect to enter into clinical and commercial supply agreements with respect to our provision of uproleselan and GMI-1687 to Apollomics. We retain all rights for both compounds in the rest of the world.

Pfizer

In October 2011, we entered into the Pfizer Agreement, under which we granted Pfizer an exclusive worldwide license to develop and commercialize products containing rivipansel for all fields and uses. Pfizer was required to use commercially reasonable efforts, at its expense, to develop, obtain regulatory approval for and commercialize rivipansel for SCD in the United States. On August 2, 2019, Pfizer announced that its pivotal Phase 3 clinical trial to evaluate the efficacy and safety of rivipansel in patients aged six and older with SCD who were hospitalized for a vaso-occlusive crisis and required treatment with intravenous opioids did not meet its primary or key secondary efficacy endpoints. Pfizer terminated the Pfizer Agreement, effective as of April 5, 2020, and we now hold all rights to the potential future development and commercialization of rivipansel. We are not eligible to receive any future payments from Pfizer following the termination of the Pfizer Agreement.

Intellectual Property

We strive to protect the intellectual property that we believe is important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our drug candidates and their methods of use. We have issued patents directed to rivipansel and methods of use that are expected to expire between 2023 and 2030. We also have issued patents which cover uproleselan and methods of use that are expected to expire between 2032 and 2033. In addition, we have several pending patent applications covering uproleselan and/or methods of using it, the last expiring of which, if issued, currently would be predicted to expire in 2040. We also have an issued patent which covers GMI-1359 and methods of use that is expected to expire in 2036. In addition, we have several pending patent applications covering GMI-1359 and/or methods of using it, the last expiring of which, if issued, currently would be predicted to expire in 2040. We also rely on trade secret protection for our confidential and proprietary information and careful monitoring of such information to protect aspects of our business.

Impact of COVID-19 on Our Business

The imposition of "lockdown," "social distancing" and "shelter in place" directives by state and federal governments in the United States as well as governments in other regions of the world in response to the COVID-19 pandemic, including in locations in which our Phase 3 clinical trial of uproleselan is being conducted, resulted in slowed clinical site initiation, patient recruitment and enrollment rates in April 2020. Enrollment rates more recently showed an encouraging upward trend. However, the COVID-19 infection rates continue to rise, especially in the United States, which could negatively affect enrollment going forward. We cannot at this time fully assess the effect of the COVID-19 pandemic on our continued enrollment and whether the pandemic would potentially materially adversely impact the timing of completion of enrollment of our Phase 3 clinical trial. We continue to closely monitor the COVID-19 situation and any potential impact to our planned activities.

We have also implemented business continuity plans designed to address and mitigate the impact of the COVID-19 pandemic on our employees and our business. While to date we have experienced

limited impacts beyond the earlier delays in recruitment in our ongoing uproleselan Phase 3 clinical trial, given the global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic, our business, financial condition, results of operations and growth prospects could be materially adversely affected. We continue to closely monitor the COVID-19 situation as we evolve our business continuity plans and response strategy. In March 2020, our workforce transitioned to working remotely in accordance with federal and state declarations. We are currently preparing plans to reopen our office to allow employees to return to the office based on a phased approach that is consistent with federal and state guidelines, with a focus on employee safety and optimal work environment.

Risks Associated with our Business

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled "Risk Factors" immediately following this prospectus summary and those described under similar headings in the documents incorporated by reference into this prospectus and the accompanying prospectus. These risks include:

- We have incurred significant losses since our inception. We expect to continue to incur losses over the next several years and may never achieve or maintain profitability.
- We will need substantial additional funding to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our drug development programs or potential commercialization efforts.
- Our business could be adversely affected by the effects of health epidemics or pandemics—including the recent COVID-19 outbreak—in regions where we or third parties on whom we rely have significant manufacturing facilities, clinical trial sites or other business operations.
- Our research and development is focused on discovering and developing novel glycomimetic drugs, and we are taking an innovative approach to discovering and developing drugs, which may never lead to marketable drugs.
- We have only two drug candidates that are in clinical trials. All of our other drug candidates are still in preclinical development. If we or our collaborators are unable to commercialize our drug candidates or experience significant delays in doing so, our business will be materially harmed.
- If we or our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.
- Our success depends in part on current and future collaborations. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.
- We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.
- If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize our drug candidates and our ability to generate revenue will be materially impaired.
- The trading price of our common stock has been and is likely to continue to be volatile.

Corporate Information

We were incorporated under the laws of the State of Delaware in April 2003 and commenced operations in May 2003. Our principal executive offices are located at 9708 Medical Center Drive, Rockville, Maryland 20850. Our telephone number is (240) 243-1201. Our website is located at http://www.glycomimetics.com. We do not incorporate by reference into this prospectus the information on, or accessible through, our website, and you should not consider it as part of this prospectus.

THE OFFERING

Common Stock Offered By Us	Shares of our common stock having an aggregate offering price of up to $100,000,000.
Manner of Offering	"At-the-market" offering that may be made from time to time through our sales agent, Cowen and Company, LLC. See "Plan of Distribution" on page 17 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from this offering to fund the manufacturing of GMI-1271, to conduct ongoing and future clinical trials of GMI-1271 and GMI-1359, to fund the research and development of other drug candidates in our preclinical pipeline, including drug discovery, and for working capital and other general corporate purposes. See "Use of Proceeds" on page 11 of this prospectus supplement.
Risk Factors	Investing in our common stock involves significant risks. See "Risk Factors" on page 8 of this prospectus supplement, and under similar headings in other documents incorporated by reference into this prospectus supplement and the accompanying prospectus.
Nasdaq Global Market Symbol	"GLYC"

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described below and under the section titled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2019 and in our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2020 and June 30, 2020, as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus supplement and any free writing prospectus with respect to this offering filed by us with the SEC, before deciding whether to invest in our common stock. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

Additional Risks Related to This Offering

You may experience dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Because the sales of the shares offered hereby will be made directly into the market or in negotiated transactions, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing shareholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

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

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 price 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 price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

Our management might apply the net proceeds from this offering in ways with which you do not agree and in ways that may impair the value of your investment.

We currently intend to use the net proceeds from this offering to fund the manufacturing of GMI-1271, to conduct ongoing and future clinical trials of GMI-1271 and GMI-1359, to fund the research and development of other drug candidates in our preclinical pipeline, including drug discovery, and for working capital and other general corporate purposes. Pending these uses, we expect to invest the net proceeds in short-term, interest-bearing securities. Our management has broad discretion as to the use of these proceeds and you will be relying on the judgment of our management regarding the application of these proceeds. We might apply these proceeds in ways with which you do not agree, or in ways that do not yield a favorable return. If our management applies these proceeds in a manner that does not yield a significant return, if any, on our investment of these net proceeds, it could compromise our ability to pursue our growth strategy and adversely affect the market price of our common stock.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, the documents we file with the SEC that are incorporated by reference in this prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering, contain "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the Sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent Annual Report on Form 10-K and in our Quarterly Reports on Form 10-Q, as well as any amendments thereto, filed with the SEC.

Any statements in this prospectus supplement, or incorporated herein, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. These forward-looking statements include statements regarding:

- our plans to develop and commercialize our glycomimetic drug candidates;
- our and our collaborators' ongoing and planned clinical trials for our drug candidates uproleselan and GMI-1359, including the timing of initiation of and enrollment in the trials, the timing of availability of data from the trials and the anticipated results of the trials;
- the timing of completion of enrollment in our Phase 3 clinical trial of uproleselan in individuals with relapsed/refractory AML:
- the timing of and our ability to obtain and maintain regulatory approvals for our drug candidates;
- the clinical utility of our drug candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional drug candidates with significant commercial potential that are consistent with our commercial objectives;
- our estimates regarding future revenues, expenses and needs for additional financing; and
- our beliefs about our capital expenditure requirements and the length of time over which our capital resources will be sufficient to meet our anticipated cash requirements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "project," "predict," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading "Risk Factors" contained in this prospectus supplement, in any free writing prospectuses we may authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K and quarterly reports on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus supplement in its entirety. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to

update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus, together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary 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 after the date of this prospectus supplement. 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. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Cowen as a source of financing.

We currently intend to use the net proceeds from this offering primarily to fund the manufacturing of GMI-1271, to conduct ongoing and future clinical trials of GMI-1271 and GMI-1359, to fund the research and development of other drug candidates in our preclinical pipeline, including drug discovery, and for working capital and other general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement. Pending these uses, we expect to invest the net proceeds in short-term, interest-bearing securities.

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus supplement, our certificate of incorporation authorizes us to issue 100,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share. As of June 30, 2020, 46,714,698 shares of common stock were outstanding and no shares of preferred stock were outstanding.

The following summary description of our capital stock is based on the provisions of our certificate of incorporation, as well as our bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our certificate of incorporation, bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our certificate of incorporation and bylaws, which are exhibits to the registration statement of which this prospectus supplement is a part, see "Where You Can Find Additional Information."

Common Stock

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of our common stock do not have cumulative voting rights in the election of directors. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock.

Additional shares of authorized common stock may be issued, as authorized by our board of directors from time to time, without stockholder approval, except as may be required by applicable stock exchange requirements.

The rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any preferred stock that we may designate and issue in the future.

Registration Rights

We and the some of the holders of our common stock have entered into an investor rights agreement. The registration rights provisions of this agreement provide those holders with demand, piggyback and Form S-3 registration rights with respect to the shares of our common stock currently held by them.

Demand Registration Rights

The holders of at least 40% of the shares held by the parties to the investor rights agreement have the right to demand that we file up to a total of two registration statements, as long as the anticipated aggregate offering price, net of underwriting discounts and commissions, would exceed $10.0 million. These registration rights are subject to specified conditions and limitations, including the right of the underwriters, if any, to limit the number of shares included in any such registration under specified circumstances. Upon such a request, we are required to effect the registration as soon as reasonably possible.

Piggyback Registration Rights

If we propose to register any of our securities under the Securities Act either for our own account or for the account of other stockholders, the parties to the investor rights agreement with piggyback registration rights will each be entitled to notice of the registration and will be entitled to include their shares of common stock in the registration statement. These piggyback registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under specified circumstances.

Registration on Form S-3

If we are eligible to file a registration statement on Form S-3, the parties to the investor rights agreement are entitled, upon their written request, to have such shares registered by us on a Form S-3 registration statement at our expense, provided that such requested registration has an anticipated aggregate offering size to the public of at least $1.0 million and subject to other specified conditions and limitations.

Expenses of Registration

We will pay all expenses relating to any demand, piggyback or Form S-3 registration, other than underwriting discounts and commissions, subject to specified conditions and limitations.

Termination of Registration Rights

The registration rights granted under the investor rights agreement will terminate upon the seventh anniversary of the completion of our initial public offering, which would be in January 2021, or, if earlier, with respect to a particular holder, at such time as that holder and its affiliates may sell all of their shares of common stock pursuant to Rule 144 under the Securities Act of 1933, as amended, without any restrictions on volume.

Preferred Stock

Pursuant to our amended and restated certificate of incorporation, or the Restated Certificate, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or stock exchange listing rules), to designate and issue up to 5,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the designations, powers, preferences, privileges and relative participating, optional or special rights and the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights of the common stock, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

The board of directors, without stockholder approval, can issue preferred stock with voting, conversion or other rights that could adversely affect the voting power and other rights of the holders of common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of the common stock and may adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

Our board of directors will fix the designations, voting powers, preferences and rights of the each series, as well as the qualifications, limitations or restrictions thereof, of the preferred stock of each series that we offer under this prospectus and applicable prospectus supplements in the certificate of

designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock.

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as

a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Antitakeover Effects of Provisions of Charter Documents and Delaware Law

Charter Documents. Our Restated Certificate and Amended and Restated Bylaws, or Bylaws, each as amended to date, include a number of provisions that may have the effect of deterring hostile takeovers or delaying or preventing changes in control or management of our company. First, our board of directors is classified into three classes of directors. Under Delaware law, directors of a corporation with a classified board may be removed only for cause unless the corporation's certificate of incorporation provides otherwise. Our Restated Certificate does not provide otherwise. In addition, the Restated Certificate provides that all stockholder action must be effected at a duly called meeting of stockholders and not by a consent in writing. Further, our Bylaws limit who may call special meetings of the stockholders. Our Restated Certificate does not include a provision for cumulative voting for directors. Under cumulative voting, a minority stockholder holding a sufficient percentage of a class of shares may be able to ensure the election of one or more directors. Finally, our Bylaws establish procedures, including advance notice procedures, with regard to the nomination of candidates for election as directors and stockholder proposals. These and other provisions of our Restated Certificate and Bylaws and Delaware law could discourage potential acquisition proposals and could delay or prevent a change in control or management of our company.

Delaware Takeover Statute. We are subject to Section 203 of the General Corporation Law of the State of Delaware, or DGCL, which regulates acquisitions of some Delaware corporations. Section 203 generally prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years following the date of the transaction in which the person became an interested stockholder, unless:

- the board of directors of the corporation approved the business combination or the other transaction in which the person became an interested stockholder prior to the date of the business combination or other transaction;
- upon consummation of the transaction that resulted in the person becoming an interested stockholder, the person owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding shares owned by persons who are directors and also officers of the corporation and shares issued under employee stock plans under 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 the person became an interested stockholder, the board of directors of the corporation approved the business combination and the stockholders of the corporation authorized the business combination at an annual or special meeting of stockholders by the affirmative vote of at least $66^2/_3\%$ of the outstanding stock of the corporation not owned by the interested stockholder.

Section 203 of the DGCL defines a "business combination" to include any of the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the corporation's assets or outstanding stock involving the interested stockholder;

- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any of its stock to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of its stock owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an "interested stockholder" as any person who, together with the person's 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 voting stock.

Section 203 of the DGCL could depress our stock price and delay, discourage or prohibit transactions not approved in advance by our board of directors, such as takeover attempts that might otherwise involve the payment to our stockholders of a premium over the market price of our common stock.

Choice of Forum

Our Restated Certificate provides that the Court of Chancery of the State of Delaware will be the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our Restated Certificate, or our Restated Bylaws; or
- any action asserting a claim against us that is governed by the internal affairs doctrine.

The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our Restated Certificate to be inapplicable or unenforceable in such action.

Transfer Agent And Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, and its address is 6201 15th Street, Brooklyn, NY 11219. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

Listing on the Nasdaq Global Market

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

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen, under which we may issue and sell from time to time up to $100,000,000 of our common stock after the date of this prospectus supplement through Cowen as our sales agent. Sales of our common stock, if any, will be made at market prices 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 the Exchange or any other trading market for our common stock. If authorized Cowen may purchase shares of our common stock as principal.

Cowen 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 Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. In addition, we have agreed to reimburse Cowen for fees and disbursements related to its legal counsel in an amount not to exceed $50,000, and for certain other expenses, including Cowen's FINRA counsel fees in an amount up to $12,500. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately $100,000.

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, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on the Exchange on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, Cowen may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on the Exchange and trades under the symbol "GLYC." The transfer agent of our common stock is American Stock Transfer & Trust Company.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement will be passed upon by Cooley LLP, Reston, Virginia. Goodwin Procter LLP, New York, New York, is counsel for Cowen in connection with this offering.

EXPERTS

The financial statements of GlycoMimetics, Inc. appearing in GlycoMimetics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2019, and the effectiveness of GlycoMimetics, Inc.'s internal control over financial reporting as of December 31, 2019 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of our internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is a part of a registration statement we filed with the SEC. This prospectus supplement does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person 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 supplement is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of the securities offered by this prospectus supplement.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including GlycoMimetics, Inc. The address of the SEC website is www.sec.gov.

We maintain a website at www.glycomimetics.com. Information contained in or accessible through our website does not constitute a part of this prospectus supplement.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for the documents incorporated by reference in this prospectus supplement is 001-36177. The documents incorporated by reference into this prospectus supplement contain important information that you should read about us.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on February 28, 2020;
- our Quarterly Report on Form 10-Q for the three months ended March 31, 2019 filed with the SEC on May 1, 2020;

- our Quarterly Report on Form 10-Q for the three months ended June 30, 2019 filed with the SEC on July 31, 2020;
- our Current Reports on Form 8-K filed with the SEC on January 7, 2020, February 10, 2020, February 28, 2020, May 26, 2020, and October 7, 2020 to the extent the information in such reports is filed and not furnished;
- our Proxy Statement filed with the SEC on April 16, 2020, to the extent the information therein is filed and not furnished; and
- the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on November 5, 2013, including any amendments or reports filed for the purposes of updating this description.

We also incorporate by reference into this prospectus supplement all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

We will provide to each person, including any beneficial owner, to whom a prospectus supplement is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus supplement but not delivered with this prospectus supplement, including exhibits which are specifically incorporated by reference into such documents. Requests should be directed to: GlycoMimetics, Inc., Attn: Investor Relations, 9708 Medical Center Drive, Rockville, Maryland 20850, telephone: (240) 243-1201.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

DISCLOSURE OF COMMISSION'S POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITY

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the Company pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

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October 7, 2020