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

FORM 8-K

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

Date of Report (Date of earliest event reported):
June 7, 2020

KEZAR LIFE SCIENCES, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-38542**	**47-3366145**
(state or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

4000 Shoreline Court, Suite 300 **South San Francisco, California** **(Address of principal executive offices)**	**94080** **(Zip Code)**

Registrant's telephone number, including area code: (650) 822-5600

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

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

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

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

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

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

Title of each class	Trading symbol	Name of each exchange on which registered
Common Stock, $0.001 par value	**KZR**	**The Nasdaq Stock Market LLC**

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

Emerging growth company ☒

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

Item 1.02. Termination of a Material Definitive Agreement.

As previously disclosed, on July 3, 2019, Kezar Life Sciences, Inc. (the "Company") entered into an Open Market℠ Sales Agreement (the "Sales Agreement"), with Jefferies LLC ("Jefferies"), to sell, at its option, shares of common stock, par value $0.001 per share ("Common Stock"), having aggregate gross sales proceeds of up to $50 million, from time to time, through an "at the market" equity offering program under which Jefferies acted as sales agent.

On June 7, 2020, the Company delivered written notice to Jefferies, effective as of such date, to terminate the Sales Agreement pursuant to Section 7(b)(i) thereof. Prior to termination, the Company had not sold, and the Company will not sell, any shares of Common Stock pursuant to the Sales Agreement.

A copy of the Sales Agreement was filed as Exhibit 1.2 to the Company's Registration Statement on Form S-3, filed with the Securities and Exchange Commission (the "SEC") on July 3, 2019 (the "Form S-3"). The description of the Sales Agreement contained in this Current Report on Form 8-K does not purport to be complete and is qualified in its entirety by reference to the copy of the Sales Agreement filed as Exhibit 1.2 to the Form S-3.

Item 8.01 Other Events.

On June 8, 2020, the Company filed with the SEC a preliminary prospectus supplement in connection with a proposed public offering of shares of Common Stock. The preliminary prospectus supplement contains an updated description of certain aspects of the Company's business. Accordingly, the Company is filing this information with this Current Report on Form 8-K for the purpose of supplementing and updating disclosures contained in the Company's prior filings with the SEC. The updated disclosures are filed herewith as Exhibit 99.1 and are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit	Description
99.1	Updated Company Disclosures.

SIGNATURES

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

KEZAR LIFE SCIENCES, INC.

By: /s/ Marc L. Belsky
Marc L. Belsky
Chief Financial Officer and Secretary

Dated: June 8, 2020

As used in this Exhibit 99.1, unless the context indicates otherwise, references to "Kezar," "the Company," "we," "us," "our" and similar references refer to Kezar Life Sciences, Inc. and its wholly owned Australian subsidiary, Kezar Life Sciences Australia Pty Ltd.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Exhibit 99.1 contains forward-looking statements. In some cases, you can identify these statements by forward-looking words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "could," "should," "would," "potential," "project," "plan," "expect," "seek," "should," "target" or similar expressions, or the negative or plural of these words or expressions. These forward-looking statements include statements concerning the following:

- statements regarding the impact of the COVID-19 pandemic and its effects on our operations, research and development, clinical trials and financial position, and its potential effects on the operations of third-party manufacturers, contract research organizations, other service providers, and collaborators with whom we conduct business;
- our plans to develop and commercialize our product candidates;
- the initiation, timing, progress and expected results of our current and future clinical trials and our research and development programs;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to successfully acquire or in-license additional product candidates or other technology on reasonable terms;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- the timing and likelihood of obtaining regulatory approval of our current and future product candidates;
- our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business and product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights and the duration of our patent rights covering our product candidates;
- developments or disputes concerning our intellectual property or other proprietary rights;
- the scalability and commercial viability of our manufacturing methods and processes;
- our expectations regarding government and third-party payor coverage and reimbursement;
- our ability to compete in the markets for our product candidates;
- the impact of government laws and regulations;
- developments relating to our competitors and our industry; and
- the factors that may impact our financial results.

These statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in the sections titled "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 most recent Quarterly Report on Form 10-Q, as well as any amendments thereto, filed with the SEC. You should not rely upon forward-looking statements as predictions of future events.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we are under no duty to update or revise any of the forward-looking statements in this Exhibit 99.1, whether as a result of new information, future events or otherwise.

Company Overview

We are a clinical-stage biotechnology company, discovering and developing novel small molecule therapeutics to treat unmet needs in autoimmunity and cancer. Our lead product candidate, KZR-616, a first-in-class selective immunoproteasome inhibitor, has completed testing in healthy volunteers, and we are now leveraging its broad therapeutic potential in three Phase 2 clinical trials across five separate autoimmune indications: lupus nephritis (the MISSION trial), autoimmune hemolytic anemia, or AIHA, immune thrombocytopenia, or ITP (the MARINA trial), dermatomyositis, or DM, and polymyositis, or PM (the PRESIDIO trial). We are also continuing to enroll patients in the Phase 1b portion of the MISSION trial, a Phase 1b/2 clinical trial in systemic lupus erythematosus, also known as lupus or SLE, and lupus nephritis.

We believe that the immunoproteasome is a validated target for the treatment of a wide variety of autoimmune diseases based on its ability to target cells in both the adaptive and innate immune system as bolstered by compelling published activity seen with non-selective proteasome inhibitors administered to patients with severe autoimmune diseases. Based on results from our Phase 1a studies in healthy volunteers and the preliminary results from the Phase 1b portion of the MISSION trial, KZR-616 has largely avoided adverse effects associated with currently marketed non-selective proteasome inhibitors, as exhibited in clinical studies conducted by third parties, including side effects which we believe could prevent them from being utilized as a chronic treatment in autoimmune disorders. We intend to develop KZR-616 to address chronic, severe and underserved autoimmune diseases.

Additionally, we are advancing our novel research platform targeting the Sec61 translocon and the protein secretion pathway to discover and develop small molecule therapeutics targeting oncology indications. Our first clinical candidate in this program, KZR-261, has demonstrated broad anti-tumor activity in preclinical models of both solid and hematologic malignancies. KZR-261 is undergoing laboratory studies and manufacturing activities in support of an investigational new drug, or IND, application, which we anticipate submitting to the FDA in the first quarter of 2021 for a Phase 1 clinical trial in solid tumors. We believe this discovery platform has the potential to yield oral small molecule candidates to act as cytotoxic anti-cancer agents or to block the secretion of novel targets of interest in immuno-oncology or inflammation and that, if successfully developed and approved, could serve as alternatives to currently marketed biologic therapeutics.

KZR-616: Selective Immunoproteasome Inhibitor

We believe that KZR-616 has potential to be developed for the treatment of multiple autoimmune disease indications. In the last decade, research directed by our Chief Scientific Officer, along with work performed in multiple academic laboratories, has led to over 15 peer-reviewed publications showing that selective immunoproteasome inhibition resulted in a broad anti-inflammatory response, reducing autoimmune disease in animal models of lupus, lupus nephritis, rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, Type 1 diabetes and other indications. This immunomodulatory response was broadly seen across many cell types of the immune system, including both T cells and B cells, and was demonstrated in a safe

and non-immunosuppressive manner. This is distinct from other agents currently used to treat autoimmunity, which typically target a single cytokine or immune cell type or are broadly immunosuppressive.

Autoimmunity and Selective Inhibition of the Immunoproteasome

Autoimmune disease is an immune response directed against the body's own healthy cells and tissues. Approximately 50 million people in the United States suffer from more than 100 diagnosed autoimmune diseases according to the American Autoimmune Related Diseases Association, Inc. In indications large and small, there remain significant unmet medical needs and indications with no approved drugs beyond broadly prescribed corticosteroids and similar immunosuppressive regimens. These result in increased risk of infection and malignancy and a wide variety of side effects. In diseases such as lupus nephritis, these regimens do not induce high rates of clinically meaningful responses.

Found in all cells of the body, proteasomes regulate intracellular protein degradation and are essential for many cellular processes such as cell division, cell differentiation and cytokine production. There are two main forms of the proteasome: the constitutive proteasome and the immunoproteasome. In most tissues of the body, the constitutive proteasome is the predominant form. In cells of the immune system, the immunoproteasome is the predominant form. While both forms of the proteasome mediate protein degradation, the two forms of the proteasome accomplish this utilizing different active sites. These active sites are responsible for cleaving and degrading proteins. Selective inhibition of the immunoproteasome has the potential to reduce inflammation by targeting dysfunctional immune cells involved in autoimmunity, such as T cells and B cells, without causing widespread immunosuppression.

Safety and Efficacy of Approved Proteasome Inhibitors

The three proteasome inhibitors approved for the treatment of multiple myeloma, Velcade (bortezomib), Kyprolis (carfilzomib) and Ninlaro (ixazomib), are potent "dual inhibitors" of both the immunoproteasome and the constitutive proteasome. This dual-targeting profile is necessary to make them effective treatments for multiple myeloma. However, dual proteasome inhibition is associated with hematologic issues such as thrombocytopenia, neutropenia and anemia, as well as constitutional toxicities such as fatigue and myalgia. In addition, Velcade and Ninlaro are associated with risk of peripheral neuropathy, likely due to the off-target activity of these drugs against proteins found in peripheral neurons.

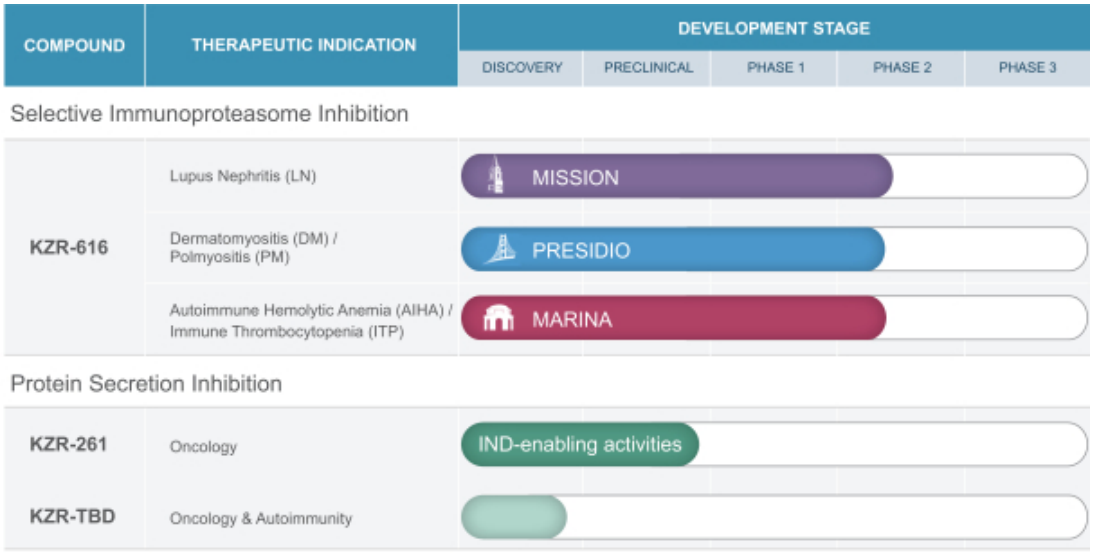
Velcade has demonstrated clinical activity in several autoimmune diseases, including lupus, lupus nephritis, rheumatoid arthritis, immune thrombocytopenia, autoimmune hemolytic anemia, primary Sjögren's syndrome and graft-versus-host disease. In preclinical models, proteasome inhibition with Velcade blocked production of most inflammatory cytokines, including many of those targeted by current biologic drugs. However, long-term, chronic administration of Velcade in the setting of autoimmune diseases is not considered feasible due to its side effect profile, in particular hematologic toxicities and risk of peripheral neuropathy. As a result, we believe that this promising drug target has remained untapped for use in the chronic treatment of autoimmune diseases.

We believe we are the only company with a selective immunoproteasome inhibitor that is in clinical trials for the treatment of autoimmune disorders. In addition, we believe that KZR-616, if successfully developed and approved, may have the ability to become the standard of care across a broad range of autoimmune diseases based on the following expected key attributes:

- broad immunomodulatory activity that may allow it to outperform approved therapies and to be effective in indications where other drugs have failed;
- low infection rates observed in clinical trials to date, which indicates a potential lack of immunosuppression, a key drawback to other approved therapies in autoimmunity; and
- avoidance of systemic toxicities associated with dual proteasome inhibitors and the peripheral neuropathy associated with Velcade and Ninlaro.

Our Pipeline

The following table sets forth the status and initial focus of our lead product candidate and protein secretion program:



Clinical Development of KZR-616

We are focusing our initial development of KZR-616 in severe orphan autoimmune diseases where limited treatment options exist. Currently, there are no approved treatments for lupus nephritis or AIHA in the United States or Europe, and there are limited approved treatments for DM, PM and ITP in the United States and Europe. We estimate the addressable patient population in the United States for lupus, lupus nephritis, DM/PM and AIHA/ITP to be 460,000, 100,000 to 200,000, 70,000 and 140,000, respectively.

We currently have three active Phase 2 trials across five separate autoimmune diseases of high unmet need: the MISSION trial in patients with lupus nephritis; the PRESIDO trial in patients with DM and PM; and the MARINA trial in patients with AIHA and ITP. Based upon the updated results from the Phase 1b portion of MISSION and the recent slowdown in recruitment and enrollment activities across our clinical trials due to the COVID-19 pandemic, we are actively reviewing and adapting some of our clinical trial plans in order to optimize the development pathway for KZR-616. Based on the positive safety and tolerability, pharmacology, and clinical activity results seen to date, we plan to focus future development on the 45 mg and 60 mg dose levels of KZR-616.

Phase 2 Clinical Trials

The Phase 2 portion of MISSION is intended to inform and enable late-stage clinical trials of KZR-616 in lupus nephritis. In order to expedite the advancement of KZR-616 into the next phase of development, we plan to submit an amendment to the current clinical trial protocol in the third quarter of 2020. Based on the data generated to date in two patients with active, proliferative LN, the primary endpoint will be changed from safety and tolerability to an efficacy endpoint of renal response measured by 50% or greater reduction in urine protein creatine ratio, or UPCR, at six months, which has been observed to be predictive of long-term outcomes in patients with lupus nephritis. Additionally, the inclusion/exclusion criteria will be expanded to include patients with LN with histologic Class III or IV +/- Class V being treated with current standard-of-care regardless of background therapy. The clinical trial will include a single treatment arm evaluating a 60 mg dose (with first dose of 30 mg) of KZR-616 administered subcutaneously once weekly for 24 weeks. The trial will be open-label with an opportunity for interim analyses. We expect to enroll 20 patients. Upon the successful completion of the

Phase 2 portion of MISSION, we intend to initiate a robust late-stage randomized placebo-controlled trial in patients with active, proliferative lupus nephritis.

PRESIDIO is a Phase 2 randomized, placebo-controlled, double-blind, crossover, multicenter trial to evaluate the safety, tolerability, efficacy, PK and PD of KZR-616 in patients with active PM or DM. During the 32-week treatment period, patients receive either 45 mg of KZR-616 or placebo subcutaneously once weekly for 16 weeks followed by a crossover to the other treatment arm for an additional 16 weeks. We expect to enroll 24 patients in the trial. We believe that KZR-616 has the potential to be developed into a treatment for patients with DM and PM, which is in-part supported by preclinical data in a mouse model of PM and DM that demonstrated immunoproteasome inhibition and improved muscle function.

MARINA is a Phase 2 randomized, dose-blind, multicenter trial designed to evaluate the safety, tolerability, efficacy, PK and PD of KZR-616 in patients with active AIHA or ITP. In order to expedite the advancement of KZR-616 in these orphan diseases, we plan to submit an amendment to the current clinical trial protocol in the third quarter of 2020. Under the amended protocol, patients with AIHA or ITP will receive KZR-616 subcutaneously once weekly for 13 weeks, with one dose at 30 mg and the remaining doses at 45 mg. We expect to enroll 30 patients in the trial. We believe that whole blood RNASeq data from MISSION, which showed a decrease in multiple inflammatory gene signature and prolonged increase in erythropoietic gene signatures in SLE patients, support the broad potential anti-inflammatory activity of KZR-616 and an application in patients with AIHA and ITP.

Phase 1 Clinical Trials

We have conducted two Phase 1a studies evaluating KZR-616 in 100 healthy volunteers. Results from these studies, involving administration of two different formulations of KZR-616, demonstrated that KZR-616 was well tolerated in up to 75 mg (the highest tested dose). We believe that these results support development of KZR-616 in autoimmune disorders based on the following observations:

- consistent and reproducible pharmacology;
- a distinct safety profile from dual proteasome inhibitors as a class; and
- an encouraging safety and tolerability profile.

The Phase 1b portion of MISSION is an open-label, dose escalation and dose-finding study in patients with active lupus with or without lupus nephritis who have received at least one standard therapeutic regimen. We are evaluating doses of 45 mg, 60 mg and 75 mg. Patients receive 13 weeks of weekly subcutaneous treatment of KZR-616, followed by 12 weeks of follow-up. Cohorts 2a, 2b and 2c utilized step-up dosing to 60 mg, which was observed to improve overall tolerability. Data generated to date from the Phase 1b portion of the MISSION trial continues to support the advancement of KZR-616 into Phase 2 trials across multiple autoimmune indications. As of the May 4, 2020 data cutoff, the Phase 1b portion of MISSION has enrolled 39 patients across five of six cohorts. We are currently recruiting the final cohort evaluating a 75 mg dose. Results generated and released to date demonstrate that KZR-616:

- was well tolerated for 13 weeks of treatment;
- largely avoided toxicities seen with dual proteasome inhibitors in third-party clinical trials;
- exhibited low rates of infection (which suggest immunomodulatory activity without inducing immunosuppressive side effects);
- induced broad improvement across seven measured parameters of disease activity across organ systems;
- showed a broad anti-inflammatory gene expression response as evidenced by whole blood RNASeq data;
- demonstrated consistent, dose proportional PK; and
- reached target levels of immunoproteasome inhibition with all dose levels.

Two SLE patients with biopsy-proven lupus nephritis were included in the Phase 1b portion of MISSION. Both patients showed a greater than 50% reduction in proteinuria as measured by UPCR, as well as reductions in

Systemic Lupus Erythematosus Disease Active Index, or SLEDAI-2K, and reductions in double-stranded DNA, or anti-dsDNA, antibody levels.

Patient 1 (Cohort 2a) [1]	UPCR	SLEDAI-2K	Anti-dsDNA antibodies (IU/ml)
Baseline	3.85	17	137
Week 13	2.89	8	53
Week 17	0.6	8	73
Week 25	1.0	8	61

(1) This patient was enrolled into Cohort 2a and was treated at 45 mg after initial doses of 30 mg. Prior to the start of therapy, her regime included leflunomide, hydroxychloroquine and 10 mg/day prednisone; and she had failed prior treatment with tacrolimus. She entered the study with a positive antinuclear antibody test, low complement levels, proliferative lupus nephritis, and a nephrotic range of proteinuria with a 3.85 mg/mg UPCR, a baseline SLEDAI score of 17, and anti-double-stranded DNA (anti-dsDNA) antibodies levels of 137 (IU/ml), indicative of severe disease. The UPCR dropped to 0.6 mg/mg at week 17 (four weeks after the last dose of KZR-616), the SLEDAI score dropped to 8 at week 13, which was maintained through the follow-up period to week 25, and anti-dsDNA levels dropped to 53 at week 13 and were relatively maintained to week 25.

Patient 2 (Cohort 2c) [2]	UPCR	SLEDAI-2K	Anti-dsDNA antibodies (IU/ml)
Baseline	2.39	14	123.5
Week 5	1.03	10	82
Week 13	0.69	NA	52

(2) This patient was enrolled into Cohort 2c and was treated at 60 mg with an initial step-up dose of 30 mg. Prior to the start of therapy, her regime included 2 g/day mycophenylate mofetil (MMF;CellCept™), hydroxychloroquine and 10 mg/day prednisone. She has completed 13 weeks of dosing and is currently in the follow-up phase of the study. She entered the study with active proliferative lupus nephritis, a nephrotic range of proteinuria with a 2.39 mg/mg UPCR, a baseline SLEDAI score of 14, and anti-dsDNA antibodies of 123.5 (IU/mL), indicative of severe disease. At week 5, the UPCR dropped to 1.03 mg/mg, SLEDAI improved by four points, and anti-dsNDA antibody levels dropped to 82. At week 13, the UPCR dropped to 0.69 mg/mg and the anti-dsDNA dropped to 52.

Broad and consistent improvements have been seen across multiple measures and assessments of disease activity. Among patients completing treatment, all seven measures of disease activity improved (decrease in score) in the majority of patients from Baseline to Week 13. Improvement in disease activity has persisted following the end-of-treatment.

	Mean Score for Patients Completing Study 1, 2, 2a and 2b (n=22)*		
Assessment of SLE Disease Activity	Baseline	End of Treatment (Week 13)	End of Study (Week 25)
Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)	9.5	6.7	7.1
Cutaneous Lupus Erythematosus Severity Index-Activity (CLASI-A)	6.0	3.6	3.6
Tender Joint Count (TJC)	12.5	5.9	6.0
Swollen Joint Count (SJC)	8.5	3.2	2.2
Physician Global Assessment (PhGA)	57.3	40.6	38.2
Patient Global Assessment (PtGA)	58.7	41.7	41.8
Patient Assessment of Pain (PtP)	59.8	45.7	42.4

* As of the data cutoff, no patients in Cohort 2c had reached 13 weeks of treatment.

Below is the table of safety reporting from the Phase 1 portion of the MISSION study. Step-up dosing to 60 mg of KZR-616 has improved overall tolerability, including the mitigation of early dose effects of nausea and vomiting. Most treatment emergent adverse events, or TEAEs, have been mild or moderate and were found to occur early and diminish with later doses. There have been no clinically significant laboratory adverse events. To date, no patients have discontinued treatment in Cohorts 2b and 2c, which utilize a lyophilized formulation of KZR-616 and step-up dosing to 60 mg. The most common TEAEs have been transient injection site reactions.

N (%) of patients	Cohort 2a (n=14)	Cohort 2b (n=6)	Cohort 2c* (n=6)	All Patients (Cohorts 1-2c) (n=39)
TEAEs	12 (85.7)	4 (66.7)	5 (83.3)	34 (87.2)
Injection Site Reactions	9 (64.3)	2 (33.3)	4 (66.7)	25 (64.1)
Nausea	5 (35.7)	1 (16.7)	2 (33.3)	14 (35.9)
Vomiting	4 (28.6)	1 (16.7)	1 (16.7)	12 (30.8)
TEAEs [3] Grade 3	2 (14.3)	1 (16.7)	0 (0.0)	4 (10.3)
Infectious TEAEs [3] Grade 3	1 (7.1)	1 (16.7)	0 (0.0)	2 (5.1)
Infectious TEAEs; All Grades	5 (37.5)	2 (33.3)	0 (0.0)	8 (20.5)
Serious TEAEs	2 (14.3)	1 (16.7)	0 (0.0)	4 (10.3)
Any Discontinuation	4 (28.6)	0 (0.0)	0 (0.0)	10 (25.6)

We caution that these data from the Phase 1b portion of the MISSION trial are preliminary, particularly with respect to the two lupus nephritis patients described above, and will require confirmation in additional patients as well as longer follow-up to draw any clinical conclusion. In addition, these preliminary data should not be viewed as an indication, belief or guarantee that other patients enrolled in the MISSION trial will achieve similar results or that the preliminary results from this patient will be maintained. For more information about the risks of preliminary clinical data, including the risk that the preliminary data from this single patient enrolled in the MISSION trial to date may not be maintained or replicated in that patient or in any other enrolled patients, see "Risk Factors—Risks Related to the Development and Commercialization of Our Product Candidates—*Interim top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data*" incorporated by reference in this prospectus supplement.

Protein Secretion and the Sec61 Translocon

We are conducting research and discovery efforts targeting protein secretion pathways as potential therapies for oncology and immuno-oncology indications. We believe that targeting this pathway has the potential to inhibit multiple therapeutically relevant targets with a single small molecule.

In mammalian cells, the secretion of proteins such as cytokines and the expression of cell surface transmembrane proteins such as cytokine receptors involve a process called cotranslational translocation. For nearly all secreted and transmembrane proteins (approximately 5,000 to 7,000 proteins), this process occurs via the Sec61 translocon, a highly conserved multi-subunit protein complex found in the membrane of the endoplasmic reticulum of all cells. Inhibition of the Sec61 translocon with small molecules blocks the secretion of some or all proteins, which can result in several physiologic outcomes, including altered cellular function, inhibition of cytokine release and/or cell death. Our scientists have been researching the protein secretion pathway and ways to therapeutically target this key aspect of cellular function for more than five years. We have developed several novel experimental platforms to study small molecule inhibitors of Sec61, which can result in several physiologic outcomes, including altered cellular function, inhibition of cytokine release and/or cell death. We believe this platform has the potential to yield small molecule alternatives to currently marketed biologic therapeutics to act as cytotoxic anti-cancer agents or to block the secretion of novel targets of interest in inflammation or immuno-oncology.

Our preclinical research on the Sec61 transolocon has demonstrated high degrees of potency against a large number of therapeutically relevant oncology and immuno-oncology targets that are Sec61 client proteins, translating into broad anti-tumor activity. Our discovery-stage Sec61 inhibitors have shown to induce anti-tumor activity against multiple hematologic tumor types without inducing cell death in normal cells or significant toxicity in animals. Genomic and proteomic analysis reveal a proteotoxic stress response as a potential biomarker for sensitivity across multiple tumor types, and we have observed synergy with proteasome inhibitors in multiple myeloma models.

KZR-261

KZR-261, a novel, first-in-class protein secretion inhibitor, is the first clinical candidate to be nominated from our research and discovery efforts targeting protein secretion pathways. KZR-261 is a broad-spectrum, anti-tumor agent that acts through direct interaction and inhibition of Sec61 activity. The compound was discovered at Kezar through a medicinal chemistry campaign in which several scaffolds were progressed through our proprietary workflow of protein secretion assays. As a result, we have established a unique and broad library of protein secretion inhibitors and a strong patent position around KZR-261 and its analogs. We have observed encouraging data with KZR-261 that exhibit its potential to be a new anti-cancer agent for the treatment of solid and hematologic malignancies. It has been shown to induce simultaneous inhibition of multiple, clinically relevant proteins including oncogenic drivers, angiogenic factors and immune checkpoints. The preclinical data generated with KZR-261 increases our confidence that inhibiting the Sec61 translocon may treat a variety of solid and hematologic tumor types. IND-enabling studies are currently underway, and we expect to file an IND application for the treatment of solid tumors in the first quarter of 2021.