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

FORM 10-K

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15 (d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2021

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission file number 0-20713

CASI PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	58-1959440
(State of Incorporation)	(I.R.S. Employer Identification No.)
9620 Medical Center Drive, Suite 300, Rockville, MD	20850
(Address of principal executive offices)	(Zip Code)

(240) 864-2600

Registrant's telephone number, including area code

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

Common Stock, $0.01 par value	Trading Symbol	NASDAQ
(Title of each class)	CASI	(Name of each exchange on which registered)

Securities registered pursuant to Section 12(g) of the Act: NONE

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15 (d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15 (d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer ☐	Accelerated filer ☐	Non-accelerated filer ☒	Smaller reporting company ☒
			Emerging growth company ☐

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

As of June 30, 2021, the aggregate market value of the shares of common stock held by non-affiliates was $179,150,437.

As of March 18, 2022, 136,589,826 shares of the Company's common stock were outstanding.

Documents Incorporated By Reference

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days of the end of the fiscal year ended December 31, 2021. The proxy statement is incorporated herein by reference into the following parts of the Form 10-K:

Part III, Item 10, Directors, Executive Officers and Corporate Governance;
Part III, Item 11, Executive Compensation;
Part III, Item 12, Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters;
Part III, Item 13, Certain Relationships and Related Transactions, and Director Independence; and
Part III, Item 14, Principal Accounting Fees and Services.

CASI PHARMACEUTICALS, INC.
FORM 10-K - FISCAL YEAR ENDED DECEMBER 31, 2021

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TRADEMARKS AND SERVICE MARKS

We own or have rights to trademarks and trademark applications for use in connection with the operation of our business, including, but not limited to, CASI and CASI PHARMACEUTICALS. All other trademarks appearing in this Annual Report on Form 10-K that are not identified as marks owned by CASI are the property of their respective owners.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements also may be included in other statements that we make. All statements that are not descriptions of historical facts are forward-looking statements. These statements can generally be identified by the use of forward-looking terminology such as "believes," "expects," "intends," "may," "will," "should," or "anticipates" or similar terminology. These forward-looking statements include, among others, statements regarding the timing of our commercial launch of products, clinical trials, our cash position and future expenses, and our future revenues.

Actual results could differ materially from those currently anticipated due to a number of factors, including: the risk that we may be unable to continue as a going concern as a result of our inability to raise sufficient capital for our operational needs; the possibility that we may be delisted from trading on The Nasdaq Capital Market if we fail to satisfy applicable continued listing standards, including compliance with the Nasdaq bid price rule; the volatility in the market price of our common stock; the outbreak of the COVID-19 pandemic and its effects on global markets and supply chains; the risk of substantial dilution of existing stockholders in future stock issuances; the difficulty of executing our business strategy on a global basis including China; our inability to enter into strategic partnerships for the development, commercialization, manufacturing and distribution of our proposed product candidates or future candidates; legal or regulatory developments in China that adversely affect our ability to operate in China, our lack of experience in manufacturing products and uncertainty about our resources and capabilities to do so on a clinical or commercial scale; risks relating to the commercialization, if any, of our products and proposed products (such as marketing, safety, regulatory, patent, product liability, supply, competition and other risks); our inability to predict when or if our product candidates will be approved for marketing by the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), National Medical Products Administration (NMPA), or other regulatory authorities; our inability to enter into strategic partnerships for the development, commercialization, manufacturing and distribution of our proposed product candidates or future candidates; the risks relating to the need for additional capital and the uncertainty of securing additional funding on favorable terms; the risks associated with our product candidates, and the risks associated with our other early-stage products under development; the risk that result in preclinical and clinical models are not necessarily indicative of clinical results; uncertainties relating to preclinical and clinical trials, including delays to the commencement of such trials; our ability to protect our intellectual property rights; our ability to design and implement a development plan for our ANDAs held by CASI Wuxi; the lack of success in the clinical development of any of our products; and our dependence on third parties; the risks related to our dependence on Juventas to conduct the clinical development of CNCT19 and to partner with us to co-market CNCT19; risks related to our dependence on Juventas to ensure the patent protection and prosecution for CNCT19; risks relating to the commercialization, if any, of our proposed products (such as marketing, safety, regulatory, patent, product liability, supply, competition and other risks); risks relating to interests of our largest stockholders and our Chairman and CEO that differ from our other stockholders; and risks related to the development of a new manufacturing facility by CASI Wuxi. Such factors, among others, could have a material adverse effect upon our business, results of operations and financial condition.

We caution investors that actual results or business conditions may differ materially from those projected or suggested in forward-looking statements as a result of various factors including, but not limited to, those described above and in Section IA, "Risk Factors" of this Annual Report on Form 10-K for the fiscal year ended December 31, 2021 (this "Annual Report") and our other filings with the Securities and Exchange Commission ("SEC"). We cannot assure you that we have identified all the factors that create uncertainties. Moreover, new risks emerge from time to time and it is not possible for our management to predict all risks, nor can we assess the impact of all risks on our business or the extent to which any risk, or combination of risks, may cause actual results to differ from those contained in any forward-looking statements. Readers should not place undue reliance on forward-looking statements, which only relate to events or information as of the date made. We undertake no obligation to publicly release the result of any revision of these forward-looking statements to reflect events or circumstances after the date they are made or to reflect the occurrence of unanticipated events. Additional information about the factors and risks that could affect our business, financial condition and results of operations, are contained in our filings with the U.S. Securities and Exchange Commission ("SEC"), which are available at www.sec.gov.

PART I

ITEM 1. BUSINESS.

CASI Pharmaceuticals, Inc. ("CASI" or the "Company", or "we" or "our") (Nasdaq: CASI) is a U.S. biopharmaceutical company focused on developing and commercializing innovative therapeutics and pharmaceutical products in China, the United States, and throughout the world. We were incorporated in 1991, and in 2012, with new leadership, we shifted our business strategy to China and has since built an infrastructure in China that includes sales and marketing, medical affairs, regulatory and clinical development and in the foreseeable future, manufacturing. We are focused on acquiring, developing and commercializing products that augment our hematology oncology therapeutic focus as well as other areas of unmet medical need. We are executing our plan to become a biopharmaceutical leader by launching medicines in the greater China market, leveraging our China-based regulatory, clinical and commercial competencies and our global drug development expertise. The majority of our operations are now located in China and are conducted primarily through two of our subsidiaries: (i) CASI Pharmaceuticals (China) Co., Ltd. ("CASI China"), which is wholly owned and is located in Beijing, China, and (ii) CASI Pharmaceuticals (Wuxi) Co., Ltd. ("CASI Wuxi"), which is located in Wuxi, China. Our Beijing office is primarily responsible for our day-to-day operations, and our commercial team of over 100 hematology/oncology sales and marketing specialists is based in China. CASI Wuxi is part of the long-term strategy to support our future clinical and commercial manufacturing needs, to manage our supply chain for certain products, and to develop a GMP manufacturing facility in China.

We launched our first commercial product, EVOMELA® (Melphalan for Injection) in China in August 2019. In China, EVOMELA® is approved for use as a conditioning treatment prior to stem cell transplantation and as a palliative treatment for patients with multiple myeloma. The other core hematology/oncology assets in our pipeline include:

- *CNCT19* is an autologous CD19 CAR-T investigative product ("CNCT19") being developed by our partner Juventas Cell Therapy Ltd. ("Juventas") for which we have exclusive World-Wide co-commercial and profit-sharing rights. CNCT19 is being developed as a potential treatment for patients with hematological malignancies which express CD19 including, B-cell acute lymphoblastic leukemia ("B-ALL") and B-cell non-Hodgkin lymphoma ("B-NHL"). The CNCT19 Phase 1 studies in patients with B-ALL and B-NHL in China have been completed by Juventas, the Phase 2 B-ALL and B-NHL registration studies are both currently enrolling in China since the fourth quarter of 2020.

- *BI-1206* is an antibody which has a novel mode-of-action, blocking the inhibitory antibody checkpoint receptor FcγRIIB to unlock anti-cancer immunity and enhance the efficacy of antibody-based immunotherapy in both hematological malignancies and solid tumors for which we have licensed exclusive greater China rights from BioInvent International AB ("BioInvent"). BI-1206 is being investigated by BioInvent in a Phase 1/2 trial, in combination with anti-PD1 therapy Keytruda® (pembrolizumab), in patients with solid tumors, and in a Phase 1/2a trial in combination with MabThera® (rituximab) in patients with relapsed/refractory non-Hodgkin lymphoma (NHL). BI-1206 has the potential to restore the activity of rituximab in patients with relapsed/refractory non-Hodgkin lymphoma. Clinical Trial Application (CTA) was approved by China National Medical Products Administration (NMPA) in December 2021. We are planning Phase 1 trials of BI-1206 as a single agent to evaluate the PK/safety profile and in combination with rituximab in patients with NHL (mantle cell lymphoma, marginal zone lymphoma, and follicular lymphoma) to assess safety and tolerability, select the Recommended Phase 2 Dose and assess early signs of clinical efficacy as part of our development program for BI-1206 in China. The studies are expected to start in the first half of 2022.

- *CB-5339* is a novel VCP/p97 inhibitor focused on valosin-containing protein (VCP)/p97 as a novel target in protein homeostasis, DNA damage response and other cellular stress pathways for therapeutic use in the treatment of patients with various malignancies. We entered into an exclusive license on March 21, 2021 with Cleave Therapeutics, Inc. ("Cleave") for the development and commercialization of CB-5339 in Mainland China, Hong Kong, Macau and Taiwan. CB-5339, an oral second-generation, small molecule VCP/p97 inhibitor, is being evaluated in a Phase 1 clinical trial in patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). CB-5339 CTA application for the multiple myeloma indication is in preparation after receiving an acceptance letter for the CB-5339 IND package from the China Center of Drug Evaluation ("CDE")

- *CID-103* is a full human IgG1 anti-CD38 monoclonal antibody recognizing a unique epitope that has demonstrated encouraging preclinical efficacy and safety profile compared to other anti-CD38 monoclonal antibodies for which we have exclusive global rights. CID-103 is being developed for the treatment of patients with multiple myeloma. The Phase 1

dose escalation and expansion study of CID-103, in patients with previously treated, relapsed or refractory multiple myeloma is ongoing in France and the UK.

We also have greater China rights to Octreotide (Long Acting Injectable), a standard of care for the treatment of acromegaly and for the control of symptoms associated with certain neuroendocrine tumors; and Thiotepa, a cytotoxic agent which has a long history of established use in the hematology/oncology setting, we have an exclusive China license and distribution rights to a novel formulation of thiotepa, which has multiple indications including use as a conditioning treatment for certain allogeneic haemopoietic stem cell transplants. However, due to the evolving standard of care environment, the rare and niche indication for these products, potential US regulatory action and our commitment to prioritize resources, we are currently evaluating our potential opportunities for these products. In addition, our assets include six FDA-approved ANDAs which we are evaluating due to generic drug pricing reforms by the Chinese government and its impact on the pricing and competitiveness of these products.

CASI has built a fully integrated, world class biopharmaceutical company dedicated to the successful development and commercialization of innovative and other therapeutic products. Our business development strategy is currently focused on acquiring additional targeted drugs and immuno-oncology therapeutics through licensing that will expand our hematology/oncology franchise. We use a market-oriented approach to identify pharmaceutical/biotechnology candidates that we believe to have the potential for gaining widespread market acceptance, either globally or in China, and for which development can be accelerated under our global drug development strategy. In many cases our business development strategy includes direct equity investments in the licensor company. We intend for our pipeline to reflect a diversified and risk-balanced set of assets that include (1) late-stage clinical drug candidates in-licensed for China or global regional rights, (2) proprietary or licensed innovative drug candidates, and (3) select high quality pharmaceuticals that fit our therapeutic focus. We have focused on US/EU approved product candidates, and product candidates with proven targets or product candidates that have reduced clinical risk with a greater emphasis on innovative therapeutics. Although oncology with a focus on hematological malignancies is our principal clinical and commercial target, we are opportunistic about other therapeutic areas that can address unmet medical needs. We will continue to pursue building a robust pipeline of drug candidates for development and commercialization in China as our primary market, and if rights are available for the rest of the world.

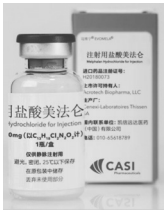
We believe our China operations offer a significant market and growth potential due to the extraordinary increase in demand for high quality medicines coupled with regulatory reforms in China that facilitate the entry of new pharmaceutical products into the country. We will continue to in-license clinical-stage and late-stage drug candidates, and leverage our cross-border operations and expertise, and hope to be the partner of choice to provide access to the China market. We expect the implementation of our plans will include leveraging our resources and expertise in both the U.S. and China so that we can maximize regulatory, development and clinical strategies in both countries.

Our commercial product, EVOMELA®, was originally licensed from Spectrum Pharmaceuticals, Inc. (“Spectrum”) and we had a supply agreement with Spectrum to support our application for import drug registration and for commercialization purposes. Spectrum completed the sale of its portfolio of FDA-approved hematology/oncology products including EVOMELA® to Acrotech Biopharma L.L.C. (“Acrotech”) on March 1, 2019. The original supply agreement with Spectrum was assumed by Acrotech; Spectrum agreed to continue with a short-term supply agreement for EVOMELA® for the initial commercial product supply in connection with the launch, with the long-term supply assumed by Acrotech.

As part of the long-term strategy to support its future clinical and commercial manufacturing needs and to manage its supply chain for certain products, on December 26, 2018, the Company, together with Wuxi Jintou Huicun Investment Enterprise, a limited partnership organized under Chinese law (“Wuxi LP”) established CASI Pharmaceuticals (WUXI) Co., Ltd. (“CASI Wuxi”) to build and operate a GMP manufacturing facility in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China.

CORE PRODUCT AND CANDIDATES IN HEMATOLOGY/ONCOLOGY

EVOMELA® (Melphalan for Injection) - Launched In China



EVOMELA® (Melphalan for Injection) is an intravenous formulation of melphalan commercialized by Acrotech (formally by Spectrum) in the multiple myeloma treatment setting in the United States, of which we have exclusive greater China rights. The EVOMELA® formulation avoids the use of propylene glycol, which is used as a co-solvent in other formulations of injectable melphalan. The use of Captisol in the EVOMELA® formulation improves the melphalan stability when reconstituted, allowing for longer preparation and infusion times. In August 2019, CASI launched EVOMELA® in China as its first commercial product. The NMPA required post-marketing study has completed and the clinical study report is being finalized for regulatory submission.

CNCT19 (CD19 CAR-T).

In June 2019, the Company acquired worldwide license and commercialization rights to CNCT19 from Juventas, a China-based domestic company engaged in cell therapy. Juventas continues to be responsible for the clinical development and regulatory submission and maintenance of CNCT19 regulatory applications and CASI is responsible for the launch and commercial activities of CNCT19 under the direction of a joint steering committee. Subsequently, the worldwide license and commercialization rights to CNCT19 acquired in June 2019 were amended.

CNCT19 is an autologous CD19 CAR-T investigative product (CNCT19) being developed by our partner Juventas for which we have co-commercial and profit-sharing rights. CNCT19 targets CD19, a B-cell surface protein widely expressed during all phases of B-cell development and a validated target for B-cell driven hematological malignancies. CD19 targeted CAR constructs from several different institutions have demonstrated consistently high antitumor efficacy in children and adults with relapsed B-cell acute lymphoblastic leukemia (B-ALL), chronic lymphocytic leukemia (CLL), and B-cell non-Hodgkin lymphoma (B-NHL).

CNCT19 is being developed as a potential treatment for patients with hematological malignancies which express CD19 including, B-cell acute lymphoblastic leukemia ("B-ALL") and B-cell non-Hodgkin lymphoma ("B-NHL"). The CNCT19 Phase 1 studies in patients with B-ALL and B-NHL in China have been completed by Juventas, with the Phase 2 B-NHL and B-ALL registration studies both currently enrolling in China since the fourth quarter of 2020.

BI-1206 (anti-FcγRIIB antibody)

BI-1206 is an antibody which has a novel mode-of-action, blocking the inhibitory antibody checkpoint receptor FcγRIIB to unlock anti-cancer immunity and enhance the efficacy of antibody-based immunotherapy in both hematological malignancies and solid tumors for which we have licensed exclusive greater China rights. BI-1206 was added to our portfolio in October 2020 pursuant to a license agreement with our partner, BioInvent International AB ("BioInvent"). BI-1206 is being investigated by BioInvent in a Phase 1/2 trial, in combination with anti-PD1 therapy Keytruda® (pembrolizumab), in patients with solid tumors, and in a Phase 1/2a trial in combination with MabThera® (rituximab) in patients with relapsed/refractory non-Hodgkin lymphoma (NHL). BI-1206 has the potential to restore the activity of rituximab in patients with relapsed/refractory non-Hodgkin lymphoma.

Clinical Trial Application (CTA) was approved by China National Medical Products Administration (NMPA) in December 2021. The Company is planning Phase 1 trials of BI-1206 as a single agent to evaluate the PK/safety profile and in combination with rituximab in patients with NHL (mantle cell lymphoma, marginal zone lymphoma, and follicular lymphoma) to assess safety and tolerability, select the Recommended Phase 2 Dose and assess early signs of clinical efficacy as part of its development program for BI-1206 in China. The studies are expected to start in the first half of 2022.

CB-5339 (VCP/p97inhibitor)

CB-5339 is a novel VCP/p97 inhibitor focused on valosin-containing protein (VCP)/p97 as a novel target in protein homeostasis, DNA damage response and other cellular stress pathways for therapeutic use in the treatment of patients with cancer. The Company entered into an exclusive license on March 21, 2021 with Cleave Therapeutics, Inc. (Cleave") for the development and commercialization of CB-5339 in Mainland China, Hong Kong, Macau and Taiwan. CB-5339, an oral second-generation, small molecule VCP/p97 inhibitor, is being evaluated in a Phase 1 clinical trial in patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). CB-5339 CTA application for the multiple myeloma indication is in preparation after receiving an acceptance letter for the CB-5339 IND package from the China CDE.

CID 103 (anti-CD38 monoclonal antibody)

CID-103 is a full human IgG1 anti-CD38 monoclonal antibody recognizing a unique epitope that has demonstrated encouraging preclinical efficacy and safety profile compared to other anti-CD38 monoclonal antibodies for which the Company has exclusive global rights. CID-103 is being developed for the treatment of patients with multiple myeloma. The Phase 1 dose escalation and expansion study of CID-103, in patients with previously treated, relapsed or refractory multiple myeloma is ongoing in the UK and France.

OTHER MISCELLANEOUS ASSETS

The Company also has greater China rights to Octreotide LAI, a standard of care for the treatment of acromegaly and for the control of symptoms associated with certain neuroendocrine tumors, and Thiotepa, a cytotoxic agent which has a long history of established use in the hematology/oncology setting, the Company has an exclusive China license and distribution rights to a novel formulation of thiotepa, which has multiple indications including use as a conditioning treatment for certain allogeneic haemopoietic stem cell transplants. However, due to the evolving standard of care environment, the rare and niche indication for these products, potential US regulatory action and the Company's commitment to prioritize resources, the Company is currently evaluating its options for these products. In addition, the Company's assets include six FDA-approved ANDAs which the Company is evaluating due to generic drug pricing reforms by the Chinese government and its impact on the pricing and competitiveness of these products.

BUSINESS DEVELOPMENT

CASI has built a fully integrated, world class biopharmaceutical company dedicated to the successful development and commercialization of innovative and other therapeutic products.

Our business development strategy is currently focused on acquiring additional targeted drugs and immuno-oncology therapeutics through licensing that will expand our hematology/oncology franchise. We use a market-oriented approach to identify pharmaceutical/biotechnology candidates that we believe to have the potential for gaining widespread market acceptance, either globally or in China, and for which development can be accelerated under our global drug development strategy. In many cases our business development strategy includes direct equity investments in the licensor company. We intend for our pipeline to reflect a diversified and risk-balanced set of assets that include (1) late-stage clinical drug candidates in-licensed for China or global regional rights, (2) proprietary or licensed innovative drug candidates, and (3) select high quality pharmaceuticals that fit our therapeutic focus. We have focused on US/EU approved product candidates, and product candidates with proven targets or product candidates that have reduced clinical risk with a greater emphasis on innovative therapeutics. Although oncology with a focus on hematological malignancies is our principal clinical and commercial target, we are opportunistic about other therapeutic areas that can address unmet medical needs. We will continue to pursue building a robust pipeline of drug candidates for development and commercialization in China as our primary market, and, if rights are available, for the rest of the world.

CASI PHARMACEUTICALS (CHINA) CO., LTD. ("CASI China")

In August 2012, we established a wholly-owned China-based subsidiary CASI Pharmaceuticals (China) Co., Ltd.. ("CASI China"). CASI China is headquartered in Beijing, and in 2020, we established an office in Shanghai. CASI China's staff currently consists of 168 full-time employees which includes our commercial team of over 100 hematology and oncology sales and marketing specialists based in China. Among its activities, our China operations oversee the Company's sales and marketing of EVOMELA® and the anticipated commercial activities of our pipeline products, technology transfer, local preclinical and clinical operation activities, as well as its NMPA regulatory activities. In addition, our Beijing operations include business development activities and executive management activities. Global management decisions are primarily being made out of CASI China where our executive team spends a significant amount of time. We expect our operations in China to continue to grow.

CASI PHARMACEUTICALS (WUXI) CO., LTD. ("CASI Wuxi")

On December 26, 2018, the Company, together with Wuxi LP established CASI Wuxi to build and operate a GMP manufacturing facility in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China. The Company controls CASI Wuxi through 80% voting and ownership rights. Accordingly, the financial statements of CASI Wuxi have been consolidated in the Company's consolidated financial statements since its inception.

In November 2019, CASI Wuxi entered into a fifty-year lease agreement for the right to use state-owned land in China for the construction of a GMP manufacturing facility. Pursuant to the agreement, CASI Wuxi has committed to invest land use right and

property, plant and equipment of RMB1 billion (equivalent to $143 million) by August 2022. In April 2020, CASI Wuxi received RMB 15.9 million (equivalent to $2.2 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as government grant for this development project which was recorded as deferred income in April 2020. In November 2021, CASI Wuxi received an additional RMB 3.0 million (equivalent to $0.5 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as a government grant for this development project which was recorded as deferred income in November 2021.

In 2020, for the design and construction work of the land, CASI Wuxi entered into several contracts for RMB 76.1 million ($12.0 million) to complete the phase 1 project of CASI Wuxi's research and development production base, the project was the estimated to be completed in October 2023. In February 2022, CASI Wuxi has reached an alignment with the Wuxi local government that it will collaborate with Wuxi LP to co-develop the land continuously in the future, and the development plan will be extended, details regarding the plan are under negotiation.

Also in 2020, CASI Wuxi entered in to a lease agreement with local government for a manufactory building next to the leased land. Since then, the Company entered into a series of contracts for the remodeling and installation work of the building and warehouse, as well as purchase of equipments. The total contract amount entered into for this building is approximately RMB 92.9 million ($14.6 million).

RELATIONSHIPS RELATING TO PROGRAMS

EVOMELA® (Melphalan Hydrochloride For Injection)

The Company has product rights and perpetual exclusive licenses from Acrotech Biopharma L.L.C. (“Acrotech”) to develop and commercialize its commercial product EVOMELA® (Melphalan Hydrochloride For Injection) in the greater China region (which includes Mainland China, Taiwan, Hong Kong and Macau). The exclusive licenses held by the Company were originally licensed from Spectrum Pharmaceuticals, and Spectrum completed the sale of its portfolio of FDA-approved hematology/oncology products including EVOMELA® to Acrotech on March 1, 2019. On December 3, 2018, the Company received NMPA’s approval for importation, marketing and sales in China and in August 2019 the Company launched EVOMELA® in China. The NMPA required post-marketing study has completed and the clinical study report is being finalized for regulatory submission.

The Company has established relationships, coupled with supply agreements, to secure the necessary resources to supply the EVOMELA® commercial drug product as well as any clinical trials materials required for our clinical development program. As an import drug product into China, we expect that the future supply of EVOMELA® will continue to be met by our partner Acrotech and its contract manufacturers.

In March 2019, the Company entered into a three-year exclusive distribution agreement with China Resources Pharmaceutical Commercial Group International Trading Co., Ltd. (“CRPCGIT”) to appoint CRPCGIT on an exclusive basis as its distributor to distribute EVOMELA® in the territory of the People’s Republic of China (excluding Hong Kong, Taiwan and Macau), subject to certain terms and conditions. The Company’s internal marketing and sales team are responsible for commercial activities, including, for example, direct interaction with Key Opinion Leaders (KOL), physicians, hospital centers and the generation of sales. The agreement was renewed in March 2022 for another two years.

CNCT19 (CAR-T CD19)

In June 2019, the Company entered into a license agreement for exclusive worldwide license to commercialize an autologous anti-CD19 T-cell therapy product (CNCT19) from Juventas (the “Juventas license agreement”). Juventas is a privated China-based company engaged in cell therapy. Upon completion of the financing, our investment in Juventas represented a 16.327% equity interest on a fully diluted basis.

In September 2020, Juventas and its shareholders (including CASI Biopharmaceuticals (WUXI) Co., Ltd. ("CASI Biopharmaceuticals”), a majority indirectly-owned subsidiary of us) agreed to certain terms and conditions required by a new third-party investor to facilitate the Series B financing of Juventas, pursuant to which the Company agreed to amend and supplement the original licensing agreement (the "Supplementary Agreement") by agreeing to pay Juventas certain percentage of net profits generated from commercial sales of CNCT19 in addition to the royalty fee payment calculated as a percentage of net sales. The Supplementary Agreement also specifies a minimum annual target net profit to be distributed to Juventas and certain other terms and obligations. In return, the Company obtained additional equity interests in Juventas.

Under the Supplementary Agreement, Juventas and the Company will jointly market CNCT19, including, but not limited to, establishing medical teams, developing medical strategies, conducting post-marketing clinical studies, establishing Standardized Cell Therapy Centers, establishing and training providers with respect to cell therapy, testing for cell therapy, and monitoring quality controls (cell collection and transfusion, etc.), and patient management (adverse reactions treatment, patients' follow-up visits, and establishment of a database). The Company also will reimburse Juventas for a portion of Juventas' marketing expenses as reviewed and approved by a joint commercial committee to be constituted. The Company will continue to be responsible for recruiting and establishing a sales team to commercialize CNCT19.

On October 26, 2021, Juventas completed its Series C financing. Upon the completion of Juventas Series C financing, the Company's equity ownership in Juventas decreased to 12.01% on a fully diluted basis, with the total fair value of the equity interest amounted to RMB 206 million ($32.3 million).

BI-1206 (anti-FcyRIIB antibody)

In October 2020, the Company entered into an exclusive licensing agreement with BioInvent International AB ("BioInvent") for the development and commercialization of novel anti-FcγRIIB antibody, BI-1206, in mainland China, Taiwan, Hong Kong and Macau. BioInvent is a biotechnology company focused on the discovery and development of first-in-class immune-modulatory antibodies for cancer immunotherapy. BI-1206 is being investigated in a Phase 1/2 trial, in combination with anti-PD1 therapy Keytruda® (pembrolizumab), in patients with solid tumors, and in a Phase 1/2a trial in combination with MabThera® (rituximab) in patients with relapsed/refractory non-Hodgkin lymphoma (NHL). Clinical Trial Application (CTA) was approved by NMPA in December 2021. The Company is planning Phase 1 trials of BI-1206 as a single agent to evaluate the PK/safety profile and in combination with rituximab in patients with NHL (mantle cell lymphoma, marginal zone lymphoma, and follicular lymphoma) to assess safety and tolerability, select the Recommended Phase 2 Dose and assess potential evidence of clinical efficacy as part of its development program for BI-1206 in China. The studies are expected to start in the first half of 2022.

Under the terms of the agreement, BioInvent and CASI will develop BI-1206 in both hematological malignancies and solid tumors, with CASI responsible for commercialization in China and associated markets. CASI made a $5.9 million upfront payment in November 2020 to BioInvent and will pay up to $83 million in development and commercial milestone payments plus tiered royalties in the high-single to mid-double-digit range on net sales of BI-1206.

In conjunction with its license agreement entered into with BioInvent, CASI made a SEK 53.8 million investment (equivalent to $6.3 million) in 1.2 million new shares of BioInvent, and 14,700,000 new warrants, each warrant with a right to subscribe for 0.04 new shares in BioInvent within a period of five years and at a subscription price of SEK 78.50 per share.

As an import drug product into China, we expect that future supply of BI-1206 will be met by our partner BioInvent and its contract manufacturers. For local development in China, we expect that our clinical materials and commercial inventory will be supplied by one or more contract manufacturers.

CB-5339 (VCP/p97inhibitor)

In March 2021, the Company entered into an exclusive license with Cleave Therapeutics, Inc. ("Cleave") for the development and commercialization of CB-5339, an oral novel VCP/p97 inhibitor, in both hematological malignancies and solid tumors, in Mainland China, Hong Kong, Macau and Taiwan. Cleave is a clinical-stage biopharmaceutical company focused on valosin-containing protein (VCP)/p97 as a novel target in protein homeostasis, DNA damage response and other cellular stress pathways for therapeutic use in the treatment of patients with cancer.

CB-5339 is being evaluated by Cleave in a Phase 1 clinical trial in patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). Under the terms of the agreement, CASI is responsible for development and commercialization in China and associated markets. Cleave received a $5.5 million upfront payment and is eligible to receive up to $74 million in development and commercial milestone payments plus tiered royalties in the high-single to mid-double-digit range on net sales of CB-5339. In conjunction with the license agreement, CASI made a $5.5 million investment in Cleave through a convertible note.

As an import drug product into China, we expect that future supply of CB-5339 will be met by our partner Cleave and its contract manufacturers. For local development in China, we expect that our clinical materials and commercial inventory will be supplied by one or more contract manufacturers.

CID-103 (anti-CD38 Monoclonal Antibody)

In April 2019, the Company entered into a license agreement with a newly established, privately held UK Company Black Belt Therapeutics Limited ("Black Belt") for exclusive worldwide rights to CID-103, an investigational anti-CD38 monoclonal antibody (Mab) (formerly known as TSK011010). In conjunction with the license agreement, CASI invested 2 million euros in Black Belt.

The Company expects that its clinical materials and commercial inventory will be supplied by one or more contract manufacturers with whom the Company has contracted with. Under the terms of the agreement, CASI obtained global rights to CID-103 for an upfront payment of 5 million euros ($5.7 million) as well as certain milestone and royalty payments. In June 2021, the Company achieved the First-Patient-In (FPI) in the Phase 1 dose escalation and expansion study of CID-103, and made $750,000 milestone payment in June 2021 and €250,000 ($305,000) payment in August 2021 under the terms of the agreement.

Thiotepa

In August 2019, the Company entered into an Exclusive License and Distribution Agreement with Riemser Pharma GmbH ("Riemser"), pursuant to which we obtained exclusive distribution rights for Thiotepa in China. Under the agreement, Riemser will be responsible for manufacturing and supplying CASI with clinical trials materials and commercial drug product, and costs of clinical trials (if any) for the registration, product launch and commercialization of Thiotepa in China. In January 2020, Riemser was acquired by Esteve Healthcare, S.L. ("ESTEVE"), an international pharmaceutical company headquartered in Barcelona.

Octreotide LAI

In October 2019, the Company entered into an exclusive distribution agreement with Pharmathen Global BV ("Pharmathen") for the development and distribution of Octreotide LAI microsphere in China. Octreotide LAI formulations, which are approved in various European countries, are considered a standard of care for the treatment of acromegaly and the control of symptoms associated with certain neuroendocrine tumors. Octreotide LAI's ANDA review is pending due to CDE's sterilization requirement is different from European standard. CASI is now working with licensor Pharmathen to improve the sterilization process in order to meeting CDE's requirement.

The terms of the agreement include an upfront payment of 1 million euros which was paid by the Company in 2019, and up to 2 million euros of additional milestone payments, of which 1.5 million euros ($1.7 million) was expensed in the year ended December 31, 2020 as acquired in-process research and development following Pharmathen's achievement of certain milestones. CASI is responsible for the development, import drug registration, product approval and commercialization in China. CASI has a 10-year non-royalty exclusive distribution period after the product launch at agreed supply costs for the first three years.

INTELLECTUAL PROPERTY

We generally seek patent protection for our technology and product candidates in the United States, Canada, China and other key markets. The patent position of biopharmaceutical companies generally is highly uncertain and involves complex legal and factual questions. Our success will depend, in part, on whether we can: (i) obtain patents to protect our own products; (ii) obtain licenses to use the technologies of third parties, which may be protected by patents; (iii) protect our trade secrets and know-how; and (iv) operate without infringing the intellectual property and proprietary rights of others.

With regards to our commercial drug EVOMELA® licensed for greater China rights from our partner, we have acquired exclusive licenses to intellectual property to enable us to develop and continue to commercialize EVOMELA® in China.

With regards to CNCT19, we have acquired an exclusive license to intellectual property from our partner Juventas to enable us to co-commercialize CNCT19 in China and well as the rest of the world. Juventas is responsible for prosecuting and maintaining the licensed intellectual property.

With regards to BI-1206, we have acquired an exclusive license to intellectual property and the know-how from our partner BioInvent to enable us to develop and commercialize BI-1206 in our greater China commercial markets. BioInvent is responsible for prosecuting and maintaining the licensed BioInvent intellectual property.

With regards to CB-5339, we have acquired an exclusive license to intellectual property and the know-how from our partner Cleave to enable us to develop and commercialize CB-5339 in our greater China commercial markets. Cleave is responsible for prosecuting and maintaining the licensed Cleave intellectual property.

With regards to our in-licensed anti-CD38 antibody candidate CID-103, we have acquired an exclusive worldwide license to patents around CID-103 and other anti-CD38 antibodies, covering multiple pending applications worldwide, directed to the antibodies themselves and treatment methods using the antibodies. We have since filed additional applications, with current pending applications including U.S., Australia, Canada, China, Europe, India, Japan, Korea, New Zealand, Singapore and Hong Kong. We intend to further expand our patent portfolio and in the submission stage of additional applications. The patent term for any patents granted from the earliest of these pending applications will expire in June 2038, assuming all annuities are paid and not considering any term extensions for regulatory approval that might be available.

With regards to our drug candidates Thiotepa and Octreotide LAI, we have acquired exclusive licenses to intellectual property and/or the know-how to enable us to develop and commercialize the drug candidates in the China market.

The Company holds certain intellectual property in connection with a proprietary aurora kinase inhibitor that we no longer devote resources to. Our intellectual property for this asset remains available for business development partnering.

We currently own a number of registered trademarks and pending trademark applications for CASI, including our corporate logo and product name in the United States, China and other jurisdictions, and we are seeking further trademark protection for CASI, including our corporate logo, product name, and other marks in jurisdictions where available and appropriate.

We review and assess our portfolio on a regular basis to secure protection and to align our intellectual property strategy with our overall business strategy.

GOVERNMENT REGULATION

U.S. Food and Drug Administration (FDA)

Our research, development, testing, manufacture, labeling, sale, marketing, advertising, and distribution of therapeutics in the United States, China and other countries are subject to extensive regulations by federal, state, local and foreign governmental authorities.

In the United States, the FDA regulates the development and commercialization of drugs and biologics. Drugs are subject to regulation under the Federal Food, Drug, and Cosmetic Act (FFDCA), and biological products, in addition to being subject to certain provisions of the FFDCA, are regulated under the Public Health Service Act (PHSA). We believe that the FDA will regulate the products currently being developed by us or our collaborators as drugs or biologics. Both the FFDCA and PHSA and corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, storage, recordkeeping, advertising and other promotion of biologics and drugs, as the case may be.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our product candidates or any future product candidates we may develop. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

Preparing drug and biologic candidates for regulatory approval is a costly and time-consuming process. Generally, a developer first must conduct preclinical studies in the laboratory and in animal model systems in accordance with applicable FDA requirements, including Good Laboratory Practice regulations, to gain preliminary information on an agent's effectiveness and to identify any safety problems. The results of these studies, together with manufacturing information and analytical data as well as protocols and detailed descriptions for proposed clinical investigations, are submitted to FDA as a part of an Investigational New Drug Application (IND) for a drug or biologic, which must become effective before human clinical trials of an investigational drug can begin. An IND application will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues, such as the conduct of the clinical trials as outlined in the IND application, and places the clinical trial(s) on a clinical hold. In such a case, the IND application sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be certain that submission of an IND application will result in the FDA allowing clinical trials to begin.

We or our collaborators must then conduct adequate and well-controlled clinical trials, in accordance with applicable IND regulations, Good Clinical Practices ("GCPs"), and other clinical-trial related regulations, to establish the safety and efficacy of the candidate for each proposed indication We or our collaborators will be required to select qualified investigators (usually physicians within medical institutions) to supervise the administration of the products, test or otherwise assess patient results, and collect and maintain patient data; monitor the investigations to ensure that they are conducted in accordance with applicable requirements, including the requirements set forth in the general investigational plan and protocols contained in the IND; and comply with applicable reporting and recordkeeping requirements. The study protocol and informed consent information for study subjects in clinical trials must also be approved by an institutional review board ("IRB") for each institution where the trials will be conducted before the trial can begin, and each IRB must monitor the study until completion. Study subjects must provide informed consent and sign an informed consent form before participating in a clinical trial.

Clinical trials of drugs or biologics are normally done in three phases, although the phases may overlap or be combined. Phase 1 trials usually involve the initial introduction of the investigational candidate into humans to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness. Phase 2 trials normally involve trials in a limited patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the candidate for specific target indications. Phase 3 trials are expanded clinical trials with larger numbers of patients which are intended to evaluate the overall benefit-risk relationship of the drug and to gather additional information for proper dosage and labeling of the drug. Phase 3 clinical trials may take several years to complete. Annual progress reports detailing the results of the clinical studies must be submitted to the FDA and IND safety reports must be submitted to the FDA and investigators within 15 calendar days for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. We or our collaborators, the FDA, or an IRB (with respect to a particular study site) may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after receiving initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of the product or, in certain circumstances, post-approval.

The FDA has various programs, including fast track designation, breakthrough therapy designation, priority review, accelerated approval, and, for regenerative medicine therapies, regenerative medicine advanced therapy designation, which are intended to expedite or simplify the process for the development, and FDA's review, of drugs and biologics (e.g., granting approval on the basis of surrogate endpoints subject to post-approval trials). Generally, drugs or biologics that may be eligible for one or more of these programs are those intended to treat serious or life-threatening diseases or conditions, those with the potential to address unmet medical needs for those disease or conditions, and/or those that provide a meaningful benefit over existing treatments. Moreover, if a sponsor submits a marketing application for a product intended to treat certain rare pediatric or tropical diseases or for use as a medical countermeasure for a material threat, and that meets other eligibility criteria, upon approval such sponsor may be granted a priority review voucher that can be used for a subsequent application. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, these programs do not change the standards for approval and may not ultimately expedite the development or approval process.

If clinical trials of a product candidate are completed successfully, the sponsor of the product may seek FDA marketing approval. If the product is classified as a new drug, an applicant must file a New Drug Application (NDA). For biological products, an applicant must file a Biologics License Application (BLA). In each case, FDA must approve the application before the product can be marketed commercially. NDAs and BLAs must include, among other things, detailed information about the product's chemistry, manufacture, controls, and proposed labeling and the results of preclinical studies and clinical trials. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of a drug, and safety, purity, and potency of a biologic, to the satisfaction of the FDA. A user fee must be paid with the submission of an NDA or BLA (unless a fee waiver applies) in order to support the cost of agency review, which is currently almost $3 million. FDA usually will inspect the facility or the facilities at which the drug is manufactured and will not approve the product unless the manufacturing and production and testing facilities are in compliance with current Good Manufacturing Practice (cGMP) regulations. In addition, FDA may also inspect clinical trial sites that generated data for the NDA or BLA as well as us or our collaborators as a clinical trial sponsor.

The testing and approval processes require substantial time and effort, and there can be no assurance that FDA will accept the application for filing or that any approval will be obtained on a timely basis, if at all. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, the FDA has ten months from the 60 day filing date in which to complete its initial review of a standard application and respond to the applicant. However, the time required by the FDA to review and approve NDAs and BLAs is variable and, to a large extent, beyond our control. Notwithstanding the submission of relevant data, the FDA may ultimately decide that an NDA or BLA does not satisfy its regulatory criteria and deny the approval. In such instance, FDA will issue a Complete Response Letter, describing all the deficiencies that the FDA has identified in an application that must be satisfactorily addressed before it can be approved. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Further, even if such additional information is submitted, the FDA may ultimately decide that the application does not satisfy the criteria for approval. The FDA may also refer the application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee, but the Agency historically has tended to follow such recommendations. In addition, the FDA may condition marketing approval on the conduct of specific post-marketing studies to further evaluate safety and effectiveness or a Risk Evaluation and Mitigation Strategy (REMS) that may include both special labeling and controls, known as Elements to Assure Safe Use, on the distribution, prescribing, dispensing and use of a drug product. After approval is obtained, a marketed product is subject to continuing regulatory requirements and review relating to cGMP, adverse event reporting, promotion and advertising, and other matters. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Products may be promoted only for the approved indications and consistent with the provisions of the approved label. Discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product, mandated labeling changes, or withdrawal of the product from the market, as well as possible civil or criminal sanctions.

Drugs and biological products may be eligible to receive certain regulatory exclusivities upon approval. For example, a drug that constitutes a new chemical entity (i.e., an active moiety that has not been previously approved in another NDA) is entitled to five years of exclusivity during which FDA may not accept an ANDA or 505(b)(2) NDA for filing referencing such chemical entity, unless a "Paragraph IV certification" is made in which case FDA may accept such applications four years after initial approval of the new chemical entity. In addition, three years of exclusivity can be awarded for applications (including supplements) containing the results of new clinical investigations (other than bioavailability studies) conducted by the applicant and essential to the FDA's approval of new versions or conditions of use of previously approved drug products, such as new indications, delivery mechanisms, dosage forms, strengths, or other conditions of use. A reference biological product is granted twelve years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. Moreover, a drug or biologic may receive orphan drug designation if intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product in the United States. If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which restricts FDA from approving any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety, by providing a major contribution to patient care, or in instances of an inability to assure drug supply.

FDA may approve generic drugs and biological products through abbreviated pathways. Generic drugs may be marketed upon approval of an ANDA, which contains information to show that the proposed product is identical in active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics, and intended use, among other things, to a previously approved drug. Approval is generally supported by data from bioequivalence studies, rather than complete preclinical and clinical studies. Biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product are eligible for an abbreviated approval pathway. Although licensure of biosimilar or interchangeable products is generally expected to require less than the full complement of product-specific preclinical and clinical data required for reference products, the FDA has considerable discretion over the kind and amount of scientific evidence required to demonstrate biosimilarity and interchangeability. Under section 610 of the Further Consolidated Appropriations Act, 2020, entitled "Actions for Delays of Generic Drugs and Biological Products", generic drug and biosimilar developers may sue brand manufacturers, or generic or biosimilar manufacturers, to obtain sufficient quantities of reference product necessary for approval of the developers' generic or biosimilar product. If a generic drug or biosimilar developer is successful in its suit, the defendant manufacturer would be required to provide sufficient quantities of product on commercially-reasonable, market-based terms and may be required to pay the developer's reasonable attorney's fees and costs as well as financial compensation under certain circumstances. While intended to facilitate the timely entry of lower-cost generic and biosimilar products,

we cannot determine what effect this new private right of action may have on the development and approval of generic drug and biosimilar products at this time.

The Generic Drug Enforcement Act of 1992 establishes penalties for wrongdoing in connection with the development or submission of an application. In general, the FDA is authorized to temporarily or permanently bar companies and individuals, from submitting or assisting in the submission of applications to FDA, and to temporarily deny approval and suspend applications to market drugs under certain circumstances. FDA's debarment authority has also been expanded to apply to certain import-related offenses. In addition to debarment, the FDA has numerous enforcement and disciplinary powers, including the authority to withdraw approval of an application or to approve an application under certain circumstances, to suspend the distribution of all drugs approved or developed in connection with certain wrongful conduct, and various civil and criminal penalties. The FDA may also withdraw product approval or take other corrective measures if, among other things, ongoing regulatory requirements are not met or if safety or efficacy questions are raised after the product reaches the market.

Manufacturers and other entities involved in the manufacturing and distribution of approved products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the product. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory requirements, and test each product batch or lot prior to its release. We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates and any future product candidates we may develop. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution or may require substantial resources to correct.

Healthcare Regulation

Federal and state healthcare laws in the United States, including fraud and abuse and health information privacy and security laws, also apply to our business. If we fail to comply with those laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected. The laws that may affect our ability to operate include, but are not limited to: the federal Anti-Kickback Statute, which prohibits, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs; and federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent. Additionally, we are subject to state law equivalents of each of the above federal laws, which may be broader in scope and apply regardless of whether the payer is a federal healthcare program, and many of which differ from each other in significant ways and may not have the same effect, further complicate compliance efforts.

Numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who are expected to prescribe our products and from whom we obtain patient health information, are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology and Clinical Health Act (HIPAA). Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we obtain and/or disclose individually identifiable health information from a HIPAA-covered entity, including healthcare providers, in a manner that is not authorized or permitted by HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business.

In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act (PPACA), created a federal requirement under the federal Open Payments program, that requires certain manufacturers to track and report to the Centers for Medicare and Medicaid Services, or CMS, annually certain payments and other transfers of value provided to physicians and teaching hospitals made in the previous calendar year. In addition, there are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and federal authorities.

For those marketed products which are covered in the United States by certain government healthcare programs (e.g., Medicare and Medicaid), we have various obligations, including government price reporting and rebate requirements, which generally require products be offered at substantial rebates/discounts to Medicaid and certain purchasers (including "covered entities" purchasing under the 340B Drug Discount Program). We are also required to discount such products to authorized users of the Federal Supply Schedule of the General Services Administration, under which additional laws and requirements apply. These programs require submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations, and the guidance governing such calculations is not always clear. Compliance with such requirements can require significant investment in personnel, systems and resources, but failure to properly calculate prices, or offer required discounts or rebates could subject us to substantial penalties.

National Medical Products Administration (NMPA, formerly the China Food and Drug Administration)

In the PRC, the NMPA is the authority under the State Administration for Market Regulation (SAMR) that monitors and supervises the administration of pharmaceuticals products, medical appliances and equipment, and cosmetics. We are also subject to regulation and oversight by different levels of the Medical Products Administration and Administration of Market Regulation in China. For clinical-stage product candidates, our development activities in China can follow two purposes: (1) to obtain clinical data to support our global FDA-regulated trials as is the case for our proprietary ENMD 2076, and (2) to obtain clinical data to support local registration with the NMPA. For late-stage product candidates that we in-license for greater China rights, such as EVOMELA®, which has been launched, CID-103, BI-1206 and CB-5339, our development activities in China are to secure clinical trial notification, and marketing approval from the Center of Drug Evaluation (CDE) under the NMPA by conducting import drug registration. The "Law of the PRC on the Administration of Pharmaceuticals," as last amended on August 26, 2019 and effective as of December 1, 2019, provides the basic legal framework for the administration of the production and sale of pharmaceuticals in China and covers the manufacturing, distributing, packaging, pricing and advertising of pharmaceutical products in China.

We are also subject to other PRC laws and regulations that are applicable to pharmaceutical manufacturers and distributors in general such as "Drug Registration Regulation (DRR)", which was updated on January 22, 2020 and became effective on July 1, 2020.

The Marketing Authorization Holder System.

Pursuant to the amended Law of the PRC on the Administration of Pharmaceuticals, the Marketing Authorization Holder System, previously implemented in a few pilot regions in China, is now implemented nationwide. Companies and research and development institutions can be drug marketing authorization holders after they receive drug approvals. The drug marketing authorization holder are responsible for their products throughout the life cycle, including nonclinical studies, clinical trials, production and distribution, post-market studies, and the monitoring, reporting, and handling of adverse reactions in connection with pharmaceuticals in accordance with the amended law.

The marketing authorization holders may engage contract manufacturers for manufacturing, provided that the contract manufacturers are licensed pharmaceutical manufacturers, and may engage pharmaceutical distribution enterprises with a valid drug distribution license to sell their products. Upon receiving the marketing authorizations from the NMPA, a drug marketing authorization holder may transfer its drug marketing authorization and the transferee should have the capability of quality management, risk prevention and control, and liability compensation to ensure the safety, effectiveness and quality controllability of drugs, and fulfill the obligations of the drug marketing authorization holder.

Product Manufacturing

For the registration of locally manufactured drugs, the drug products need to be manufactured in China through either a self-owned facility or a contract manufacturing organization. The study drug to be used for clinical trials must be manufactured in compliance with NMPA Good Manufacturing Practice (GMP) guidelines. A domestic manufacturer of pharmaceutical products and active pharmaceutical ingredient (API) must obtain the drug manufacturing license to produce pharmaceutical products and API for marketing in China. Pursuant to the newly amended Law of the PRC on the Administration of Pharmaceuticals, the GMP certification has been cancelled, but with its cancellation, drug manufacturing enterprises are still required to strictly comply with GMP requirements. GMP requirements include institution and staff qualifications, production premises and facilities, equipment, raw materials, hygiene conditions, production management, quality controls, product distributions, maintenance of records and manner of handling customer complaints and adverse reaction reports. The drug manufacturing license is valid for five years, and must be renewed at least six months before its expiration date.

In addition, before commencing business, a pharmaceutical manufacturer must also obtain a business license from the Administration of Market Regulation at the local level.

Preclinical Research and Clinical Trials.

For an investigational new drug application, a clinical trial approval issued from CDE was historically required to conduct clinical trials. However, since July 24, 2018, the NMPA announced to adopt a negative notification system for clinical trial approvals. In particular, if the applicant does not receive negative comments within 60 days after the CDE accepts the clinical trial application, the applicant can proceed with the clinical trial immediately based on the protocol submitted without waiting to receive an explicit clinical trial approval. Chemical generics, on the other hand, only need to undergo bioequivalent studies upon a filing for record with the NMPA. In order to apply for a clinical trial application approval to support local registration in China, a pharmaceutical company is required to conduct a series of preclinical research including research on chemistry, pharmacology, toxicology and pharmacokinetics of pharmaceuticals. This preclinical research should be conducted in compliance with the relevant regulatory guidelines issued by the NMPA. In particular, safety evaluation research must be conducted in compliance with China's Good Laboratory Practice.

After completion of preclinical studies and obtaining permission to conduct the clinical trial from the NMPA, clinical trials are generally conducted in three sequential phases that may overlap or be combined, known as Phase 1, Phase 2, and Phase 3 clinical trials, and Phase 4 clinical trials may be conducted at the post-marketing surveillance stage, in compliance with China's Good Clinical Practice (GCP):

Phase 1 – preliminary trial of clinical pharmacology and human safety evaluation studies. The primary objective is to observe the pharmacokinetics and the tolerance level of the human body to the new medicine as a basis for ascertaining the appropriate methods of dosage.

Phase 2 – preliminary exploration on the therapeutic efficacy. The purpose is to assess preliminarily the efficacy and safety of pharmaceutical products on patients with the target indication of the pharmaceutical products and to provide the basis for the design and dosage tests for Phase 3. The dosing and methodology of research in this phase generally adopts double-blind, random methods with limited sample sizes.

Phase 3 – confirm the therapeutic efficacy. The objective is to further verify the efficacy and safety of pharmaceutical products on patients within the target indication, to evaluate the benefits and risks and finally to provide sufficient experimentally proven evidence to support the registration application of the pharmaceutical products. In general, the trial should adopt double-blind random methods with sufficient sample sizes.

Phase 4 –assess therapeutic efficacy and adverse reactions post-approval. The purpose is, by conducting a new drug's post-marketing study, to assess therapeutic efficacy and adverse reactions when the drug is widely used, to evaluate overall benefit-risk relationships of the drug when used among the general population or specific groups and to adjust the administration dose, among others.

In April 2020, the NMPA and the National Health Commission (NHC) released the amended GCP, which took effect on July 1, 2020. The amended GCP is harmonized with the ICH-GCP. Compared to the previous GCP, the amended GCP provides comprehensive and substantive requirements on the design and conduct of clinical trials in China. In particular, the amended GCP enhances the protection for study subjects and tightens the control over bio-samples collected under clinical trials.

Collecting and Using Patients' Biospecimens and Derived Data.

Foreign-invested sponsors that collect and use patients' biospecimens in clinical trials are required to file with the China Human Genetic Resources Administrative Office, or the HGRAO, under the Ministry of Science and Technology, or the MOST. In 2017, the MOST issued the Circular on Optimizing the Administrative Examination and Approval of Human Genetic Resources, which simplified the approval for collecting and using human genetic resources for the purpose of commercializing a drug or medical device in the PRC. In June 2019, the State Council of the PRC issued the Regulation on the Administration of PRC Human Genetic Resources (effective as of July 1, 2019), which formalized the approval requirements pertinent to research collaborations between Chinese and foreign-owned entities.

Pursuant to this new HGR Regulation, a new notification system (as opposed to the advance approval approach originally in place) was put in place for clinical trials using PRC patients' biospecimens and data at clinical study sites without involving the export

of such specimens outside of China. The notification filing must specify the type, quantity, volume size and usage of the biospecimens, among others, with the HGRAO is required before conducting such clinical trials. The collection and use of PRC patients' biospecimens and data in international basic research collaboration are still subject to the approval of the HGRAO. The notification filing with the HGRAO also applies to access to clinical study data by foreign entities.

In October 2020, the Standing Committee of the NPC promulgated the PRC Biosecurity Law, which took effect on April 15, 2021. The PRC Biosecurity Law, the higher law to the HGR Regulation, reaffirms the regulatory requirements stipulated by the HGR Regulation while potentially increasing the administrative fines significantly in cases where foreign entities are alleged to have collected, preserved or exported Chinese human genetic resources.

Import Drug Registration or Multi Regional Clinical Trials.

NMPA regulations allow foreign drug developers to conduct import drug registration or multi regional clinical trials in China for a new drug as part of a global drug development program. An International Multicenter Clinical Trial (IMCT) Application needs to be filed with the CDE for conducting the clinical trials.

In October, 2017, the NMPA released the Decision on Adjusting Items concerning the Administration of Imported Drug Registration, as well as current requirement in DRR, which includes the following key points:

- Phase 1 IMCT is allowed to be conducted in China. The IMCT drug does not need to gain prior approval or have entered into either a Phase 2 or 3 clinical trial in a foreign country before the IMCT could be conducted in China, except for preventive biological products.
- If the IMCT is conducted in China and the local recruitment of patients number allied with CDE, the application for drug marketing authorization can be submitted directly after the completion of the IMCT.
- With respect to clinical trial and market authorization applications for imported innovative chemical drugs and therapeutic biological products, the marketing authorization in the country or region where the foreign drug manufacturer is located will not be required.
- With respect to drug applications that have been accepted before the release of this Decision, importation permission can be granted if such applications request exemption of clinical trials for the imported drugs based on the data generated from IMCT and if relevant requirements under the Administrative Measures of the Drug Registration are met.

The NMPA Decision on IMCT and the application for imported new drugs has streamlined and accelerated the applications for imported new drugs.

In order to apply for an IMCT Application in China, a biopharmaceutical company is required to submit a comprehensive investigation new drug application package filed with foreign regulatory agency, i.e. the FDA in our case, in a format compliant with NMPA guidance.

After obtaining the IMCT permit from the CDE, clinical trials should be conducted in compliance with both the FDA/ICH and NMPA Good Clinical Practice guidelines.

Data derived from IMCT can be used for the marketing authorization applications with the NMPA. When using IMCT data to support marketing authorization applications in China, applicants shall submit completed global clinical trial report, statistical analysis report and database, along with relevant supporting data in accordance with the ICH-CTD (International Conference on Harmonization-Common Technical Document) content and format requirements; subgroup research results summary and comparative analysis shall also be conducted concurrently.

Marketing Authorization Application

After completion of the first 3 phases of clinical trials demonstrating the safety and effectiveness of a pharmaceutical in its targeted indication, a Marketing Authorization Application needs to be filled with the NMPA, which includes research data of chemistry, manufacturing and controls, pre-clinical studies and clinical trial report in order to register the new drug. For imported drugs, the New Drug Registration Application is also known as the Import Drug License Application.

Once a marketing authorization is received, the product can be sold nationwide in China.

Pricing

The government regulates prices for pharmaceuticals (except for narcotic and Type 1 psychotropic drugs) mainly by establishing a price negotiation, consolidated procurement mechanism, and revising medical insurance reimbursement standards. The Chinese government has initiated several rounds of price negotiations with manufacturers of patented drugs, drugs with an exclusive source of supply, and oncology drugs since 2016. The average percentage of price reduction has been over 50%. Once the government agreed with the drug manufacturers on the supply prices, the drugs would be automatically listed in the National Reimbursement Drug List (NRDL) and qualified for public hospital purchase.

Reimbursement

China is a single-payor market with near universal healthcare provided by the government. Over 95% of the population receives healthcare coverage at various levels of reimbursement. Commercial insurance is available but is minimally adopted, and is seen as a supplement above and beyond government reimbursement. To obtain government reimbursement for a drug, the government must agree to add it to the NRDL or the provincial reimbursement drug lists at a negotiated price (at times at a significant discount to prevailing market price). Prior to this time, the market is self-pay, where patients will be responsible for 100% of the launch price determined by the company. We believe the self-pay market in China is expanding, given the rise in personal income levels in the country. In December 2020, the National Healthcare Security Administration (NHSA) and the PRC Ministry of Human Resources and Social Security released the National Drug Catalogue for Basic Medical Insurance, Work-Related Injury Insurance and Maternity Insurance, or the 2020 NRDL , and 119 new drugs were admitted to the 2020 NRDL. Previous updates to the NRDL occurred in 2019, 2017 and 2009. In addition, there were also NRDL price negotiations in 2018, 2019, and 2020. In 2020, the average price reduction of the 119 new drugs added to the 2020 NRDL is 50.64%. Admission to the NRDL depends on a number of factors, including on-market experience, scale of patient adoption, physician endorsement, cost effectiveness and budget impact. Provincial governments have some discretion to add additional drugs not listed in the NRDL to provincial reimbursement drug lists.

Medicines included in the NRDL are divided into two classes, Class A and Class B. Patients purchasing medicines included in the NRDL are entitled to reimbursement of the entire amount or a certain percentage of the purchase price. The percentage of reimbursement for Class B medicines differs from region to region in the PRC.

Hospital Listing

Government hospitals currently represent over 90% of the pharmaceutical market in China. In order for a new drug to be prescribed at a government hospital, it has to be listed in the hospital formulary. The process of entering into the formulary is commonly referred to as “hospital listing”, and typically requires a long lead time. These decisions are made on a hospital-by-hospital basis with timing that can range from every six months to every five years. Some hospitals also have temporary listing procedures that can accelerate timing. Private hospital and non-hospital pharmacies, which represent less than 10% of the drug market in China, do not require a formulary process to sell a drug.

Centralized Procurement and Tenders

Provincial and municipal government agencies will establish a provincial drug procurement agency to operate a mandatory collective tender process for purchases by government hospitals of a medicine included in provincial or local medicine procurement catalogs. The provincial or local medicine procurement catalogs are determined by the provincial drug procurement agency based on the National Essential Drugs List, the NRDL, local hospital formularies, etc. If a new drug has been included in a government hospital formulary, the NRDL or the provincial reimbursement drug list, the relevant hospitals must participate in collective tender processes for the purchase of such new drug. The centralized tender process is in principle conducted once every year in the relevant province or city in China. During the collective tender process, the provincial drug procurement agency will establish a committee consisting of recognized pharmaceutical experts. The committee will assess the bids submitted by the various participating pharmaceutical manufacturers, taking into consideration, among other things, the quality and price of the drug product and the service and reputation of the manufacturer. Only drug products that have been selected in the collective tender processes may be purchased by participating hospitals.

“4+7” Volume-based Drug Procurement and Tenders. In June 2018, the State Council decided to launch a new round of drug pricing and procurement reform. The reform policy aims to lower drug costs for patients, reduce transaction costs for enterprises, regulate

drug use of hospitals, and improve the centralized drug procurement and pricing system. This reform is implemented mainly by the NHSA. The NHC supports the reform by introducing policy that encourages purchasing and prescribing of the selected drug. The NMPA is responsible for the quality assurance of the drugs submitted for tenders.

The national pilot scheme for centralized volume-based drug procurement and tenders under the reform was launched in November 2018. The selected drugs must pass the GQCE on quality and effectiveness.

The centralized volume-based procurement is open to all approved enterprises that manufacture drugs on the government-set procurement list in China. The NHSA organized four rounds of volume-based procurement and tenders to this date. On February 3, 2021, the results of the fourth round of the volume-based procurement and tender were announced. All of the 45 listed products were successfully qualified to enter into a supply agreement with the group procurement organization and the average price reduction was 52%.

COMPETITION

Competition in the pharmaceutical, biotechnology and biopharmaceutical industries is intense and based significantly on scientific and technological factors, the availability of patent and other protection for technology and products, the ability and length of time required to obtain governmental approval for testing, manufacturing and marketing and the ability to commercialize products in a timely fashion. Moreover, the biopharmaceutical industry is characterized by rapidly evolving technology that could result in the technological obsolescence of any products that we develop.

We compete with many specialized biopharmaceutical firms, as well as a growing number of large pharmaceutical companies that are applying biotechnology to their operations. It is probable that the number of companies seeking to develop products and therapies for the treatment of unmet needs in oncology will increase. Many biopharmaceutical companies have focused their development efforts in the human therapeutics area, including oncology and inflammation, and many major pharmaceutical companies have developed or acquired internal biotechnology capabilities or made commercial arrangements with other biopharmaceutical companies. These companies, as well as academic institutions, governmental agencies and private research organizations, also compete with us in recruiting and retaining highly qualified scientific personnel and consultants.

The biopharmaceutical industry has undergone, and is expected to continue to undergo, rapid and significant technological change. Consolidation and competition are expected to intensify as technical advances in each field are achieved and become more widely known. In order to compete effectively, we will be required to continually expand our scientific expertise and technology, identify and retain capable personnel and pursue scientifically feasible and commercially viable opportunities.

Our competition will be determined in part by the potential indications for which our product candidates may be developed and ultimately approved by regulatory authorities. The relative speed with which we develop new products, complete clinical trials, obtain regulatory approvals, and complete the other requirements to get a pharmaceutical product on the market are critical factors in gaining a competitive advantage. We may rely on third parties to commercialize our products, and accordingly, the success of these products will depend in significant part on these third parties' efforts and ability to compete in these markets. The success of any collaboration will depend in part upon our collaborative partners' own competitive, marketing and strategic considerations, including the relative advantages of alternative products being developed and marketed by our collaborative partners and our competitors.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. In addition, many of these competitors have extensive experience in preclinical testing and human clinical trials and in obtaining regulatory approvals. The existence of competitive products, including products or treatments of which we are not aware, or products or treatments that may be developed in the future, may adversely affect the marketability of products that we may develop. Our competitors' drugs may be more effective than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing our product candidates.

EMPLOYEES

Our work force currently consists of 176 employees, all of which are full-time employees, the majority of whom are located in China. Certain of our activities, such as manufacturing and clinical trial operations, are outsourced at the present time. We may hire additional personnel, in addition to utilizing part-time or temporary consultants, on an as-needed basis. None of our employees are represented by a labor union, and we believe our relations with our employees are satisfactory.

CORPORATE HEADQUARTERS

We were incorporated under Delaware law in 1991. In 2012, with new leadership, the Company shifted its business strategy to China and has since built an infrastructure in China that includes sales and marketing, medical affairs, regulatory and clinical development and in the foreseeable future, distribution and manufacturing. The majority of the Company's operations are now located in China. Our offices are located at 9620 Medical Center Drive, Suite 300, Rockville, Maryland 20850, and our telephone number is (240) 864-2600. Our wholly-owned subsidiary, CASI China, is headquartered in Beijing, China and CASI Wuxi is headquartered in Wuxi, China. We conduct substantially all of our China commercial, regulatory and related operations through CASI China and our operations in Wuxi through CASI Wuxi. CASI China's headquarters are located at 1701-1702, China Central Office Tower 1, No.81 Jianguo Road, Chaoyang District, Beijing, 100025 China.

In 2020, we leased office space in Shanghai, China to accommodate our growing staff in that region. Our address in Shanghai is No. 2904, Shengbang International, North Sichuan Road, Hongkou District, Shanghai, China.

Management decisions are primarily being made out of CASI China where our executive team spends a substantial amount of time.

CHINA OPERATIONS

The majority of our operations are now located in China and are conducted primarily through two of our subsidiaries: (i) CASI Pharmaceuticals (China) Co., Ltd. ("CASI China"), a directly wholly owned subsidiary established in August 2012 and located in Beijing. CASI China is responsible for our day-to-day operations, development and commercialization of our product and (ii) CASI Pharmaceuticals (Wuxi) Co., Ltd. ("CASI Wuxi"), a directly wholly owned subsidiary established in November 2018 and located in Wuxi Huishan Economic Development Zone. CASI Wuxi was incorporated as the holding company for CASI's R&D center, distribution center and manufacturing facilities. CASI Wuxi has a lease on industrial land, for 7.33 hectare. In December 2018, CASI Wuxi established a new subsidiary CASI Biopharmaceuticals as an investment platform for Chinese pharmaceutical asset acquisition or cooperation.

We have about 168 FTEs in China. Over 100 employees are dedicated to commercial operations, which mainly account for EVOMELA's sales and marketing activities. The clinical and regulatory team has 18 FTEs, who oversee local preclinical and clinical operations, and NMPA regulatory activities. The Wuxi R&D and manufacturing center has 24 employees at the current stage, and the team size will expand according to the progress of the facility's construction.

AVAILABLE INFORMATION

Through our website at *www.casipharmaceuticals.com*, we make available, free of charge, our filings with the SEC, including our annual proxy statements, annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and all amendments thereto, as soon as reasonably practicable after such reports are filed with or furnished to the SEC. Additionally, our board committee charters and code of ethics are available on our website. We intend to post to this website all amendments to the charters and code of ethics. Our filings are also available through the SEC via their website, *http://www.sec.gov*. The information contained on our website is not incorporated by reference in this Annual Report on Form 10-K (this "Annual Report") and should not be considered a part of this report.

ITEM 1A. RISK FACTORS.

This section includes the most significant factors that we believe may adversely affect our business and operations. Before making an investment decision, you should carefully consider the risks described below, and all other information contained or incorporated by reference in our filings with the SEC. We expect to update these Risk Factors from time to time in the periodic and current reports that we file with the SEC. Please refer to these subsequent reports for additional information relating to the risks associated with investing in our common stock. If any of such risks and uncertainties actually occurs, our business, financial condition, and results of operations could be severely harmed. This could cause the trading price of our common stock to decline, and you could lose all or part of your investment.

Risk Factors Summary

Risks Relating to our Financial Position and Need for Additional Capital

- If we do not regain compliance with the Nasdaq bid price rule, our common stock would be delisted from the Nasdaq Capital Market, which would impair our ability to raise capital and the liquidity of our common stock could be adversely affected.
- We have incurred significant operating losses since inception and anticipate that we will continue to incur operating losses for the foreseeable future and may never achieve or maintain profitability.
- The success of CASI Wuxi is subject to uncertainty and may increase our losses, be difficult to accomplish, take longer than expected or require us to obtain additional financing.
- The current capital and credit market conditions may adversely affect our access to capital, cost of capital, and ability to execute our business plan as scheduled.
- We have limited revenue streams and we are uncertain whether additional funding will be available for our future capital needs and commitments. If we cannot raise additional funding, or access the capital markets, we may be unable to complete the development and commercialization of our products and product candidates.

Risks Relating to Our Business

- If we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.
- We are substantially dependent on the commercial success of EVOMELA™. Our medicine may fail to achieve and maintain the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community necessary for commercial success.
- We currently rely on a single source for our supply of EVOMELA which has high risk of supply chain disruption.
- Our business has been and may continue to be adversely affected by the current COVID-19 pandemic and could be impacted by future COVID-19 variants and other outbreaks of contagious diseases.
- The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a material adverse effect on our business, operations and prospects.
- We face significant competition from other biotechnology and pharmaceutical companies and our business will suffer if we fail to compete effectively.
- We may need new collaborative partners to further develop and commercialize products, and if we enter into such arrangements, we may lose control over the development and approval process.
- We may not have sufficient funds to acquire new product candidates or pay milestone payments.
- We must show the safety and efficacy of our product candidates through clinical trials, the results of which are uncertain.
- Compliance with ongoing post-marketing obligations for our approved products may uncover new safety information that could give rise to a product recall, updated warnings, or other regulatory actions that could have an adverse impact on our business.
- Undesirable adverse events caused by our medicines and drug candidates could interrupt, delay or halt clinical trials, delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval.
- Potential products may subject us to product liability for which insurance may not be available.
- If we are unable to obtain both adequate coverage and adequate reimbursement from third-party payers for our products before the competitor's product launch our revenues and prospects for profitability will suffer.
- Cybersecurity incidents could impair our ability to conduct business effectively.
- Our business depends substantially on the continuing efforts of our senior management, key employees and qualified personnel, and our business operations may be adversely and negatively impacted if we lose their services.
- Certain of our directors and officers may have business interests that may conflict with our interests and those of our stockholders.

- We or the third parties upon whom we rely on may be adversely affected by epidemic outbreaks, earthquakes, tornadoes, hurricanes or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Risks Relating to Our Reliance on Third Parties

- Independent clinical investigators and contract research organizations that we engage to conduct our clinical trials may not devote sufficient time or attention to our clinical trials or be able to repeat their past success.
- We have no current manufacturing capacity and rely on limited suppliers for some of our products.
- The design and manufacture of a manufacturing facility by CASI Wuxi may be delayed.
- If we fail to maintain an effective distribution channel for our medicines, our business and sales could be adversely affected.

Risks Related to Extensive Government Regulation

- All material aspects of the research, development, manufacturing and commercialization of pharmaceutical products are heavily regulated, and we may face difficulties in complying with or be unable to comply with such regulations, which could have a material adverse effect on our business.
- We are subject to certain U.S. healthcare laws, regulation and enforcement; our failure to comply with those laws could have a material adverse effect on our results of operations and financial condition.
- Current healthcare laws and regulations and future legislative or regulatory reforms to the healthcare system may affect our ability to sell our products profitably.
- Our medicines and any future approved drug candidates will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our medicines and drug candidates.

Risks Relating to Our Intellectual Property

- We depend on patents and other proprietary rights, some of which are uncertain. If we are unable to protect our intellectual property rights our business and competitive position would be harmed.
- Third parties may initiate legal proceedings alleging infringement of intellectual property rights, the outcome of which would be uncertain and could harm our business.
- Although China recently adopted changes to its patent law to include patent term extension and an early resolution mechanism for pharmaceutical patent disputes starting in June 2021, key provisions of the law remain unclear and/or subject to implementing regulations. The absence of effective regulatory exclusivity for pharmaceutical products in China could further increase the risk of early generic or biosimilar competition with our medicines in China.

Risks Relating to Our Common Stock

- The market price of our common stock may be highly volatile or may decline regardless of our operating performance.
- Our largest stockholders, including our directors and executive officers and investment funds with which they are associated, hold a significant amount of our outstanding common stock and, if they acted together, could influence our management and affairs.
- Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for certain legal actions between us and our stockholders, which could increase costs to bring a claim, discourage claims or limit the ability of our stockholders to bring a claim in a judicial forum viewed by the stockholders as more favorable for disputes with us or our directors, officers or other employees.

Risks Relating to Our Auditor

- The audit report included in this Annual Report on Form 10-K is prepared by auditors who are not currently inspected by the PCAOB and, as such, our stockholders are deprived of the benefits of such inspection. In addition, various legislative and regulatory developments related to U.S.-listed China based companies due to lack of PCAOB inspection and other developments due to political tensions between the United States and China may have a material adverse impact on our listing and trading in the United States and the trading prices of our shares of common stock.

- We could be delisted if our auditors are unable to meet the PCAOB inspection requirements in time.

Risks Relating to Our Business Operations in China

- We conduct a majority of our operations in China, which exposes us to risks associated with operating outside of the U.S. Changes in international trade and economic policy by the U.S. and Chinese governments could have a material adverse effect on our business and operations.
- Governmental control of currency conversion and payments of RMB out of mainland China may limit our ability to utilize our cash balances effectively and affect the value of your investment.
- Changes in China's economic, political or social conditions or government policies could have a material adverse effect on our business and operations.
- The Chinese government exerts substantial influence over the manner in which we must conduct our business activities.
- We are subject to the Enterprise Income Tax Law, and we may therefore be subject to PRC income tax on our global income.
- China regulations relating to investments in offshore companies by China residents may subject our China-resident stockholders, beneficial owners or our China subsidiaries to liability or penalties, limit our ability to inject capital into our China subsidiaries or limit our China subsidiaries' ability to increase their registered capital or distribute profits to us.
- We may be subject to fines and legal sanctions by SAFE or other China government authorities if we or our employees who are China citizens fail to comply with regulations relating to employee stock options granted by companies listed on exchanges outside of China to China citizens.

General Risk Factors

- We may engage in strategic, commercial and other corporate transactions that could negatively affect our financial condition and prospects.
- If securities or industry analysts publish inaccurate or unfavorable research about our business, our stock price could decline.
- Subsequent resales of shares of our common stock in the public market may cause the price of our common stock to fall.
- Issuances of additional shares of our common stock may cause substantial dilution of existing stockholders.

Risks Relating to our Financial Position and Need for Additional Capital

If we do not regain compliance with the Nasdaq bid price rule, our common stock would be delisted from the Nasdaq Capital Market, which would impair our ability to raise capital and the liquidity of our common stock could be adversely affected.

Our listing on the Nasdaq Capital Market is contingent upon meeting all the continued listing requirements of the Nasdaq Capital Market.

On December 30, 2021, CASI received a deficiency letter from the Listing Qualifications Department (the "Staff") of the Nasdaq Stock Market ("Nasdaq") notifying CASI that, for the previous 30 consecutive business days, the bid price of CASI's common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2) (the "Bid Price Rule").

The Nasdaq deficiency letter has no immediate effect on the listing of CASI's common stock on the Nasdaq Capital Market.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), CASI has been provided an initial period of 180 calendar days, or until June 28, 2022 (the "Compliance Date"), to regain compliance with the Bid Price Rule. If, at any time before the Compliance Date, the bid price for CASI's common stock closes at $1.00 or more per share for a minimum of 10 consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to CASI that it complies with the Bid Price Rule, unless the Staff exercises its discretion to extend this 10-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H).

If CASI does not regain compliance with the Bid Price Rule by the Compliance Date, CASI may be eligible for an additional 180 calendar day compliance period (the "Second Compliance Period"). To qualify, CASI would need to meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards of the Nasdaq Capital Market, with the exception of the Bid Price Rule, and provide written notice to the Staff of its intention to cure the deficiency during the Second Compliance Period by effecting a reverse stock split, if necessary.

However, if CASI does not regain compliance with the Bid Price Rule by the Compliance Date and it appears to the Staff that CASI will not be able to regain compliance with the Bid Price Rule during the Second Compliance Period, or CASI is otherwise not eligible for the Second Compliance Period, then Nasdaq will provide notice to CASI that CASI's common stock will be subject to delisting. At that time, CASI may appeal the Staff's delisting determination to a Nasdaq Listing Qualifications Panel (the "Panel"). CASI expects that its common stock would remain listed pending the Panel's decision. There can be no assurance that, if CASI does appeal the Staff's delisting determination to the Panel, such appeal would be successful.

CASI intends to actively monitor the closing bid price of its common stock between now and the Compliance Date and will consider available options, including a reverse stock split. In order to make available the option of a reverse stock split, CASI may submit a reverse stock split proposal to its stockholders at a special meeting of stockholders or its next annual meeting of stockholders. However, there can be no assurance that the reverse stock split will be approved or that CASI will be able to regain compliance with the Bid Price Rule. If our common stock is delisted from the Nasdaq Capital Market, our ability to raise capital in the future may be limited. Delisting could also result in less liquidity for our stockholders and a lower stock price.

If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on the OTC Bulletin Board or another over-the-counter market. Any such alternative would likely result in it being more difficult for us to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, our common stock. In addition, there can be no assurance that our common stock would be eligible for trading on any such alternative exchange or markets.

We have incurred significant operating losses since inception and anticipate that we will continue to incur operating losses for the foreseeable future and may never achieve or maintain profitability.

To date, we have been engaged primarily in research and development activities. Previously, we have not derived significant revenues from operations; however, in the years ended December 31, 2021 and 2020, we had EVOMELA® sales totaling $30.0 million and $15.0 million, respectively.

We have experienced losses in each year since inception. Through December 31, 2021, we had an accumulated deficit of $605.6 million. We expect that we will seek to raise capital to continue our operations and, although we have been successfully funded to date through the sales of our equity securities, our capital-raising efforts may not produce the funding needed to sustain our operations. If we are unable to obtain additional funding for operations, we may not be able to continue operations as proposed, requiring us to modify our business plan, curtail various aspects of our operations or cease operations. In any such event, investors may lose a portion or all of their investment.

We expect that our ongoing preclinical, clinical, marketing and corporate activities will result in operating losses for the foreseeable future. In addition, to the extent we rely on others to develop and commercialize our products, our ability to achieve profitability will depend upon the success of these other parties. To support our research and development of certain product candidates, we may seek and rely on cooperative agreements from governmental and other organizations as a source of support. If a cooperative agreement were to be reduced to any substantial extent, it may impair our ability to continue our research and development efforts. To become and remain profitable, we must successfully commercialize one or more product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing clinical trials of our product candidates, developing commercial scale manufacturing processes, obtaining marketing approval, manufacturing, marketing and selling any current and future product candidates for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate sufficient revenue to achieve profitability.

The success of CASI Wuxi is subject to uncertainty and may increase our losses, be difficult to accomplish, take longer than expected or require us to obtain additional financing.

We intend to invest $80 million in CASI Pharmaceuticals (Wuxi) Co., Ltd., that is building a manufacturing facility in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China. Since the construction began, we have incurred capital expenditures of $12.1 million. CASI Wuxi will also operate the facility upon completion. As of December 31, 2021, we have invested $31 million in cash, transferred selected ANDAs valued at $30 million and will invest an additional $19 million in cash in the future. The Company's total investment is intended to account for 80% of the equity of the CASI Wuxi. CASI Wuxi may not achieve the expected goal as the planned manufacturing facility will not be entirely within our control. It can take years to build and establish a new manufacturing facility.

Once built, the new facility might fail validation or not meet regulatory standards for a commercial manufacturing facility. In addition, we may not obtain or retain the requisite legal permits to manufacture in China, and costs or operational limitations may be imposed in connection with obtaining and complying with such permits. Our ability to establish and operate a manufacturing facility in China may be adversely affected by changes in Chinese laws and regulations such as those related to, among other things, taxation, import and export tariffs, environmental regulations, land use rights, intellectual property, employee benefits and other matters. The success of CASI Wuxi also relies on our ability to make additional payments in the future, which is uncertain. Our plan may require us to obtain additional debt or equity financing, resulting in additional debt obligations, increased interest expense or dilution of equity ownership. If we are unable to establish a new manufacturing facility, purchase equipment, hire adequate personnel to support our manufacturing efforts or implement necessary process improvements, we may be unable to produce commercial materials or meet demand, if any should develop, for our product candidates. Any one of the factors cited above, or a combination of them, could result in unanticipated costs, which could materially and adversely affect our business and planned operations and earnings in China.

The current capital and credit market conditions may adversely affect our access to capital, cost of capital, and ability to execute our business plan as scheduled.

Access to capital markets is critical to our ability to operate. Traditionally, we have funded our operations by raising capital in the equity markets. Declines and uncertainties in these markets over the past few years have restricted raising new capital in amounts sufficient to conduct our current operations and have affected our ability to continue to expand or fund additional development efforts. We require significant capital for research and development for our product candidates, clinical trials, and marketing activities. Our inability to access the capital markets on favorable terms because of our low stock price, or upon our delisting from the Nasdaq Capital Market if we fail to satisfy a listing requirement, could affect our ability to execute our business plan as scheduled. Moreover, we rely and intend to rely on third parties, including our clinical research organizations, third party manufacturers, and certain other important vendors and consultants. As a result of the current volatile and unpredictable global economic situation, there may be a disruption or delay in the performance of our third-party contractors and suppliers. If such third parties are unable to adequately satisfy their contractual commitments to us in a timely manner, our business could be adversely affected.

We have limited revenue streams and we are uncertain whether additional funding will be available for our future capital needs and commitments. If we cannot raise additional funding, or access the capital markets, we may be unable to complete the development and commercialization of our products and product candidates.

We will require substantial funds in addition to our existing working capital to develop and commercialize our products and product candidates and to otherwise meet our business objectives. We have never generated sufficient revenue during any period since our inception to cover our expenses and have spent, and expect to continue to spend, substantial funds to continue our clinical development programs and commercialization of our products and product candidates. Any one of the following factors, among others, could cause us to require additional funds or otherwise cause our cash requirements in the future to increase materially:

- progress of our clinical trials or correlative studies;
- results of clinical trials;
- changes in or terminations of our relationships with strategic partners;
- changes in the focus, direction, or costs of our research and development programs;
- competitive and technological advances;
- establishment and expansion of marketing and sales capabilities;
- manufacturing;
- the regulatory approval process; or
- product launch and distribution.

At December 31, 2021, we had cash and cash equivalents of $38.7 million. We may continue to seek additional capital through public or private financing or collaborative agreements in 2021 and beyond. Our operations require significant amounts of cash. We may be required to seek additional capital for the future growth and development of our business. We can give no assurance as to the availability of such additional capital or, if available, whether it would be on terms acceptable to us. If we are not successful in obtaining sufficient capital because we are unable to access the capital markets on favorable terms, it could reduce our research and development efforts and materially adversely affect our future growth, results of operations and financial results. There can be no assurance that we would be able to obtain any required financing on a timely basis or at all.

Risks Relating to Our Business

If we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed

The time required to obtain approval by FDA and NMPA is unpredictable and typically takes many years following the commencement of preclinical studies and clinical trials and depends on numerous factors, including the substantial discretion of the regulatory authorities.

Our drug candidates could be delayed or fail to receive regulatory approval for many reasons, including:

- failure to begin or complete clinical trials due to disagreements with regulatory authorities;
- delays in subject enrollment or interruptions in clinical trial supplies or investigational product;
- failure to demonstrate that a drug candidate is safe and effective or that a biologic candidate is safe, pure, and potent for its proposed indication;
- failure of clinical trial results to meet the level of statistical significance required for approval;
- reporting or data integrity issues related to our clinical trials;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- changes in approval policies or regulations that render our preclinical and clinical data insufficient for approval or require us to amend our clinical trial protocols;
- regulatory requests for additional analyses, reports, data, nonclinical studies and clinical trials, or questions regarding interpretations of data and results and the emergence of new information regarding our drug or biologic candidates or other products;
- failure to satisfy regulatory conditions regarding endpoints, patient population, available therapies and other requirements for our clinical trials in order to support marketing approval on an accelerated basis or at all;
- our failure to conduct a clinical trial in accordance with regulatory requirements or our clinical trial protocols; and
- clinical sites, investigators or other participants in our clinical trials deviating from a trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial.

The FDA, NMPA or a comparable regulatory authority may require more information, including additional preclinical, chemistry, manufacturing and controls, and/or clinical data, to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program.

Changes in regulatory requirements and guidance may also occur, and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to IRBs or ethics committees for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

If we experience delays in the completion of, or the termination of, a clinical trial of any of our product candidates, the commercial prospects of that candidate may be harmed, and our ability to generate product sales revenues from any of those candidates may be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our candidate development and approval process, and jeopardize our ability to commence product sales and generate related revenues for that candidate. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Our success in commercializing these drugs and biologics may be inhibited by a number of factors, including:

- our inability to obtain/maintain regulatory approvals;
- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or educate physicians on the benefits of our products;
- our lack of experience in manufacturing drugs for commercial sales;

- our or our partners' inability to secure widespread acceptance of our products from physicians, healthcare payors, patients and the medical community;
- our ability to win tenders through the collective tender processes in which we decide to participate;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization;
- generic and biosimilar competition; and
- regulatory exclusivities or patents held by competitors that may inhibit our products' entry to the market.

If we decide to rely on third parties to manufacture, sell, market and distribute our products and product candidates, we may not be successful in entering into arrangements with such third parties or may be unable to do so on terms that are favorable to us. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates, which would adversely affect our business and financial condition.

We are substantially dependent on the commercial success of EVOMELA™. Our medicine may fail to achieve and maintain the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community necessary for commercial success.

The success of our business is substantially dependent on our ability to successfully commercialize EVOMELA. On December 3, 2018, we received the NMPA approval for importation, marketing and sales in China for EVOMELA®, and on August 12, 2019, we announced the commercial launch of EVOMELA® in China. We will continue to spend our time, resources and efforts on the commercialization of EVOMELA® in China.

Reimbursement and hospital listing may be the most critical market access factors for our commercialization success in China. The NRDL is updating on annual basis via a negotiation mechanism. Although participating the NRDL pricing negotiation is voluntarily, it usually results significant price discount. The Company has no intention to list EVOMELA® in the NRDL any time before a direct competitor's compound commercially launch, therefore, our market will be limited given only a small portion of the Chinese population would be able to afford EVOMELA® through self-pay.

The government owned hospitals in China usually restrict the drug use outside the hospital formulary. Therefore, been listed in hospital formulary is critical. In order to list in the hospital formulary, the Company must participate the provincial level tendering process. Wining the tendering does not guarantee the hospital listing. If we were unable to quickly add EVOMELA® to hospitals' formulary, doctors and patients will have limited access to EVOMELA® through hospital pharmacies, the demand for EVOMELA®, and the revenues from EVOMELA® will be materially and adversely affected. On the other hand, patients are able to purchase EVOMELA with the prescription from the physician from pharmacies the product is not available in the hospital, however, the hospitals do not encourage such activities.

We currently rely on a single source for our supply of EVOMELA which has high risk of supply chain disruption

We currently rely on a single source for our supply of EVOMELA®. Early in the COVID-19 pandemic we experienced a disruption to our supply chain for EVOMELA®, we have experienced minimal supply disruptions in 2021. However, if suppliers refuse or are unable to provide products for any reason (including the occurrence of an event like the COVID-19 pandemic that makes delivery impractical), we would have to work with Acrotech to negotiate an agreement with a substitute supplier, which would likely interrupt further manufacturing of EVOMELA®, cause delays or increase our costs.

Our business has been and may continue to be adversely affected by the current COVID-19 pandemic and could be impacted by future COVID-19 variants and other outbreaks of contagious diseases

The COVID-19 pandemic has adversely affected, and may continue to adversely affect, the economies and financial markets of many countries, which may result in a period of regional, national, and global economic slowdown or regional, national, or global recessions that could affect our ability to continue to commercialize and expand distribution of EVOMELA® (Melphalan For Injection) or other drugs in our existing product pipeline. Early in the COVID-19 pandemic we experienced a disruption to our supply chain for EVOMELA®, we have experienced no supply disruption in 2021; however, there can be no assurance that restrictions will not be

imposed again. In addition, economic and other uncertainties may adversely affect other parties' willingness to negotiate and execute product licenses and thus hamper our ability to in-license clinical-stage and late-stage drug candidates in China or elsewhere.

Clinical trials, whether planned or ongoing, may be affected by the COVID-19 pandemic. Our partner, Juventas, experienced some delay in the start of the CNCT19 clinical trials due to the COVID-19 pandemic. The COVID-19 pandemic has also impacted our targeted start time of our CID-103 trial due to the lock-down of many medical facilities in Europe. Study procedures (particularly any procedures that may be deemed non-essential), site initiation, participant recruitment and enrollment, participant dosing, shipment of our product candidates, distribution of clinical trial materials, study monitoring, site inspections and data analysis may be paused or delayed due to changes in hospital or research institution policies, federal, state or local regulations, prioritization of hospital and other medical resources toward COVID-19 efforts, or other reasons related to the pandemic. In addition, there could be a potential effect of COVID-19 on the operations of the health regulatory authorities, which could result in delays of reviews and approvals, including with respect to our product candidates. Any prolongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold or used for research under the same or similar names, or similar mechanism of action or product class, but which are sold without proper licenses or approvals. Such products may be used for indications or purposes that are not recommended or approved or for which there is no data or inadequate data with regard to safety or efficacy. Such products divert sales from genuine products, often are of lower cost, often are of lower quality (having different ingredients or formulations, for example), and have the potential to damage the reputation for quality and effectiveness of the genuine product. If counterfeit pharmaceuticals illegally sold or used for research result in adverse events or side effects to consumers, we may be associated with any negative publicity resulting from such incidents. Consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. In addition, the use of counterfeit products could be used in non-clinical or clinical studies, or could otherwise produce undesirable side effects or adverse events that may be attributed to our products as well, which could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

We face significant competition from other biotechnology and pharmaceutical companies and our business will suffer if we fail to compete effectively.

If competitors were to develop superior drug candidates, our products could be rendered noncompetitive or obsolete, resulting in a material adverse effect to our business. Developments in the biotechnology and pharmaceutical industries are expected to continue at a rapid pace. Success depends upon achieving and maintaining a competitive position in the development of products and technologies. Competition from other biotechnology and pharmaceutical companies can be intense. Many competitors have substantially greater research and development capabilities, marketing, financial and managerial resources and experience in the industry.

In the generic products market, we face competition from other generic pharmaceutical companies, which may impact our selling price and revenues from such products. The FDA approval process often results in the FDA granting final approval to a number of ANDAs for a given product at the time a patent for a corresponding brand product or other market exclusivity expires. This may force us to face immediate competition when we seek to introduce a generic product into the market. If competition from other generic pharmaceutical companies intensifies, revenues may decline.

The availability of our competitors' products could limit the demand, and the price we are able to charge, for product candidates we develop. We will not achieve our business plan if the acceptance of our products is inhibited by price competition or reimbursement issues or if physicians switch to other new drug products or choose to reserve our product candidates for use in limited circumstances. The inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, financial condition and prospects.

We may need new collaborative partners to further develop and commercialize products, and if we enter into such arrangements, we may lose control over the development and approval process.

We may develop and commercialize our product candidates both with and without corporate alliances and partners. Nonetheless, we intend to explore opportunities for new corporate alliances and partners to help us develop, commercialize and market our product candidates. We may grant to our partners certain rights to commercialize any products developed under these agreements, and we may rely on our partners to conduct research and development efforts and clinical trials on, obtain regulatory approvals for, and manufacture and market any products licensed to them. Each individual partner will seek to control the amount and timing of resources devoted to these activities generally. We anticipate obtaining revenues from our strategic partners under such relationships in the form of research and development payments and payments upon achievement of certain milestones. Since we generally expect to obtain a royalty for sales or a percentage of profits of products licensed to third parties, our revenues may be less than if we retained all commercialization rights and marketed products directly. In addition, there is a risk that our corporate partners will pursue alternative technologies or develop competitive products as a means for developing treatments for the diseases targeted by our product candidates.

We may not be successful in establishing any collaborative arrangements. Even if we do establish such collaborations, we may not successfully commercialize any products under or derive any revenues from these arrangements. There is a risk that we will be unable to manage simultaneous collaborations, if any, successfully. With respect to existing and potential future strategic alliances and collaborative arrangements, we will depend on the expertise and dedication of sufficient resources by these outside parties to develop, manufacture, or market products. If a strategic alliance or collaborative partner fails to develop or commercialize a product to which it has rights, we may not recognize any revenues on that particular product.

We may not have sufficient funds to acquire new product candidates or pay milestone payments.

Our growth strategy relies on our in-license of new product candidates from third parties. Our pipeline will be dependent upon the availability of suitable acquisition candidates at favorable prices and upon advantageous terms and conditions. Even if such opportunities are present, we may not be able to successfully identify appropriate acquisition candidates. Moreover, other companies, many of which may have substantially greater financial resources are competing with us for the right to acquire such product candidates.

If a product candidate is identified, the third parties with whom we seek to cooperate may not select us as a potential partner or we may not be able to enter into arrangements on commercially reasonable terms or at all. Furthermore, the negotiation and completion of collaborative and license arrangements could cause significant diversion of management's time and resources and potential disruption of our ongoing business.

We must show the safety and efficacy of our product candidates through clinical trials, the results of which are uncertain.

Before obtaining regulatory approvals for the commercial sale of our products, we must demonstrate, through preclinical studies (animal testing) and clinical trials (human testing), that our proposed products are safe and effective for use in each target indication. Testing of our product candidates will be required, and failure can occur at any stage of testing. Clinical trials may not demonstrate sufficient safety and efficacy to obtain the required regulatory approvals or result in marketable products. The failure to adequately demonstrate the safety and efficacy of a product under development could delay or prevent regulatory approval of the potential product.

Clinical trials for the product candidates we are developing may be delayed by many factors, including that potential patients for testing are limited in number. The failure of any clinical trials to meet applicable regulatory standards could cause such trials to be delayed or terminated, which could further delay the commercialization of any of our product candidates. Newly emerging safety risks observed in animal or human studies also can result in delays of ongoing or proposed clinical trials. Any such delays will increase our product development costs. If such delays are significant, they could negatively affect our financial results and the commercial prospects for our products.

Compliance with ongoing post-marketing obligations for our approved products may uncover new safety information that could give rise to a product recall, updated warnings, or other regulatory actions that could have an adverse impact on our business.

After the FDA approves a drug or biologic for marketing, the product's sponsor must comply with several post-marketing obligations that continue until the product is discontinued. These post-marketing obligations include the reporting of adverse events to the agency within specified timeframes, the submission of product-specific annual reports that include changes in the distribution, manufacturing, and labeling information, and notification when a drug product is found to have significant deviations from its approved manufacturing specifications (among others). Our ongoing compliance with these types of mandatory reporting requirements could result in additional requests for information from the FDA and, depending on the scope of a potential product issue that the FDA may decide to pursue, potentially also result in a request from the agency to conduct a product recall or to strengthen warnings and/or revise

other label information about the product. FDA may also require or request the withdrawal of the product from the market. Any of these post-marketing regulatory actions could materially affect our sales and, therefore, have the potential to adversely affect our business, financial condition, results of operations and cash flows.

Undesirable adverse events caused by our medicines and drug candidates could interrupt, delay or halt clinical trials, delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval

Undesirable adverse events ("AEs") caused by our medicines and drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval, or could result in limitations or withdrawal following approvals. If the conduct or results of our trials or patient experience following approval reveal a high and unacceptable severity or prevalence of AEs, our trials could be suspended or terminated and regulatory authorities could order us to cease further development of, or deny approval of, our drug candidates or require us to cease commercialization following approval.

As is typical in the development of pharmaceutical products, drug-related AEs and serious AEs ("SAEs") have been reported in our clinical trials. Some of these events have led to patient deaths. Drug-related AEs or SAEs could affect patient recruitment or the ability of enrolled subjects to complete the trial and could result in product liability claims. Any of these occurrences may harm our reputation, business, financial condition and prospects significantly. In our periodic and current reports filed with the SEC and our press releases and scientific and medical presentations released from time to time we disclose clinical results for our drug candidates, including the occurrence of AEs and SAEs.

Potential products may subject us to product liability for which insurance may not be available.

The use of our potential products in clinical trials and the marketing of any pharmaceutical products may expose us to product liability claims. We have obtained a level of liability insurance coverage that we believe is adequate in scope and coverage for our current stage of development. However, our present insurance coverage may not be adequate to protect us from liabilities we might incur. In addition, our existing coverage will not be adequate as we further develop products and, in the future, adequate insurance coverage and indemnification by collaborative partners may not be available in sufficient amounts or at a reasonable cost. If a product liability claim or series of claims are brought against us for uninsured liabilities, or in excess of our insurance coverage, the payment of such liabilities could have a negative effect on our business and financial condition.

If we are unable to obtain both adequate coverage and adequate reimbursement from third-party payers for our products before the competitor's product launch our revenues and prospects for profitability will suffer.

Successful commercialization of our products is highly dependent on the extent to which coverage and reimbursement is, and will be, available from third-party payers, including governmental payers and private health insurers. Patients may not be capable of paying for our products themselves and may rely on third-party payers to pay for, or subsidize, the costs of their medications, among other medical costs. If third-party payers do not provide coverage or reimbursement for our products, our revenues and prospects for profitability will suffer. In addition, even if third-party payers provide some coverage or reimbursement for our products, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

Cybersecurity incidents could impair our ability to conduct business effectively.

Cybersecurity incidents against us or against a third party that has authorized access to our data or networks, failure of our disaster recovery systems, or consequential employee error, could have an adverse effect on our ability to communicate or conduct business, negatively impacting our operations and financial condition. This adverse effect can become particularly acute if those events affect our electronic data processing, transmission, storage, and retrieval systems, or impact the availability, integrity, or confidentiality of our data.

We depend heavily upon computer systems to perform necessary business functions. Our computer systems, networks, and data, like those of other companies, could be subject to cyberattacks and unauthorized access, use, alteration, or destruction. If one or more of these events occurs, it could potentially jeopardize the confidential, proprietary, and other information processed, stored in, and transmitted through our computer systems and networks. Such an attack could cause interruptions or malfunctions in our operations, which could result in financial losses, litigation, regulatory penalties, reputational damage, and increased costs associated with mitigation of damages and remediation. Third parties with which we do business may also be sources of cybersecurity or other technological risk.

The use of quarantines and social distancing restrictions to reduce the spread of COVID-19, including employees who have transitioned to working remotely, may present additional cybersecurity risks to us. Policies of extended periods of remote working, whether by us or third parties with which we do business with, could strain technology resources, introduce operational risks and otherwise heighten the risks described above.

Our business depends substantially on the continuing efforts of our senior management, key employees and qualified personnel, and our business operations may be adversely and negatively impacted if we lose their services.

Our future success depends substantially on the continued efforts of our senior management team and key employees. Our employees play key roles in the areas of product development, marketing, sales, and general and administrative functions. Competition for qualified staff or other key employees in the biopharmaceutical industry in China is intense, particularly for individuals with multinational experience. If one or more of our members of senior management or key employees are unable or unwilling to continue their services with us, we might not be able to replace them easily, at an acceptable cost or in a timely manner, if at all.

Many of the companies with which we compete for experienced personnel have greater resources than we have and some of these companies may offer more lucrative compensation packages. If any of our key personnel joins a competitor or forms a competing company, we may lose customers, know-how and key professionals and staff members. Even if we enter into employment agreements and non-compete agreements with our employees, certain provisions under these agreements may be deemed invalid or unenforceable under PRC laws. Our continued ability to compete effectively depends on our ability to attract new employees and to retain and motivate our existing employees. Since the demand and competition for talent is intense in our industry, we may need to offer higher compensation and other benefits in order to attract and retain key personnel in the future, which could increase our compensation expenses. If we do not succeed in attracting additional highly skilled personnel or retaining or motivating our existing personnel, we may be unable to grow effectively.

Certain of our directors and officers may have business interests that may conflict with our interests and those of our stockholders.

Certain of our directors and officers have relationships with venture capital or similar funds that invest in life sciences companies that may compete with us. James Huang, a director, is the founding partner of Panacea Venture, a global venture fund focusing on investments in innovative and transformative early and growth stage healthcare and life science companies. Dr. Quan Zhou, another director, previously served as the president of IDG Technology Venture Investment Inc. and has been the managing member of IDG Technology Venture Investments, LP and its successor fund since 2000 and the director of various IDG-Accel China funds since 2005.

Our Chairman and CEO, Dr. Wei-Wu He, is the founder and managing partner of Emerging Technology Partners, LLC ("ETP"), a life science focused venture fund, and its related investing entities. Through funds affiliated with ETP, Dr. He is a founder and significant shareholder of Juventas and currently serves as chairman of Juventas' board of directors. Mr. Huang, through Panacea Venture, also is an investor in Juventas. In addition, we have an equity investment in Juventas.

Although we require that all transactions with Juventas must be approved by a committee of independent directors, our commercial license, loan to, and other transactions with Juventas could create conflicts of interests for Dr. He or Mr. Huang. Even though we are an investor in Juventas, Dr. He and Mr. Huang may have different business and personal interests than our other stockholders. In particular, Dr. He, as a founder of Juventas, has a direct interest in the financial success of Juventas that may encourage him to support strategies to further the financial success of Juventas that could potentially adversely impact us. To the extent we fail to appropriately deal with any such conflicts of interests, it could negatively impact our reputation and ability to raise additional funds and the willingness of counterparties to do business with us, all of which could have an adverse effect on our business, financial condition, results of operations, and cash flows.

We or the third parties upon whom we rely on may be adversely affected by epidemic outbreaks, earthquakes, tornadoes, hurricanes or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

We have offices in Rockville, Maryland, and a wholly owned subsidiary in Beijing, China through which substantially all of our operations are conducted. We also rely and intend to rely on third parties, including our clinical research organizations, third party manufacturers, and certain other important vendors and consultants in China and in United States. The occurrence of one or more epidemic outbreaks such as Ebola, Zika, SARS-CoV, COVID-19 or measles, natural disasters, such as tornadoes, hurricanes, fires, floods, hail storms and earthquakes, unusual weather conditions, terrorist attacks or disruptive political events in regions where we operate our business could adversely affect the operations of the third parties we rely on and our business, results of operations, financial condition and our prospects.

If an epidemic outbreak, natural disaster, power outage or other event occurred that prevented us or the third parties we rely on from using all or a significant portion of our or their offices, damaged critical infrastructure or disrupted operations, it may be difficult, or in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plan we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Risks Relating to Our Reliance on Third Parties

Independent clinical investigators and contract research organizations that we engage to conduct our clinical trials may not devote sufficient time or attention to our clinical trials or be able to repeat their past success.

We depend on independent clinical investigators and contract research organizations ("CROs") to assist in the conduct of our clinical trials under their agreements with us. The investigators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. If independent investigators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard or deviates from regulatory requirements, GCPs, or the protocol, it could delay the approval of our FDA applications and our introduction of new products. The CROs we contract with to assist with the execution of our clinical trials play a significant role in the conduct of the trials and the subsequent collection and analysis of data. Failure of the CROs to meet their obligations, as well as any failure of us or our collaborators to effectively monitor and audit our CROs and clinical trials, could adversely affect clinical development of our products.

We have no current manufacturing capacity and rely on limited suppliers for some of our products.

We plan to operate a manufacturing facility in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China. We do not currently have the capacity to manufacture products and we have limited experience in these activities. The manufacturing processes for the pipeline we are developing have not yet been tested at commercial levels, and it may not be possible to manufacture these materials in a cost-effective manner. If we elect to perform these functions, we will be required to either develop these capacities, or contract with others to perform some or all of these tasks. We may be dependent to a significant extent on corporate partners, licensees, or other entities for manufacturing of our products. If we engage directly in manufacturing, we will require substantial additional funds and personnel and will be required to comply with extensive regulations. We may be unable to develop or contract for these capacities when required to do so in connection with our business.

We depend on our third-party manufacturers to perform their obligations effectively and on a timely basis. These third parties may not meet their obligations and any such non-performance may delay clinical development or submission of products for regulatory approval, or otherwise impair our competitive position. Any significant problem experienced by one of our suppliers could result in a delay or interruption in the supply of materials to us until such supplier resolves the problem or an alternative source of supply is located. Any delay or interruption would likely lead to a delay or interruption of manufacturing operations, which could negatively affect our operations. Although we have identified alternative suppliers for our product candidates, we have not entered into contractual or other arrangements with them. If we needed to use an alternate supplier for any product, we would experience delays while we negotiated an agreement with them for the manufacture of such product. In addition, we may be unable to negotiate manufacturing terms with a new supplier as favorable as the terms we have with our current suppliers.

Problems with any manufacturing processes, including deviations from cGMP, could result in product defects, which could require us to delay shipment of products or recall products previously shipped, as well as regulatory action. In addition, any prolonged interruption in the operations of the manufacturing facilities of one of our sole-source suppliers could result in the cancellation of shipments. A number of factors could cause interruptions, including equipment malfunctions or failures, or damage to a facility due to natural disasters or otherwise. We expect our future manufacturing processes to be, highly complex and subject to a lengthy regulatory approval process. Alternative qualified production capacity may not be available on a timely basis or at all. Difficulties or delays in our manufacturing could increase our costs and damage our reputation.

The manufacture of pharmaceutical products can be an expensive, time consuming, and complex process. Manufacturers often encounter difficulties in scaling-up production of new products, including quality control and assurance and shortages of personnel. Delays in formulation and scale-up to commercial quantities could result in additional expense and delays in our clinical trials, regulatory submissions, and commercialization.

Failure of manufacturing facilities producing our product candidates to maintain regulatory approval could delay or otherwise hinder our ability to market our product candidates. Any manufacturer of our product candidates will be subject to applicable cGMP prescribed by the FDA or other rules and regulations prescribed by the NMPA and other foreign regulatory authorities. We and any of

our collaborators may be unable to enter into or maintain relationships either domestically or abroad with manufacturers whose facilities and procedures comply or will continue to comply with cGMP and who are able to produce our products in accordance with applicable regulatory standards. Failure by a manufacturer of our products to comply with cGMP could result in significant time delays or our inability to obtain marketing approval or, should we have market approval, for such approval to continue. Changes in our manufacturers could require new product testing and facility compliance inspections. In the U.S., failure to comply with cGMP or other applicable legal requirements can lead to federal seizure of violated products, injunctive actions brought by the federal government, inability to export product, and potential criminal and civil liability on the part of a company and its officers and employees.

The design and manufacture of a manufacturing facility by CASI Wuxi may be delayed.

Together with our partner, Wuxi Jintou Huicun Investment Enterprise, a limited partnership organized under Chinese law, we established CASI Wuxi, to build and operate a GMP manufacturing facility in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China. Under the terms of our agreement, we have agreed to invest $80 million in CASI Wuxi. As of December 31, 2021, we have invested $31 million in cash and transferred selected ANDAs valued at $30 million to CASI Wuxi . We are required to invest an additional $19 million in cash for the following two years. We have an 80% interest in CASI Wuxi and our partner has a 20% interest.

In November 2019, CASI Wuxi entered into a lease agreement for the right to use state-owned land in China for the construction of a manufacturing facility. Pursuant to this agreement, CASI Wuxi has committed to invest in land use rights and property, plant and equipment of RMB1 billion (equivalent to US $143 million) by August 2022. The lease agreement also specifies dates by which certain milestones must be met, including a construction start date in August 2020. Construction of the manufacturing facility began in the fourth quarter of 2020. In February 2022, we have reached an alignment with the Wuxi local government that we will collaborate with Wuxi LP to co-develop the land continuously in the future, and the development plan will be extended, details regarding the plan are under negotiation.

The undertaking of building and establishing a new manufacturing facility can take years. Once completed, the new facility might fail validation or not meet regulatory standards for a commercial manufacturing facility. In addition, the facility may not obtain or retain the requisite legal permits to manufacture in China, and costs or operational limitations may be imposed in connection with obtaining and complying with such permits. Accordingly, there can be no assurance that CASI Wuxi will meet the expenditure requirements and other deadlines set forth in the lease agreement.

The success of CASI Wuxi also relies on our ability to make additional payments in the future, which is uncertain. Our plan may require us to obtain additional debt or equity financing, resulting in additional debt obligations, increased interest expense or dilution of equity ownership.

The timing of the development and investment plans for a manufacturing facility are subject to further discussions with the government. We may seek to renegotiate the terms of our investment in CASI Wuxi, as well as the terms of the various agreements to which CASI Wuxi is a party. There can be no assurance that we will be able to obtain more favorable terms.

If we fail to maintain an effective distribution channel for our medicines, our business and sales could be adversely affected

We rely on third-party distributors to distribute our approved medicines. Our ability to maintain and grow our business will depend on our ability to maintain an effective distribution channel that ensures the timely delivery of our medicines. However, we have relatively limited control over our distributors, who may fail to distribute our drugs in the manner we contemplate. If price controls or other factors substantially reduce the margins our distributors can obtain through the resale of our medicines to hospitals, medical institutions and sub-distributors, they may terminate their relationship with us. While we believe alternative distributors are readily available, there is a risk that, if the distribution of our medicines is interrupted, our sales volumes and business prospects could be adversely affected.

Risks Related to Extensive Government Regulation

All material aspects of the research, development, manufacturing and commercialization of pharmaceutical products are heavily regulated, and we may face difficulties in complying with or be unable to comply with such regulations, which could have a material adverse effect on our business

All jurisdictions in which we conduct or intend to conduct our pharmaceutical-industry activities regulate these activities in great depth and detail. We are currently focusing our activities in the major markets of the United States, China and Europe. These geopolitical areas all strictly regulate the pharmaceutical industry, and in doing so they employ broadly similar regulatory strategies,

including regulation of product development and approval, manufacturing, and marketing, sales and distribution of products. However, there are differences in the regulatory regimes-some minor, some significant-that make for a more complex and costly regulatory compliance burden for a company like ours that plans to operate in each of these regions.

The process of obtaining regulatory approvals and compliance with appropriate laws and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process, or after approval, may subject us to administrative or judicial sanctions. These sanctions could include a regulator's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, voluntary or mandatory product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. The failure to comply with these regulations could have a material adverse effect on our business.

We are subject to certain U.S. healthcare laws, regulation and enforcement; our failure to comply with those laws could have a material adverse effect on our results of operations and financial condition.

We are subject to certain U.S. healthcare laws and regulations and enforcement by the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, without limitation:

- the federal Anti-Kickback Statute ("AKS"), which governs our business activities, including our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities. The AKS prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. Remuneration has been broadly interpreted to include anything of value, including for example, gifts, discounts, coupons, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others;
- the FFDCA, and its regulations which prohibit, among other things, the introduction or delivery for introduction into interstate commerce of any food, drug, device, biologic, or cosmetic that is adulterated or misbranded;
- the PHSA, which prohibits, among other things, the introduction into interstate commerce of biological product unless a biologics license is in effect for that product;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA and its implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal and state government price reporting laws that require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on our marketed drugs (participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, and could potentially affect our ability to offer certain marketplace discounts); and

- federal and state financial transparency laws, which generally require certain types of expenditures in the U.S. to be tracked and reported (compliance with such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships with healthcare providers and healthcare entities, which could potentially have a negative effect on our business and/or increase enforcement scrutiny of our activities).

In addition, certain marketing practices, including off-label promotion, may also violate certain federal and state healthcare fraud and abuse laws, FDA rules and regulations, as well as false claims laws. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we, or our officers or employees, may be subject to penalties, including administrative civil and criminal penalties, damages, fines, withdrawal of regulatory approval, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to sell our products or operate our business and also adversely affect our financial results.

Current healthcare laws and regulations and future legislative or regulatory reforms to the healthcare system may affect our ability to sell our products profitably.

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payers in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

We expect that healthcare reform measures, including the potential repeal and replacement of the Patient Protection and Affordable Care Act ("PPACA"), that may be adopted in the future, may have a significant impact on our business. Most recently, the Tax Cuts and Jobs Acts was enacted, which, among other things, removed penalties for not complying with the individual mandate to carry health insurance. Additionally, all or a portion of PPACA and related subsequent legislation may be modified, repealed or otherwise invalidated through judicial challenge, which could result in lower numbers of insured individuals, reduced coverage for insured individuals and adversely affect our business. If PPACA is repealed or replaced, it is unclear how the replacement statute may impact our business. If PPACA is not repealed or replaced, it will continue to impose requirements on our business.

Moreover, certain politicians have announced intentions to propose initiatives to regulate the prices of pharmaceutical products. We cannot know what form any such legislation may take or the market's perception of how such legislation would affect us. Any reduction in reimbursement from government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our current products and/or those for which we may receive regulatory approval in the future.

Our medicines and any future approved drug candidates will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our medicines and drug candidates.

Our medicines and any additional drug candidates that are approved will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-marketing information, including both federal and state requirements in China, the US and other regions. As such, we and our collaborators will be subject to ongoing review and periodic inspections to assess compliance with applicable post-approval regulations. Additionally, to the extent we want to make certain changes to the approved medicines, product labeling, or manufacturing processes, we will need to submit new applications or supplements to regulatory authorities for approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, NMPA and comparable regulatory authority requirements, ensuring that quality control and manufacturing procedures conform to GMP regulations. As such, we and our contract manufacturers are and will be subject to continual review and inspections to assess compliance with GMP and adherence to commitments made in any NDA or BLA, other marketing application, and previous responses to any inspection observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. The failure to comply with these requirements could have a material adverse effect on our business.

The regulatory approvals for our medicine and any approvals that we receive for our drug candidates are and may be subject to limitations on the approved indicated uses for which the medicine may be marketed or to the conditions of approval, which could adversely affect the drug's commercial potential or contain requirements for potentially costly post-marketing testing and surveillance

to monitor the safety and efficacy of the drug or drug candidate. The FDA, NMPA, EMA or comparable regulatory authorities may also require a REMS program or comparable program as a condition of approval of our drug candidates or following approval. In addition, if the FDA, NMPA, EMA or a comparable regulatory authority approves our drug candidates, we will have to comply with requirements including, for example, submissions of safety and other post-marketing information and reports, establishment registration, as well as continued compliance with GMP and good clinical practice ("GCP") for any clinical trials that we conduct post-approval.

The FDA, NMPA, EMA or comparable regulatory authorities may seek to impose a consent decree or withdraw marketing approval if compliance with regulatory requirements is not maintained or if problems occur after the drug reaches the market. Later discovery of previously unknown problems with our medicines or drug candidates or with our drug's manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our medicines, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, untitled or warning letters, or holds on clinical trials;
- refusal by the FDA, NMPA, EMA or comparable regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals or withdrawal of approvals;
- product seizure or detention, or refusal to permit the import or export of our medicines and drug candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA, NMPA, EMA and other regulatory authorities strictly regulate the marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for their approved indications and for use in accordance with the provisions of the approved label. The FDA, NMPA, EMA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA, NMPA, EMA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad, particularly in China, where the regulatory environment is constantly evolving. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained and we may not achieve or sustain profitability.

In addition, if we obtain accelerated approval or conditional approval of any of our drug candidates, as we have done with the initial approval of EVOMELA® in China we will be required to conduct a confirmatory study (also called Post Marketing Study "PMS") to verify the predicted clinical benefit and may also be required to conduct post-marketing safety studies. Other comparable regulatory authorities may have similar requirements. The results from the confirmatory study may not support the clinical benefit, which could result in the approval being withdrawn. While operating under accelerated approval, we will be subject to certain restrictions that we would not be subject to upon receiving regular approval.

Risks Relating to Our Intellectual Property

We depend on patents and other proprietary rights, some of which are uncertain. If we are unable to protect our intellectual property rights our business and competitive position would be harmed.

We have in-licensed rights to a variety of product candidates. Our success, competitive position and future revenues with respect to these product candidates will depend, in part, on our ability to protect our intellectual property. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. We attempt to protect our proprietary position by maintaining trade secrets and by filing U.S. and foreign patent applications related to our in-licensed technology, inventions and improvements that are important to the development of our business. Our failure to do so may adversely affect our business and competitive position.

The patent positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. We may not be able to protect our intellectual property rights throughout the world. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the U.S. or in many jurisdictions outside of the U.S. Changes in either the patent laws or interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property and therefore we cannot predict with certainty whether any patent

applications that we have filed or that we may file in the future will be approved, will cover our products or product candidates or that any resulting patents will be enforced. In addition, third parties may challenge, seek to invalidate, limit the scope of or circumvent any of our patents, once they are issued. Thus, any patents that we own or license from third parties or CASI Wuxi or development partners may not provide any protection against competitors. Any patent applications that we have filed or that we may file in the future, or those we may license from third parties or CASI Wuxi or development partners, may not result in patents being issued. Moreover, disputes between our licensing or joint development partners and us may arise over license scope, or ownership, assignment, inventorship and/or rights to use or commercialize patent or other proprietary rights, which may adversely impact our ability to obtain and protect our proprietary technology and products. Also, patent rights may not provide us with adequate proprietary protection or competitive advantages against competitors with similar technologies or products.

Third parties may initiate legal proceedings alleging infringement of intellectual property rights, the outcome of which would be uncertain and could harm our business

Third parties may assert patent or other intellectual property infringement claims against us or our licensors arising from the manufacture, use and sale of our current or future product candidates in China or in any other jurisdictions we ultimately commercialize in. The validity of our current or future patents or patent applications or those of our licensors may be challenged in litigation, interference or derivation proceedings, opposition, post grant review, inter parts review, or other similar enforcement and revocation proceedings, provoked by third parties or brought by us, may be necessary to determine the validity of our patents or patent applications or those of our licensors. Our patents could be found invalid, unenforceable, or their scope significantly reduced.

An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

Although China recently adopted changes to its patent law to include patent term extension and an early resolution mechanism for pharmaceutical patent disputes starting in June 2021, key provisions of the law remain unclear and/or subject to implementing regulations. The absence of effective regulatory exclusivity for pharmaceutical products in China could further increase the risk of early generic or biosimilar competition with our medicines in China.

In China, laws on patent term extension, patent linkage, and data exclusivity (referred to as regulatory data protection) are still developing. Therefore, a lower-cost generic drug can emerge onto the market much more quickly. Chinese regulators have set forth a framework for integrating patent linkage and data exclusivity into the Chinese regulatory regime, as well as for establishing a pilot program for patent term extension. The Economic and Trade Agreement Between the United States of America and the People's Republic of China announced in January 2020 (the "Trade Agreement") also provides for a mechanism for early resolution of patent disputes and patent term extension systems. To be implemented, this framework will require adoption of legislation and regulations. In October 2020, China adopted amendments to its Patent Law (the "Amended PRC Patent Law"), which will become effective on June 1, 2021. The Amended PRC Patent Law contains both patent term extension and a mechanism for early resolution of patent disputes, which may be comparable to patent linkage in the United States. However, the provisions for patent term extension and an early resolution mechanism are unclear and/or remain subject to the approval of implementing regulations that are still in draft form or have not yet been proposed, leading to uncertainty about their scope and implementation.

Until the relevant implementing regulations for patent term extension and an early resolution mechanism in the Amended PRC Patent Law are implemented, and until data exclusivity is adopted and implemented, we may be subject to earlier generic competition.

Risks Relating to Our Common Stock

The market price of our common stock may be highly volatile or may decline regardless of our operating performance.

The volatile price of our stock makes it difficult for investors to predict the value of their investments, to sell shares at a profit at any given time, or to plan purchases and sales in advance. Our common stock price has fluctuated from year-to-year and quarter-to-quarter and will likely continue to be volatile. During 2021, our stock price ranged from $0.77 to $3.63. We expect that the trading price of our common stock is likely to be highly volatile in response to a variety of factors that are beyond our control, such as:

- our ability to maintain regulatory approval for EVOMELA® and obtain regulatory approval for our other product candidates;

- issues in importation, marketing and sales of EVOMELA®;
- the success of CASI Wuxi to build and operate a manufacturing facility in China;
- the clinical development of CNCT19, BI-1206 and CID-103;
- publicity regarding actual or potential clinical test results relating to products under development by our competitors or us;
- initiating, completing or analyzing, or a delay or failure in initiating, completing or analyzing, preclinical or clinical trials or animal trials or the design or results of these trials for products in development;
- the entry into, or termination of, key agreements, including key commercial partner agreements;
- the initiation of, material developments in, or conclusion of litigation to enforce or defend any of our intellectual property rights or defend against the intellectual property rights of others;
- achievement or rejection of regulatory approvals for products in development by our competitors or us;
- announcements of technological innovations or new commercial products by our competitors or us;
- developments concerning our collaborations and supply chain;
- regulatory developments in the United States and foreign countries;
- economic or other crises and other external factors;
- COVID-19 pandemic, especially as a result of investor concerns and uncertainty related to the impact of the outbreak on the economics of countries worldwide;
- the loss of key employees;
- period-to-period fluctuations in our revenues and other results of operations;
- changes in financial estimates by securities analysts; or
- publicity or activity involving possible future acquisitions, strategic investments, partnerships or alliances.

We will not be able to control many of these factors, and we believe that period-to-period comparisons of our financial results will not necessarily be indicative of our future performance. The valuations of many biotechnology companies without consistent product revenues and earnings are extraordinarily high based on conventional valuation standards, such as price to earnings and price to sales ratios. These trading prices and valuations may not be sustained. In the future, our operating results in a particular period may not meet the expectations of any securities analysts whose attention we may attract, or those of our investors, which may result in a decline in the market price of our common stock. Any negative change in the public's perception of the prospects of biotechnology companies could depress our stock price regardless of our results of operations. These factors may materially and adversely affect the market price of our common stock.

Our largest stockholders, including our directors and executive officers and investment funds with which they are associated, hold a significant amount of our outstanding common stock and, if they acted together, could influence our management and affairs.

A small number of our stockholders, including our directors and executive officers and investment funds with which they are associated, hold a significant amount of our outstanding common stock. In addition, our executive officers and directors and investment funds with which they are associated could determine to make additional purchases of common stock, to the extent permitted by law. In the future, our executive officers and directors also could be issued shares of common stock as determined by the Compensation Committee and the Board in connection with current or future equity incentive plans.

These stockholders, if they acted together, could significantly influence the vote on all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. We cannot assure you that our largest stockholders will not seek to influence our business and affairs in a manner that is contrary to the interests of our other stockholders. In addition, the significant concentration of ownership in our common stock may adversely affect the trading price for our common stock because investors often perceive disadvantages in owning stock in companies with significant stockholders.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for certain legal actions between us and our stockholders, which could increase costs to bring a claim, discourage claims or limit the ability of our stockholders to bring a claim in a judicial forum viewed by the stockholders as more favorable for disputes with us or our directors, officers or other employees.

Our amended and restated bylaws, effective September 10, 2020, provide that unless CASI consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any (i) any derivative action or proceeding brought on behalf of CASI, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of CASI to CASI or CASI's stockholders, (iii) any action asserting a claim arising under any provision of the General Corporation Law of the State of Delaware, CASI's certificate of incorporation or CASI's Amended and Restated By-Laws or (iv) any action asserting a claim governed by the internal affairs doctrine. The choice of forum provision may increase costs to bring a claim, discourage claims or limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us or our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated bylaws to be inapplicable or unenforceable in an action, CASI may incur additional costs associated with resolving such action in other jurisdictions. In addition, unless CASI consents in writing to the selection of an alternative forum, the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933.

Risks Relating to Our Auditor

The audit report included in this Annual Report on Form 10-K are prepared by auditors who are not currently inspected by the PCAOB and, as such, our stockholders are deprived of the benefits of such inspection. In addition, various legislative and regulatory developments related to U.S.-listed China based companies due to lack of PCAOB inspection and other developments due to political tensions between the United States and China may have a material adverse impact on our listing and trading in the United States and the trading prices of our shares of common stock.

Our auditor, the independent registered public accounting firm that issued the audit report included in this Annual Report on Form 10-K, as an auditor of companies that are traded publicly in the United States and a firm registered with the Public Company Accounting Oversight Board ("PCAOB"), is subject to laws in the United States pursuant to which the PCAOB conducts regular inspections to assess its compliance with applicable professional standards. Our auditor is located in, and organized under the laws of, the PRC, which is a jurisdiction where the PCAOB has been unable to conduct inspections without the approval of the Chinese authorities.

On April 21, 2020, the SEC and the PCAOB released a joint statement highlighting the risks associated with investing in companies based in or having substantial operations in emerging markets including China. The joint statement emphasized the risks associated with lack of access for the PCAOB to inspect auditors and audit work papers in China and higher risks of fraud in emerging markets.

On May 18, 2020, Nasdaq filed three proposals with the SEC to (i) apply a minimum offering size requirement for companies primarily operating in a "Restrictive Market," (ii) adopt a new requirement relating to the qualification of management or the board of directors for Restrictive Market companies, and (iii) apply additional and more stringent criteria to an applicant or listed company based on the qualifications of the company's auditor.

On December 18, 2020, the President signed the "Holding Foreign Companies Accountable Act" (the "HFCAA") into law. This legislation requires certain issuers of securities to establish that they are not owned or controlled by a foreign government. Specifically, an issuer must make this certification if the PCAOB is unable to audit specified reports because the issuer has retained a foreign public accounting firm not subject to inspection by the PCAOB. Furthermore, if the PCAOB is unable to inspect the issuer's public accounting firm for three consecutive years, the issuer's securities are banned from trading on a national exchange or through other methods.

On March 24, 2021, the SEC adopted interim final rules relating to the implementation of certain disclosure and documentation requirements of the HFCA Act. We will be required to comply with these rules if the SEC identifies us as having a "non-inspection" year under a process to be subsequently established by the SEC. On December 2, 2021, the SEC adopted final amendments to its rules implementing the HFCA Act (the "Final Amendments"). The Final Amendments finalize the interim final rules adopted in March with two major modifications. First, the Final Amendments clarify how the requirements apply to variable interest entities. Second, the Final Amendments include requirements to disclose information, including the auditor name and location, the percentage of shares of the issuer owned by governmental entities, whether governmental entities in the applicable foreign jurisdiction with respect to the auditor has a controlling financial interest with respect to the issuer, the name of each official of the Chinese Communist Party who is a member

of the board of the issuer, and whether the articles of incorporation of the issuer contains any charter of the Chinese Communist Party. The Final Amendments also establish procedures the SEC will follow in identifying issuers and prohibiting trading by certain issuers under the HFCA Act.

On June 22, 2021, the U.S. Senate passed the Accelerating Holding Foreign Companies Accountable Act (the "AHFCA Act"), which if enacted into law would amend the HFCA Act and require the SEC to prohibit an issuer's securities from trading on any U.S. stock exchanges if its auditor is not subject to PCAOB inspections for two consecutive years instead of three.

On November 5, 2021, the SEC approved the PCAOB's Rule 6100, Board Determinations Under the Holding Foreign Companies Accountable Act. Rule 6100 will establish a framework for the PCAOB's determinations under the HFCA Act that the PCAOB is unable to inspect or investigate completely registered public accounting firms located in a foreign jurisdiction because of a position taken by an authority in that jurisdiction. On December 16, 2021, the PCAOB issued a report to notify the SEC its determinations that it is unable to inspect or investigate completely registered public accounting firms headquartered in Mainland China and identifies the registered public accounting firms in Mainland China that are subject to such determinations. Our auditor is identified by the PCAOB and is subject to the determination.

The lack of access to the PCAOB inspection in China prevents the PCAOB from fully evaluating audits and quality control procedures of the auditors based in China. As a result, investors may be deprived of the benefits of such PCAOB inspections. The inability of the PCAOB to conduct inspections of auditors in China makes it more difficult to evaluate the effectiveness of these accounting firm's audit procedures or quality control procedures as compared to auditors outside of China that are subject to the PCAOB inspections, which could cause investors and potential investors in our common stock to lose confidence in our audit procedures and reported financial information and the quality of our financial statements**.**

We could be delisted if our auditors are unable to meet the PCAOB inspection requirements in time.

The HFCAA requires the SEC to prohibit securities of any foreign companies from being listed on U.S. securities exchanges or traded "over-the-counter" if a company retains a foreign accounting firm that cannot be inspected by the PCAOB for three consecutive years, beginning in 2021. The AHFCAA would shorten this period to two consecutive years, also beginning in 2021. Our independent registered public accounting firm is located in and organized under the laws of the PRC, a jurisdiction where the PCAOB is currently unable to conduct inspections without the approval of the Chinese authorities, and therefore our auditors are not currently inspected by the PCAOB. As such, the requirements under the HFCAA will apply to us beginning in 2022, and we will be subject to the related reporting requirements in 2023 and (as discussed below) the trading restrictions would apply to us in 2024.

The enactment of the HFCAA, the AHFCAA and any additional rulemaking efforts to increase U.S. regulatory access to audit information in China could cause investor uncertainty for affected SEC registrants, including us, and the market price of our shares of common stock could be materially adversely affected. Additionally, whether the PCAOB will be able to conduct inspections of our auditors in the next three years, or at all, is subject to substantial uncertainty and depends on a number of factors out of our control. If we are unable to meet the PCAOB inspection requirement in time, we could be delisted from the Nasdaq Capital Market and our shares of common stock will not be permitted for trading "over-the-counter" market. Such a delisting would substantially impair your ability to sell or purchase our shares of common stock when you wish to do so, and the risk and uncertainty associated with delisting would have a negative impact on the price of our shares. Also, such a delisting would significantly affect our ability to raise capital on terms acceptable to us, or at all, which would have a material adverse impact on our business, financial condition and prospects.

Risks Relating to Our Business Operations in China

We conduct a majority of our operations in China, which exposes us to risks associated with operating outside of the U.S. Changes in international trade and economic policy by the U.S. and Chinese governments could have a material adverse effect on our business and operations.

We have operations and conduct business in China, and we plan to continue to expand these operations. Therefore, we are subject to risks related to operating in foreign countries, which include complex foreign laws or regulatory requirements or unexpected changes to those laws or requirements; other laws and regulatory requirements to which our business activities abroad are subject, such as the Foreign Corrupt Practices Act; changes in the political or economic condition of a specific country or region; fluctuations in the value of foreign currency versus the U.S. dollar; our ability to deploy overseas funds in an efficient manner; tariffs, trade protection measures, import or export licensing requirements, trade embargoes, and sanctions (including those administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury), and other trade barriers; difficulties in attracting and retaining qualified personnel; and cultural differences in the conduct of business. There is currently significant uncertainty about the future relationship between the U.S. and various other countries, including China, with respect to trade policies, treaties, government regulations and tariffs.

Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current political climate could adversely impact our business.

Governmental control of currency conversion and payments of RMB out of mainland China may limit our ability to utilize our cash balances effectively and affect the value of your investment.

Our China subsidiaries have cash and cash equivalents of 122.9 million China Renminbi ("RMB"), valued at $19.3 million in U.S. dollars as of December 31, 2021. On a consolidated basis this balance accounts for 50% of our total cash and cash equivalents. The Chinese government imposes controls on the convertibility of RMB into foreign currencies and, in certain cases, the remittance of RMB out of mainland China. Control on payments out of mainland China may restrict the ability of our China subsidiaries to remit RMB to us. Approval from China's State Administration of Foreign Exchange ("SAFE") and the People's Bank of China ("PBOC") may be required where RMB are to be converted into foreign currencies, including U.S. dollars, and approval from SAFE and the PBOC or their branches may be required where RMB are to be remitted out of mainland China. Specifically, under the existing restrictions, without prior approval from SAFE and the PBOC, the cash balance of our China subsidiaries is not available to us for activities outside of China, including the support of our in-licensing efforts. Furthermore, because repatriation of funds requires the prior approval of SAFE and the PBOC, such repatriation could be delayed, restricted or limited.

Changes in China's economic, political or social conditions or government policies could have a material adverse effect on our business and operations.

Chinese society and the Chinese economy continue to undergo significant change. Adverse changes in the political and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes, any of which could materially and adversely affect our liquidity, access to capital and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China.

The Chinese government exerts substantial influence over the manner in which we must conduct our business activities.

The China government has exercised and continues to exercise substantial control over virtually every sector of the Chinese economy through regulation and state ownership. Our ability to operate in China may be harmed by changes in its laws and regulations, including those relating to taxation, import and export tariffs, environmental regulations, land use rights, property, healthcare regulations, and other matters. We believe that our operations in China are in material compliance with all applicable legal and regulatory requirements. However, the central or local governments of the jurisdictions in which we operate may impose new, stricter regulations or interpretations of existing regulations that would require additional expenditures and efforts on our part to ensure our compliance with such regulations or interpretations.

Accordingly, government actions in the future, including any decision not to continue to support recent economic reforms and to return to a more centrally planned economy or regional or local variations in the implementation of economic policies, could have a significant effect on economic conditions in China or particular regions thereof and could require us to divest ourselves of any interest we then hold in Chinese properties, subsidiaries, or joint ventures.

We are subject to the Enterprise Income Tax Law, and we may therefore be subject to PRC income tax on our global income.

Under the PRC Enterprise Income Tax Law and its implementing rules, both of which came into effect on January 1, 2008, enterprises established under the laws of jurisdictions outside of China with "de facto management bodies" located in China may be considered PRC tax resident enterprises for tax purposes and may be subject to the PRC enterprise income tax at the rate of 25% on their global income. "De facto management body" refers to a managing body that exercises substantive and overall management and control over the production and business, personnel, accounting books and assets of an enterprise. The State Administration of Taxation issued the Notice Regarding the Determination of Chinese-Controlled Offshore-Incorporated Enterprises as PRC Tax Resident Enterprises on the basis of de facto management bodies, or Circular 82, on April 22, 2009. Circular 82 provides certain specific criteria for determining whether the "de facto management body" of a Chinese-controlled offshore-incorporated enterprise is located in China.

Although Circular 82 only applies to offshore enterprises controlled by PRC enterprises, not those controlled by foreign enterprises or individuals, the determining criteria set forth in Circular 82 may reflect the State Administration of Taxation's general position on how the "de facto management body" test should be applied in determining the tax resident status of offshore enterprises, regardless of whether they are controlled by PRC enterprises. If we were to be considered a PRC resident enterprise, we would be subject to PRC enterprise income tax at the rate of 25% on our global income. In such case, our profitability and cash flow may be materially reduced as a result of our global income being taxed under the Enterprise Income Tax Law. Although we believe that none of our entities outside of China should be considered a PRC resident enterprise for PRC tax purposes. the tax resident status of an enterprise is subject to determination by the PRC tax authorities and uncertainties remain with respect to the interpretation of the term "de facto management body."

China regulations relating to investments in offshore companies by China residents may subject our China-resident stockholders, beneficial owners or our China subsidiaries to liability or penalties, limit our ability to inject capital into our China subsidiaries or limit our China subsidiaries' ability to increase their registered capital or distribute profits to us.

The State Administration of Foreign Exchange, or SAFE, promulgated the Circular on Relevant Issues Concerning Foreign Exchange Control on Domestic Residents' Offshore Investment and Financing and Roundtrip Investment through Special Purpose Vehicles, or SAFE Circular 37, on July 4, 2014, which replaced the former circular commonly known as "SAFE Circular 75" promulgated by SAFE on October 21, 2005. SAFE Circular 37 requires China residents to register with local branches of SAFE in connection with their direct establishment or indirect control of an offshore entity, for the purpose of overseas investment and financing, with such China residents' legally owned assets or equity interests in domestic enterprises or offshore assets or interests, referred to in SAFE Circular 37 as a "special purpose vehicle." SAFE Circular 37 further requires amendment to the registration in the event of any significant changes with respect to the special purpose vehicle, such as increase or decrease of capital contributed by China individuals, share transfer or exchange, merger, division or other material event. In the event that a China shareholder holding interests in a special purpose vehicle fails to fulfill the required SAFE registration, the China subsidiaries of that special purpose vehicle may be prohibited from making profit distributions to the offshore parent and from carrying out subsequent cross-border foreign exchange activities, and the special purpose vehicle may be restricted in its ability to contribute additional capital into its China subsidiary. Moreover, failure to comply with the various SAFE registration requirements described above could result in liability under China law for evasion of foreign exchange controls. According to the Notice on Further Simplifying and Improving Policies for the Foreign Exchange Administration of Direct Investment released on February 13, 2015 by SAFE, local banks will examine and handle foreign exchange registration for overseas direct investment, including the initial foreign exchange registration and amendment registration, under SAFE Circular 37 from June 1, 2015.

According to SAFE Circular 37, our stockholders or beneficial owners, who are China residents, are subject to SAFE Circular 37 or other foreign exchange administrative regulations in respect of their investment in our company. We may not be aware of the identities of all of our stockholders or beneficial owners who are China residents, and we do not know whether they are aware of SAFE Circular 37. We do not have control over our stockholders or beneficial owners and there can be no assurance that all of our China-resident stockholders or beneficial owners will comply with SAFE Circular 37 and subsequent implementation rules, and there is no assurance that the registration under SAFE Circular 37 and any amendment will be completed in a timely manner, or will be completed at all. The failure of our stockholders or beneficial owners who are China residents to register or amend their foreign exchange registrations in a timely manner pursuant to SAFE Circular 37 and subsequent implementation rules, or the failure of future stockholders or beneficial owners who are China residents to comply with the registration procedures set forth in SAFE Circular 37 and subsequent implementation rules, may subject such stockholders or beneficial owners or our China subsidiaries to fines and legal sanctions. Failure to register or comply with relevant requirements may also limit our ability to contribute additional capital to our China subsidiaries and limit our China subsidiaries' ability to distribute dividends to us. Because a majority of our operating activities take place in and our strategic focus is on China, any such limitations would have a material adverse effect on our business, financial condition and results of operations.

We may be subject to fines and legal sanctions by SAFE or other China government authorities if we or our employees who are China citizens fail to comply with regulations relating to employee stock options granted by companies listed on exchanges outside of China to China citizens.

On February 15, 2012, SAFE promulgated the Circular on Relevant Issues Concerning the Foreign Exchange Administration for Domestic Individuals' Participating in the Share Incentive Plans of Overseas-Listed Companies, or SAFE Circular 7, replacing earlier rules promulgated in 2007. Under SAFE Circular 7, China resident individuals who participate in a share incentive plan of a company that is listed on an overseas exchange are required to register with SAFE and complete certain other procedures. All participants to a plan need to retain a China agent through Chinese subsidiaries of the overseas listed company to handle foreign exchange

registration, account opening, funds transfer and remittance and other related matters. An overseas agent should also be designated to handle matters in connection with the exercise or sale of share awards and proceeds transferring for the share incentive plan participants. We believe that our share incentive plans for our China resident employees are in compliance with SAFE Circular 7; however, any failure to comply with these or similar regulations in the future may subject us or our Chinese employees to fines and legal sanctions imposed by SAFE or other government authorities and may prevent us from further granting options under our share incentive plans to our employees. Such events could adversely affect our business operations.

General Risk Factors

We may engage in strategic, commercial and other corporate transactions that could negatively affect our financial condition and prospects.

We may consider strategic, commercial, and other corporate transactions as opportunities present themselves. There are risks associated with such activities. These risks include, among others, incorrectly assessing the quality of a prospective strategic partner, encountering greater than anticipated costs in integration, being unable to profitably deploy assets acquired in the transaction, such as drug candidates, possible dilution to our stockholders, and the loss of key employees due to changes in management. Further, strategic transactions may place additional constraints on our resources by diverting the attention of our management from our business operations. To the extent we issue securities in connection with additional transactions, these transactions and related issuances may have a dilutive effect on existing shareholders. Our financial condition and prospects after an acquisition depend in part on our ability to successfully integrate the operations of the acquired business or technologies. We may be unable to integrate operations successfully or to achieve expected cost savings. Any cost savings which are realized may be offset by losses in revenues or other charges to earnings.

If securities or industry analysts publish inaccurate or unfavorable research about our business, our stock price could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who may cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our common stock price would likely decline.

Subsequent resales of shares of our common stock in the public market may cause the market price of our common stock to fall.

The market value of our common stock could decline as a result of sales by investors from time to time, or perceptions that such sales may occur, of a substantial amount of the shares of common stock held by them.

Issuances of additional shares of our common stock may cause substantial dilution of existing stockholders.

We may issue additional shares of common stock or other securities that are convertible into or exercisable for common stock in connection with future acquisitions, future sales of our securities for capital raising purposes, future strategic relationships, or for other business purposes. The future issuance of any additional shares of our common stock may create downward pressure on the trading price of our common stock. There can be no assurance that we will not be required to issue additional shares, warrants or other convertible securities in the future in conjunction with any capital raising efforts, including at a price (or exercise prices) below the price at which shares of our common stock are then traded.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934 and are not required to provide the information under this item.

ITEM 2. PROPERTIES.

As of December 31, 2021, we hold leases for land, office and laboratory space, as follows:

China:

- The primary office of CASI China is located in Beijing, China with approximately 14,000 square feet of office space.
- In November 2019, CASI Wuxi entered into a fifty-year lease agreement for the right to use state-owned land in Wuxi China. The land parcel is approximately 666,000 square feet, and the GMP manufacturing facility is now under construction.
- CASI Wuxi has workshop space of approximately 90,000 square feet.
- CASI China has office space in Shanghai of approximately 1,600 square feet.

United States:

- We have office space in Rockville, Maryland of approximately 6,100 square feet.

We believe that our facilities are adequate for current needs; however, the Company is in the process of expanding operations in China and, accordingly, intends to increase facilities to meet our foreseeable and long-term needs. We do not own any real property.

ITEM 3. LEGAL PROCEEDINGS.

CASI is subject in the normal course of business to various legal proceedings in which claims for monetary or other damages may be asserted. Management does not believe such legal proceedings, unless otherwise disclosed herein, are material.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Market for Common Equity

Our common stock trades on The Nasdaq Capital Market under the symbol "CASI." As of March 18, 2022, there were 254 holders of record of our common stock.

Dividend Policy

The Company has never declared or paid dividends on its common stock or any other securities and does not anticipate paying any dividends in the foreseeable future.

ITEM 6. SELECTED FINANCIAL DATA.

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934 and are not required to provide the information under this item.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

The following discussion should be read in conjunction with the Consolidated Financial Statements and Notes thereto appearing elsewhere in this report. See also "Risk Factors" in Item 1A of this Annual Report.

OVERVIEW

We are a U.S. biopharmaceutical company focused on developing and commercializing innovative therapeutics and pharmaceutical products in China, the United States, and throughout the world. We were incorporated in 1991, and in 2012, with new leadership, the Company shifted its business strategy to China and has since built an infrastructure in China that includes sales and marketing, medical affairs, regulatory and clinical development and in the foreseeable future, manufacturing. In 2014, the Company changed its name to "CASI Pharmaceuticals, Inc." We are focused on acquiring, developing and commercializing products that augment our hematology oncology therapeutic focus as well as other areas of unmet medical need. The Company is executing our plan to become a biopharmaceutical leader by launching medicines in the greater China market, leveraging our China-based regulatory, clinical and commercial competencies and our global drug development expertise. The majority of the Company's operations are now located in China and are conducted primarily through two of our subsidiaries: (i) CASI Pharmaceuticals (China) Co., Ltd.. ("CASI China"), which is wholly owned and is located in Beijing, China, and (ii) CASI Pharmaceuticals (Wuxi) Co., Ltd.. ("CASI Wuxi"), which is located in Wuxi, China. Our Beijing office is primarily responsible for our day-to-day operations and our commercial team of over 100 hematology/oncology sales and marketing specialists based in China. CASI Wuxi is part of the long-term strategy to support our future clinical and commercial manufacturing needs, to manage our supply chain for certain products, and to develop a GMP manufacturing facility in China.

We launched our first commercial product, EVOMELA® (Melphalan for Injection) in China in August 2019. In China, EVOMELA® is approved for use as a conditioning treatment prior to stem cell transplantation and as a palliative treatment for patients with multiple myeloma. The other core hematology/oncology assets in the Company's pipeline include:

- *CNCT19* is an autologous CD19 CAR-T investigative product (CNCT19) being developed by the Company's partner Juventas for which the Company has exclusive World-Wide co-commercial and profit-sharing rights. CNCT19 is being developed as a potential treatment for patients with hematological malignancies which express CD19 including, B-cell acute lymphoblastic leukemia ("B-ALL") and B-cell non-Hodgkin lymphoma ("B-NHL"). The CNCT19 Phase 1 studies in patients with B-ALL and B-NHL in China have been completed by Juventas, the Phase 2 B-ALL and B-NHL registration studies are both currently enrolling in China the fourth quarter of 2020.

- *BI-1206* is an antibody which has a novel mode-of-action, blocking the inhibitory antibody checkpoint receptor FcγRIIB to unlock anti-cancer immunity and enhance the efficacy of antibody-based immunotherapy in both hematological malignancies and solid tumors for which the Company has licensed exclusive greater China rights from BioInvent International AB ("BioInvent"). BI-1206 is being investigated by BioInvent in a Phase 1/2 trial, in combination with anti-PD1 therapy Keytruda® (pembrolizumab), in patients with solid tumors, and in a Phase 1/2a trial in combination with MabThera® (rituximab) in patients with relapsed/refractory non-Hodgkin lymphoma (NHL). BI-1206 has the potential to restore the activity of rituximab in patients with relapsed/refractory non-Hodgkin lymphoma. Clinical Trial Application (CTA) was approved by China National Medical Products Administration (NMPA) in December 2021. The Company is planning Phase 1 trials of BI-1206 as a single agent to evaluate the PK/safety profile and in combination with rituximab in patients with NHL (mantle cell lymphoma, marginal zone lymphoma, and follicular lymphoma) to assess safety and tolerability, select the Recommended Phase 2 Dose and assess early signs of clinical efficacy as part of its development program for BI-1206 in China. The studies are expected to start in the first half of 2022.

- *CB-5339* is a novel VCP/p97 inhibitor focused on valosin-containing protein (VCP)/p97 as a novel target in protein homeostasis, DNA damage response and other cellular stress pathways for therapeutic use in the treatment of patients with various malignancies. The Company entered into an exclusive license on March 21, 2021 with Cleave Therapeutics, Inc. (Cleave") for the development and commercialization of CB-5339 in Mainland China, Hong Kong, Macau and Taiwan. CB-5339, an oral second-generation, small molecule VCP/p97 inhibitor, is being evaluated in a Phase 1 clinical trial in patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). CB-5339 CTA application for the multiple myeloma indication is in preparation after receiving an acceptance letter for the CB-5339 IND package from the China CDE.

- *CID-103* is a full human IgG1 anti-CD38 monoclonal antibody recognizing a unique epitope that has demonstrated encouraging preclinical efficacy and safety profile compared to other anti-CD38 monoclonal antibodies for which the Company has exclusive global rights. CID-103 is being developed for the treatment of patients with multiple myeloma. The Phase 1 dose escalation and expansion study of CID-103, in patients with previously treated, relapsed or refractory multiple myeloma is ongoing in the UK and France.

The Company also has greater China rights to Octreotide (Long Acting Injectable), a standard of care for the treatment of acromegaly and for the control of symptoms associated with certain neuroendocrine tumors; and Thiotepa, a cytotoxic agent which has a long history of established use in the hematology/oncology setting, the Company has an exclusive China license and distribution rights to a novel formulation of thiotepa, which has multiple indications including use as a conditioning treatment for certain allogeneic haemopoietic stem cell transplants. However, due to the evolving standard of care environment, the rare and niche indication for these products, potential US regulatory action and the Company's commitment to prioritize resources, the Company is currently evaluating its options for these products. In addition, the Company's assets include six FDA-approved ANDAs which the Company is evaluating due to generic drug pricing reforms by the Chinese government and its impact on the pricing and competitiveness of these products.

CASI has built a fully integrated, world class biopharmaceutical company dedicated to the successful development and commercialization of innovative and other therapeutic products. Our business development strategy is currently focused on acquiring additional targeted drugs and immuno-oncology therapeutics through licensing that will expand our hematology/oncology franchise. We use a market-oriented approach to identify pharmaceutical/biotechnology candidates that we believe to have the potential for gaining widespread market acceptance, either globally or in China, and for which development can be accelerated under our global drug development strategy. In many cases our business development strategy includes direct equity investments in the licensor company. We intend for our pipeline to reflect a diversified and risk-balanced set of assets that include (1) late-stage clinical drug candidates in-licensed for China or global regional rights, (2) proprietary or licensed innovative drug candidates, and (3) select high quality pharmaceuticals that fit our therapeutic focus. We have focused on US/EU approved product candidates, and product candidates with proven targets or product candidates that have reduced clinical risk with a greater emphasis on innovative therapeutics. Although oncology with a focus on hematological malignancies is our principal clinical and commercial target, we are opportunistic about other therapeutic areas that can address unmet medical needs. We will continue to pursue building a robust pipeline of drug candidates for development and commercialization in China as our primary market, and if rights are available for the rest of the world.

We believe our China operations offer a significant market and growth potential due to the extraordinary increase in demand for high quality medicines coupled with regulatory reforms in China that facilitate the entry of new pharmaceutical products into the country. We will continue to in-license clinical-stage and late-stage drug candidates, and leverage our cross-border operations and expertise, and hope to be the partner of choice to provide access to the China market. We expect the implementation of our plans will

include leveraging our resources and expertise in both the U.S. and China so that we can maximize regulatory, development and clinical strategies in both countries.

The Company's commercial product, EVOMELA®, was originally licensed from Spectrum Pharmaceuticals, Inc. ("Spectrum") and the Company had a supply agreement with Spectrum to support the Company's application for import drug registration and for commercialization purposes. Spectrum completed the sale of its portfolio of FDA-approved hematology/oncology products including EVOMELA® to Acrotech Biopharma L.L.C. ("Acrotech") on March 1, 2019. The original supply agreement with Spectrum was assumed by Acrotech; Spectrum agreed to continue with a short-term supply agreement for EVOMELA® for the initial commercial product supply in connection with the Company's launch, with the long-term supply assumed by Acrotech.

As part of the long-term strategy to support our future clinical and commercial manufacturing needs and to manage our supply chain for certain products, on December 26, 2018, we established CASI Wuxi, between the Company and Wuxi LP, to develop a future GMP manufacturing facility that will be located in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China. In November 2019, CASI Wuxi entered into a fifty-year lease agreement for the right to use state-owned land in China for the construction of a GMP manufacturing facility. Pursuant to the agreement, CASI Wuxi has committed to invest land use right and property, plant and equipment of RMB1 billion (equivalent to $143 million) by August 2022. In April 2020, CASI Wuxi received RMB 15.9 million (equivalent to $2.2 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as government grant for this development project which was recorded as deferred income in April 2020. In November 2021, CASI Wuxi received an additional RMB 3.0 million (equivalent to $0.5 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as a government grant for this development project which was recorded as deferred income in November 2021. In 2020, for the design and construction work of the land, CASI Wuxi entered into several contracts for RMB 76.1 million ($12.0 million) to complete the phase 1 project of CASI Wuxi's research and development production base, the project was the estimated to be completed in October 2023. In February 2022, CASI Wuxi has reached an alignment with the Wuxi local government that it will collaborate with Wuxi LP to co-develop the land continuously in the future, and the development plan will be extended, details regarding the plan are under negotiation. Also in 2020, CASI Wuxi entered in to a lease agreement with local government for a manufactory building next to the leased land. Since then, the Company entered into a series of contracts for the remodeling and installation work of the building and warehouse, as well as purchase of equipments. The total contract amount entered into for this building is approximately RMB 92.9 million ($14.6 million).

During the peak of the COVID-19 pandemic in 2020, we experienced disruptions to the EVOMELA® marketing and sales activities as well as to the supply chain for EVOMELA®. The COVID-19 pandemic also impacted our targeted start time of our CID-103 trial due to the lock down of many medical facilities in Europe. During 2021, we have experienced minimal disruption to our business activities or supply chain as a result of the COVID-19 pandemic. Furthermore, in June 2021 we achieved the First-Patient-In (FPI) in the Phase 1 dose escalation and expansion study of CID-103 in patients with previously treated, relapsed or refractory multiple myeloma. The study is designed to assess the safety, tolerability, pharmacology and clinical activity of CID-103.

We currently rely on a single source for the supply of EVOMELA®. The continuation of the COVID-19 pandemic or the emergence of new COVID-19 variants or new pandemics may affect the economies and financial markets of many countries, which may result in a period of economic slowdown or recessions. In such an event, our ability to continue to commercialize and expand distribution of EVOMELA® could be adversely affected if the supplier refuses or is unable to provide products for any reason (including the occurrence of an event like the COVID-19 pandemic that makes delivery impractical). We would have to work with Acrotech to negotiate an agreement with a substitute supplier, which, assuming a substitute supplier was available, would likely interrupt the manufacturing of EVOMELA®, cause supply chain delays and increase costs.

The COVID-19 pandemic has adversely affected, and may continue to adversely affect, the economies and financial markets of many countries, which may result in a period of regional, national, and global economic slowdown or regional, national, or global recessions that could affect our ability to continue to commercialize and expand distribution of EVOMELA® (Melphalan For Injection) or other drugs in our existing product pipeline. Early in the COVID-19 pandemic, we experienced a disruption to our supply chain for EVOMELA®, we have experienced no supply disruption in 2021; however, there can be no assurance that restrictions will not be imposed again. In addition, economic and other uncertainties may adversely affect other parties' willingness to negotiate and execute product licenses and thus hamper our ability to in-license clinical-stage and late-stage drug candidates in China or elsewhere.

CRITICAL ACCOUNTING POLICIES AND THE USE OF ESTIMATES

The preparation of our financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. Actual results could differ materially from those estimates. Our critical accounting policies, including the items in our financial statements requiring significant estimates and judgments, are as follows:

Stock-Based Compensation

We record compensation expense associated with service and performance-based stock options in accordance with provisions of authoritative guidance. The estimated fair value of service-based awards is measured on the grant date and is generally amortized on a straight-line basis over the requisite service period and based on the proportionate amount of the requisite service period that has been rendered during each reporting period. The estimated fair value of performance-based awards is measured on the grant date and is recognized when it is determined that it is probable that the performance condition will be achieved. If the required vesting conditions are not met resulting in the forfeiture of the share-based awards, previously recognized compensation expense relating to those awards are reversed as occurred.

Grant date fair value was determined using an option pricing model which is affected by the fair value of underlying ordinary shares as well as assumptions regarding a number of complex and subjective variables, such as expected volitality, expected term of options, risk-free rate, and expected dividend yield.

Fair value measurement of investment in equity interests of Juventas Cell Therapy Ltd. using the measurement alternative

The investment in the equity interests of Juventas was accounted for as an investment in equity securities using the measurement alternative at its cost, minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer, as the fair value of the equity securities of Juventas is not readily determinable. The fair value of such investment was determined based on the price in the orderly transaction for newly issued equity interests of Juventas, which is further adjusted to reflect the differences between the newly issued equity interests of Juventas and the Company's investment.

RESULTS OF OPERATIONS

Years Ended December 31, 2021 and 2020.

Operating Items

Revenues

Product Sales

Revenues consist of product sales of EVOMELA® that launched during August 2019. Revenue was $30.0 million for the year ended December 31, 2021, compared to $15.0 million for the year ended December 31, 2020. Revenues increased by 100% in the year ended December 31, 2021, as compared to same period in 2020 due to the continued growth in EVOMELA® sales.

Lease Income

Lease income consists primarily of an equipment lease with Juventas (a related party). Lease income was $148,000 for the year ended December 31, 2021 compared to $140,000 for the year ended December 31, 2020.

Operating Expenses

Costs of Revenues

Costs of revenues consists primarily of the cost of inventories of EVOMELA® and sales-based royalties related to the sale of EVOMELA®.

Costs of revenues were $12.6 million for the year ended December 31, 2021, as compared to $9.5 million for the year ended December 31, 2020. The increase of costs of revenues primarily resulted from the increase of EVOMELA sales during the same period. Included in our costs of revenues are royalty amounts of $5.9 million for the year ended December 31, 2021 and $3.0 million for the year ended December 31, 2020. The other primary components of our costs of revenues are cost of goods sold, which were approximately $6.6 million and $6.6 million for the years ended December 31, 2021 and 2020, and as a percentage of revenues were 22% in the year ended December 31, 2021, compared to 44% in the year ended December 31, 2020, with such decrease as a percentage of revenue mainly due to the alternate manufacturer in place, resulting in a considerable decrease in the unit cost of inventories of EVOMELA.

Research and Development Expenses

Research and development (R&D) expenses consist primarily of compensation and other expenses related to research and development personnel, research collaborations, costs associated with internal and contract preclinical testing and clinical trials of our product candidates, including the costs of drug substance and drug product, regulatory maintenance costs of ANDAs, facilities expenses, and amortization expense of acquired ANDAs.

Research and development expenses for the year ended December 31, 2021 were $14.4 million, compared with $11.5 million for the year ended December 31, 2020. The increase in R&D expenses primarily due to an increase in R&D expenses incurred related to the development of CID-103, BI-1206 and CB-5339.

General and Administrative Expenses

General and administrative expenses include compensation and other expenses related to executive, finance, business development and administrative personnel, professional services, investor relations and facilities.

General and administrative expenses for the year ended December 31, 2021 were $23.8 million, compared with $19.7 million for the year ended December 31, 2020. The increase in general and administrative expenses was primarily due to an increase in headcount and payroll expenses amounted to $2.7 million and an increase in professional fees amounted to $1.9 million.

Selling and Marketing Expenses

Selling and marketing expenses are the direct costs related to the sales of EVOMELA® that was launched in China in August 2019, such as sales force salaries, bonuses, advertising, and other marketing efforts.

Selling and marketing expenses for the year ended December 31, 2021, were $14.7 million, compared with $7.8 million for the year ended December 31, 2020. The increase is primarily due to the increase of sales commission in accordance with the increase sales of EVOMELA.

Gain on disposal of intangible assets

There was no gain on disposal of intangible assets for the year ended December 31, 2021.

Gain on disposal of intangible assets for the year ended December 31, 2020 was $1.2 million. The gain on disposal during 2020 was primarily due to the $1.2 million gain on the sale of twenty-one ANDAs during the year.

Impairment of intangible assets

There was no impairment of intangible assets for the year ended December 31, 2021.

Impairment of intangible assets for the year ended December 31, 2020 was $1.5 million. The impairment of intangible assets was primarily due to the reduction of the carrying value of intangible assets to their fair value.

Acquired in-process Research and Development Expenses

Acquired in-process R&D expenses for the year ended December 31, 2021 were $6.6 million, compared with $17.8 million for the year ended December 31, 2020. The amount reported for the year ended December 31, 2021 consisted of the upfront payment of $5.5 million to Cleave for the development of CB-5339 and milestone payments to Alesta of $1.06 million for the development of

CID-103. The amount reported for the year ended December 31, 2020 comprised of milestone fees paid to Pharmathen of $1.7 million, to Juventas of $10.3 million and to BioInvent of $5.9 million, respectively.

Non-Operating Items

Interest income, net

Interest income, net for the year ended December 31, 2021 was $0.3 million compared with $0.9 million for the year ended December 31, 2020. The decrease in interest income, net, is mainly due to that the amount reported for the year ended December 31, 2020 included interest income from loans made to Juventas (a related party) which was repaid in September 2020.

Other income

Other income for the year ended December 31, 2021 was $558,000, compared with $82,000 for the year ended December 31, 2020. Other income of $51,000 and $35,000 recorded in the years ended December 31, 2021 and 2020, relate to CASI Wuxi's receipt of RMB 15.9 million (equivalent to $2.2 million) in April 2020, and RMB 3.0 million (equivalent to $0.5 million) in November 2021 from the Jiangsu Province Wuxi Huishan Economic Development Zone as government grant for the development of leased state-owned land in China for the construction of a manufacturing facility. The grants were recorded as deferred income and amortized over the term of the lease of the land. Other income of $471,807 recorded in the year ended December 31, 2021 relates to the loan to the Company under the Paycheck Protection Program (PPP) that was forgiven in September 2021.

Foreign exchange gains and losses

Foreign exchange gains (losses) for the year ended December 31, 2021 was gain of $0.3 million compared with losses of $1.3 million for the year ended December 31, 2020. The foreign exchange gains (losses) are primarily due to accounts receivable with CRPCGIT and USD denominated cash accounts that are held by our Chinese subsidiaries.

Change in fair value of investments

The change in fair value of investments for the years ended December 31, 2021 and 2020 was $5.7 million and $4.3 million respectively. The changes represent unrealized gains or losses on the Company's investments in equity securities and long-term investment.

Impairment loss of long-term investments

Impairment loss of long-term investments for the year ended December 31, 2021 was $865,000 relating to the investment in a privately held UK Company, Black Belt Tx". The Company did not record any impairment loss of long-term investments during the year ended December 31, 2020.

LIQUIDITY AND CAPITAL RESOURCES

To date, the Company has been engaged primarily in research and development activities. As a result, the Company has incurred and expect to continue to incur operating losses in 2022 and the foreseeable future.

The Company will require significant additional funding to fund operations beyond the first quarter of 2023 until such time, if ever, it becomes profitable. The Company intends to augment its cash balances by pursuing other forms of capital infusion, including strategic alliances or collaborative development opportunities with organizations that have capabilities and/or products that are complementary to its capabilities and products in order to continue the development of its potential product candidates that they intend to pursue to commercialization. If the Company seeks strategic alliances, licenses, or other alternative arrangements, such as arrangements with collaborative partners or others, to raise further financing, it may need to relinquish rights to certain of its existing product candidates, or products they would otherwise seek to develop or commercialize on its own, or to license the rights to its product candidates on terms that are not favorable to it.

The Company will also continuously invest in its development of the Wuxi land and construction of the manufacturing building. Commencing from the fourth quarter of 2020, in relation to the development of the Wuxi land and construction of the manufacturing

building, the Company entered into a series of contracts for the development and construction work. Total commitment under these contracts was RMB 69.1 million ($10.8 million) as of December 31, 2021.

The Company will continue to seek to raise additional capital to fund its commercialization efforts, expansion of its operations, capital expenditure, research and development, and for the acquisition of new product candidates, if any. The Company intends to and is currently actively communicating to explore one or more of the following alternatives to raise additional capital:

- raising bank loans;
- selling additional equity securities;
- out-licensing product candidates to one or more corporate partners;
- completing an outright sale of non-priority assets; and/or
- engaging in one or more strategic transactions.

The Company also will continue to manage its cash resources prudently and cost-effectively.

There can be no assurance that adequate additional financing under such arrangements will be available to the Company on terms that they deem acceptable, if at all. If additional funds are raised by issuing equity securities, dilution to existing stockholders may result, or the equity securities may have rights, preferences, or privileges senior to those of the holders of its common stock. If they fail to obtain additional capital when needed, they may be required to delay or scale back their commercialization efforts, advancement of the Spectrum products, and the ANDA products, or plans for other product candidates, if any.

Since its inception in 1991, the Company has incurred significant losses from operations and, as of December 31, 2021, has incurred an accumulated deficit of $605.6 million. As of December 31, 2021, the Company had a consolidated balance of cash and cash equivalents of $38.7 million. The Company believes that it has sufficient resources to fund its operations at least one year beyond the date that the audited consolidated financial statements are issued.

FINANCING ACTIVITIES

Stock repurchase program

On December 15, 2021, our board of directors approved a stock repurchase program for the repurchase of up to USD 10 million of our common stock (and no more than 12,500,000 shares of our common stock) through open market purchases in compliance with Rule 10b-18 under the Securities Exchange Act of 1934 and through trading plans established pursuant to Rule 10b5-1 of the Securities Exchange Act. Under any Rule 10b5-1 trading plan we might adopt, our third-party broker, subject to Securities and Exchange Commission regulations regarding certain price, market, volume and timing constraints, would have authority to purchase our common stock in accordance with the terms of the plan. The actual timing, number and value of shares repurchased under the stock repurchase program will depend on a number of factors, including constraints specified in any Rule 10b5-1 trading plans, price, general business and market conditions, and alternative investment opportunities. Subject to the purchase terms under our existing and future Rule 10b5-1 trading plans, the stock repurchase program does not obligate the Company to acquire any specific number of shares in any period, and may be expanded, extended, modified or discontinued at any time. The Company has funded and anticipates funding for stock repurchase program to come from available corporate funds, including cash on hand and future cash flow. As of March 18, 2022, the Company has repurchased 3,207,661 shares of common stock for an aggregate of $2.5 million under a Rule 10b5-1 trading plan that will terminate on March 31, 2022.

March 2021 Underwritten Public Offering

On March 24, 2021, the Company closed an underwritten public offering of 15,853,658 shares of the Company's common stock (the "Offering") at a price to the public of $2.05 per share. The gross proceeds to CASI from the Offering were $32.5 million before deducting the underwriting discounts and commissions and offering expenses payable by CASI.

The Offering was made by means of a written prospectus supplement and accompanying prospectus forming part of a shelf registration statement on Form S-3, previously filed with the SEC on November 20, 2020, which was declared effective on December 2, 2020. We have filed a final prospectus supplement, dated March 24, 2021, with the SEC relating to the Offering.

The Company is using the net proceeds of this offering for working capital and general corporate purposes, which include, but are not limited to advancing the Company's product portfolio, acquiring the rights to new product candidates and general and administrative expenses.

July 2020 Underwritten Public Offering

On July 24, 2020, the Company closed an underwritten public offering of 23 million shares of common stock (the "Offering") and received gross proceeds of $43.7 million before deducting the underwriting discounts and commissions and offering expenses payable by CASI. Certain insiders, including CASI's Chairman and CEO, and CASI's President, purchased shares of common stock in the Offering at the public offering price and on the same terms as the other purchasers in this Offering. CASI's Chairman and CEO purchased 2,952,426 shares directly and ETP Global Fund LP purchased 1,200,000 shares. CASI's President purchased 20,152 shares.

Sales Agreements

On February 23, 2018, the Company entered into a Common Stock Sales Agreement (the "Sales Agreement"), as amended, with H.C. Wainwright & Co., LLC ("HCW") that would allow the Company to sell up to $20 million of shares of common stock in "at-the-market" transactions, subject to compliance with the terms and conditions of the Sales Agreement. During the year ended December 31, 2021, the Company has not offered and sold any shares of common stock under the Sales Agreement, and a total of 143,248 shares, resulting in net proceeds to the Company of $475,000 have been issued since inception. During the year ended December 31, 2021, the Company has not offered and sold any shares of common stock under the Sales Agreement. Concurrently with and upon the execution of the new Stock Sales Agreement mentioned below, the Sales Agreement dated as of February 23, 2018, between CASI and HCW, was terminated by mutual agreement of the parties.

On July 19, 2019, the Company entered into an Open Market Sale Agreement[SM] with Jefferies LLC, as sales agent (the "Open Market Agreement") pursuant to which the Company may elect to sell from time to time, at its option, up to $30 million in shares of the Company's common stock, subject to the terms and conditions of the Open Market Agreement. In 2019, the Company issued 59,000 shares under the Open Market Agreement resulting in net proceeds to the Company of $182,000. In 2020, there were 434,000 shares issued under the Open Market Agreement with net proceeds of $1,357,000. During the year ended December 31, 2021, the Company has not offered and sold any shares of common stock under the Open Market Agreement. As of March 25, 2022, the Company has issued 493,000 shares with net proceeds of $1,539,000. As of March 25, 2022, $28.5 million remained available under the Open Market Agreement.

On October 29, 2021, the Company has entered into a common stock sales agreement ("Stock Sales Agreement"), with H.C. Wainwright & Co., LLC, relating to shares of common stock of the Company. In accordance with the terms of the sales agreement, the Company may offer and sell shares of common stock in "at-the-market" transactions, subject to compliance with the terms and conditions of the Stock Sales Agreement, with an aggregate offering price of no more than $20,000,000. During the year ended December 31, 2021, the Company has not offered or sold any shares of common stock under the sales agreement. As of March 25, 2022, the Company has not offered or sold any shares of common stock under the sales agreement.

INTEREST RATE CHANGES

Management does not believe that our working capital needs are sensitive to changes in interest rates.

OFF-BALANCE-SHEET ARRANGEMENTS

We had no off-balance sheet arrangements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934 and are not required to provide the information under this item.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

The response to this item is submitted in a separate section of this report. See Index to Consolidated Financial Statements on page F-1.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Disclosure Controls and Procedures

As of December 31, 2021, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Principal Financial Officer of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in the Securities Exchange Act of 1934 Rules 13a-15(e) and 15d-15(e)). Our Chief Executive Officer, and Principal Financial Officer have concluded that our disclosure controls and procedures are effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission and that such information is accumulated and communicated to our management (including our Chief Executive Officer, and Principal Financial Officer) to allow timely decisions regarding required disclosures. Based on such evaluation, our Chief Executive Officer, and Principal Financial Officer have concluded these disclosure controls and procedures are effective as of December 31, 2021.

Changes in Internal Control Over Financial Reporting

There have not been any changes in our internal control over financial reporting during the fourth quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Securities Exchange Act Rules 13a-15(f) and 15d-15(f). Our internal control over financial reporting is designed to provide reasonable assurance to our management and board of directors regarding the reliability of financial reporting and the preparation and fair presentation of financial statements for external purposes in accordance with generally accepted accounting principles. Any internal control over financial reporting, no matter how well designed, has inherent limitations. As a result of these inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those internal controls determined to be effective can provide only reasonable assurance with respect to reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Under the supervision and with the participation of our management, including our Chief Executive Officer, and Principal Financial Officer, we conducted an assessment of the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control — Integrated Framework 2013*. Based on our assessment, we concluded that our internal control over financial reporting was effective as of December 31, 2021.

ITEM 9B. OTHER INFORMATION.

Annual Meeting of Stockholders

Our 2022 Annual Meeting of Stockholders will be held on May 25, 2022. Further information will be provided in our proxy statement that will be filed with the SEC and mailed to stockholders of record as soon as practicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

We have adopted a Code of Ethics, as defined in applicable SEC rules, that applies to directors, officers and employees, including our chief executive officer and principal financial officer. The Code of Ethics is available on the Company's website at *www.casipharmaceuticals.com*.

ITEM 11. EXECUTIVE COMPENSATION.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.

The information required under this item, with the exception of information relating to compensation plans under which equity securities of the Company are authorized for issue, which appears below, is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Options under Employee Benefit Plans. The following table discloses certain information about the options issued and available for issuance under all outstanding Company option plans, as of December 31, 2021.

	(a)	(b)	(c)
Plan category	***Number of securities to be issued upon exercise of outstanding options, warrants and rights***	***Weighted-average exercise price of outstanding options, warrants and rights***	***Number of securities remaining available for future issuance under equity compensation plans [excluding securities reflected in column (a)]***
Equity compensation plans approved by security holders	33,243,790	$ 2.04	10,515,448

Warrants issued under the unauthorized plans represent compensation for consulting services rendered by the holders.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES.

(a) 1. FINANCIAL STATEMENTS - See index to Consolidated Financial Statements.

2. Schedules

All financial statement schedules are omitted because they are not applicable, not required under the instructions or all the information required is set forth in the financial statements or notes thereto.

3. Exhibits

1.1 Open Market Sale Agreement SM by and between CASI Pharmaceuticals, Inc. and Jefferies LLC dated July 19, 2019 (incorporated by reference from Exhibit 1.1 to our Current Report on Form 8-K filed on July 19, 2019)

1.2 Common Stock Sales Agreement, dated October 29, 2021, by and between CASI Pharmaceuticals, Inc. and H.C. Wainwright & Co., LLC (incorporated by reference to Exhibit 1.1 on our Form 8-K filed with the Securities and Exchange Commission on October 29, 2021)

3.1 Restated Certificate of Incorporation of CASI Pharmaceuticals, Inc. (incorporated by reference to exhibit 3.1 on our Form 10-Q for the quarter ended June 30, 2019 filed with the Securities and Exchange Commission on August 9, 2019)

3.2 Amended and Restated Bylaws dated September 10, 2020 (incorporated by reference to Exhibit 3.2 of our 10-Q/A filed with the Securities and Exchange Commission on February 10, 2021)

4.1 Description of Common Stock (incorporated by reference to Exhibit 4.1 of our Form 10-K filed with the Securities and Exchange Commission on March 30, 2021)

4.2 Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 of our Form 8-K filed with the Securities and Exchange Commission on October 19, 2017)

4.3 Form of Warrant (incorporated by reference to Exhibit 4.1 of our Form 8-K filed with the Securities and Exchange Commission on March 23, 2018)

4.4 Form of Warrant (incorporated by reference to Exhibit 4.1 of our Form 8-K filed with the Securities and Exchange Commission on September 14, 2018)

10.1 Form of Change in Control Agreement* (incorporated by reference to Exhibit 10.1 of our Form 8-K filed with the Securities and Exchange Commission on April 17, 2007)

10.2 First Amendment to Change in Control Agreement by and between the Company and Alexander Zukiwski* (incorporated by reference to Exhibit 10.3 of our Form 8-K filed with the Securities and Exchange Commission on December 10, 2021)

10.3 License Agreement, dated as of September 17, 2014, by and between CASI Pharmaceuticals, Inc. and Spectrum Pharmaceuticals, Inc. ++ (incorporated by reference to Exhibit 10.4 of our Form 10-K filed with the Securities and Exchange Commission on March 30, 2021)

10.4 License Agreement, dated as of September 17, 2014, by and between CASI Pharmaceuticals, Inc. and Spectrum Pharmaceuticals Cayman, L.P. ++ (incorporated by reference to Exhibit 10.5 of our Form 10-K filed with the Securities and Exchange Commission on March 30, 2021)

10.5 License Agreement, dated as of September 17, 2014, by and between CASI Pharmaceuticals, Inc. and Talon Therapeutics, Inc. ++ (incorporated by reference to Exhibit 10.6 on our Form 10-K filed with the Securities and Exchange Commission on March 30, 2021)

10.6 Employment Agreement by and between CASI Pharmaceuticals, Inc. and Alex Zukiwski, dated as of April 3, 2017* (incorporated by reference to Exhibit 10.1 of our Form 10-Q filed with the Securities and Exchange Commission on August 14, 2017)

10.7 First Amendment to the Employment Agreement by and between CASI Pharmaceuticals, Inc. and Alexander Zukiwski, dated as of December 9, 2021* (incorporated by reference to Exhibit 10.1 on our Form 8-K filed with the Securities and Exchange Commission on December 10, 2021)

10.8 Asset Purchase Agreement dated as of January 26, 2018 by and between CASI Pharmaceuticals, Inc. and Sandoz Inc. ++ (incorporated by reference to Exhibit 10.8 of our Form 10-K filed with the Securities and Exchange Commission on March 30, 2021)

10.9 Memorandum of Understanding, dated November 16, 2018, by and between Management Committee of Wuxi Huishan Economic Development Zone and CASI Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.20 of our Form 10-K filed with the Securities and Exchange Commission on March 29, 2019)

10.10 Investment Agreement, dated November 16, 2018, by and between Administrative Committee of Wuxi Huishan Economic Development Zone, Jiangsu Province and CASI Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.21 on our Form 10-K filed with the Securities and Exchange Commission on March 29, 2019)

10.11 Supplementary Agreement, dated November 16, 2018, by and between Administrative Committee of Wuxi Huishan Economic Development Zone, Jiangsu Province and CASI Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.22 on our Form 10-K filed with the Securities and Exchange Commission on March 29, 2019)

10.12 Shareholders' Agreement, dated November 16, 2018, between CASI Pharmaceuticals, Inc. and Wuxi Jintou Huicun Investment Enterprise (Limited Partnership) (incorporated by reference to Exhibit 10.23 on our Form 10-K filed with the Securities and Exchange Commission on March 29, 2019)

10.13 Lease Contract, by and between Wuxi Huishan New City Life Science & Technology Industry Development Co., Ltd. and CASI Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.24 on our Form 10-K filed with the Securities and Exchange Commission on March 29, 2019)

10.14 Joint Venture Contract on Establishment of CASI (Wuxi) Pharmaceuticals Co. Ltd. by and between CASI Pharmaceuticals, Inc. and Wuxi Jintou Huicun Investment Enterprise Limited Partnership, dated as of November 16, 2018 (incorporated by reference to Exhibit 10.25 on our Form 10-K filed with the SEC on March 29, 2019)

10.15 Labor Contract, effective as of September 1, 2018, between CASI (Beijing) Pharmaceuticals, Inc. and Wei (Larry) Zhang* (incorporated by reference to Exhibit 10.26 to the Company's Form 10-K filed with the SEC on March 29, 2019)

10.16 CASI Pharmaceuticals, Inc. 2011 Long Term Incentive Plan, as amended* (previously filed with, and incorporated herein by reference to the Company's Definitive Proxy Statement filed on April 30, 2019)

10.17 CASI Pharmaceuticals, Inc. 2021 Long Term Incentive Plan, as amended* (previously filed with, and incorporated herein by reference to the Company's Definitive Proxy Statement filed on May 10, 2021)

10.18 Exclusive Distribution Agreement, effective as of March 5, 2019, by and among CASI Pharmaceuticals, Inc, China Resources Guokang Pharmaceuticals Co., Ltd. and CASI (Beijing) Biopharmaceuticals Technology Co., Ltd. (incorporated by reference to Exhibit 10.1 to the Quarterly Report filed May 15, 2019)

10.19 Offer Letter from CASI Pharmaceuticals, Inc. to Dr. He dated March 22, 2019, effective April 2, 2019* (incorporated by reference to Exhibit 10.2 to the Quarterly Report filed May 15, 2019)

10.20 License Agreement by and between CASI Pharmaceuticals, Inc. and Black Belt Therapeutics Limited entered into as of April 16, 2019 (incorporated by reference to Exhibit 10.3 to the Quarterly Report filed May 15, 2019)+

10.21 Exclusive License Agreement by and between CASI Pharmaceuticals, Inc. and Juventas Cell Therapy Ltd effective June 15, 2019 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 9, 2019)+

10.22 Investment Agreement in respect of Juventas Cell Therapy Ltd effective June 15, 2019 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on August 9, 2019)+

10.23 Contract for Assignment of the Right to the Use of the State-owned Construction Land (no. 3202842019CR0019) dated November 15, 2019 (incorporated by reference to Exhibit 10.22 on our Annual Report on Form 10-K filed on March 16, 2020).

10.24 Form of CASI Pharmaceuticals, Inc. Performance-Contingent 2011 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in China)* (incorporated by reference to Exhibit 4.1 on our Quarterly Report on Form 10-Q filed May 15, 2019)

10.25 Form of CASI Pharmaceuticals, Inc. Performance-Contingent 2021 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in China)* (incorporated by reference to Exhibit 10.1 on our Quarterly Report on Form 10-Q filed August 12, 2021)

10.26 Form of CASI Pharmaceuticals, Inc. 2011 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in China)* (incorporated by reference to Exhibit 4.2 on our Quarterly Report on Form 10-Q filed May 15, 2019)

10.27 Form of CASI Pharmaceuticals, Inc. 2021 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in China) (incorporated by reference to Exhibit 10.2 on our Quarterly Report on Form 10-Q filed August 12, 2021)

10.28 Form of CASI Pharmaceuticals, Inc. Performance-Contingent 2011 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in the US)* (incorporated by reference to Exhibit 4.3 on our Quarterly Report on Form 10-Q filed May 15, 2019)

10.29 Form of CASI Pharmaceuticals, Inc. Performance-Contingent 2021 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in the US)* (incorporated by reference to Exhibit 10.3 on our Quarterly Report on Form 10-Q filed August 12, 2021)

10.30 Form of CASI Pharmaceuticals, Inc. 2011 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in the US)* (incorporated by reference to Exhibit 4.4 on our Quarterly Report on Form 10-Q filed May 15, 2019)

10.31 Form of CASI Pharmaceuticals, Inc. 2021 Long-Term Incentive Plan Non-Qualified Stock Option Grant Agreement (for Optionees in the US)* (incorporated by reference to Exhibit 10.4 on our Quarterly Report on Form 10-Q filed August 12, 2021)

10.32 Supplementary Agreement to the Exclusive License Agreement effective as of September 29, 2020++ (incorporated by reference to Exhibit 10.1 on our Quarterly Report on Form 10-Q filed on November 9, 2020)

10.33 Investment Agreement by and between Juventas Cell Therapy Ltd and CASI Biopharmaceuticals (WUXI) Co., Ltd. effective as of September 22, 2020++ (incorporated by reference to Exhibit 10.2 on our Quarterly Report on Form 10-Q filed on November 9, 2020)

10.34 License and Development Agreement, dated March 5, 2021, between the Company and Cleave Therapeutics Inc., (incorporated by reference to Exhibit 10.1 on our Quarterly Report on Form 10-Q filed on May 13, 2021)++

10.35 License and Development Agreement for BI-1206 dated October 26, 2020 by and between the Company and BioInvent, International AB ++ (incorporated by reference to Exhibit 10.30 to the Annual Report on Form 10-K filed on March 30, 2021)

21 Subsidiaries of the Registrant **

23.1 Consent of Independent Registered Public Accounting Firm **

31.1 Rule 13a-14(a) Certification of Chief Executive Officer **

31.2 Rule 13a-14(a) Certification of Principal Financial Officer **

32.1 Rule 13a-14(b) Certification by Chief Executive Officer **

32.2 Rule 13a-14(b) Certification by Principal Financial Officer **

101** Interactive Data Files The following financial information from the Registrant's Annual Report on Form 10-K for the year ended December 31, 2021, formatted in Inline eXtensible Business Reporting Language (XBRL): (i) Consolidated Balance Sheets as of December 31, 2021 and 2020, (ii) Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2010 and 2020, (iii) Consolidated Statements of Stockholders' Equity for the years ended December 31, 2020 and 2019 (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2021 and 2020 and (v) Notes to Consolidated Financial Statements.

104 Cover Page Interactive Data File (formatted in Inline XBRL and Contained in Exhibit 101)

* Management Contract or any compensatory plan, contract or arrangement.

+ Certain portions of this exhibit have been omitted based upon a request for confidential treatment under 17 C.F.R. section 200.80(b)(4) and 240.24b-2. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been filed separately with the Commission pursuant to our confidential treatment request.

++ Information in this exhibit identified by brackets is confidential and has been excluded pursuant to Item 601(B)(10)(IV) of Regulation S-K because it (i) is not material and (ii) would likely cause competitive harm to CASI Pharmaceuticals, Inc. if publicly disclosed.

** Filed herewith

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 28, 2022

CASI Pharmaceuticals, Inc.

By:/s/Wei-Wu He
Wei-Wu He
Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1934, this report has been signed below by the following persons in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Wei-Wu He Wei-Wu He	Chief Executive Officer and Chairman (Principal Executive Officer)	March 28, 2022
/s/ Larry (Wei) Zhang Larry (Wei) Zhang	President (Principal Financial Officer)	March 28, 2022
/s/ James Z. Huang James Z. Huang	Director	March 28, 2022
/s/ Franklin C. Salisbury Franklin C. Salisbury	Director	March 28, 2022
/s/ Rajesh C. Shrotriya Rajesh C. Shrotriya	Director	March 28, 2022
/s/ Y. Alexander Wu Y. Alexander Wu	Director	March 28, 2022
/s/ Quan Zhou Quan Zhou	Director	March 28, 2022

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The following consolidated financial statements of CASI Pharmaceuticals, Inc. are included in Item 8:

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
CASI Pharmaceuticals, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of CASI Pharmaceuticals, Inc. and subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Fair Value Measurement of Investment in Equity Interests of Juventas Cell Therapy Ltd. Using the Measurement Alternative

As discussed in Note 3 to the consolidated financial statements, as of December 31, 2021, the Company's investment in Juventas Cell Therapy Ltd. ("Juventas")'s equity interests was US$32,308. The investment is measured using the measurement alternative at its cost, minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. The Company recognized gain of fair value change for equity interests of US$ 5.5 million for the year ended December 31, 2021, based on the price in an orderly transaction for newly issued equity interests of Juventas, which is further adjusted to reflect the differences between the newly issued equity interests of Juventas and the Company's investment.

We identified the fair value measurement of the investment in equity interests of Juventas as a critical audit matter. Specialized skill and knowledge and subjective auditor judgment were needed to evaluate the expected volatility used to determine the fair value.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design of certain internal controls related to the Company's process to estimate the fair value of the investment in equity interests of Juventas, including controls over the Company's evaluation of expected volatility applied to the valuation model . We involved valuation professionals with specialized skills and knowledge who assisted in:

- evaluating the expected volatility determined by the Company by comparing such volatility to an expected volatility that was independently developed using publicly available market data for comparable entities

- developing an estimate of the fair value of the investment in equity interests of Juventas using the independently developed expected volatility and comparing it to the value determined by the Company.

/s/ KPMG Huazhen LLP

We have served as the Company's auditor since 2019.

Beijing, China
March 28, 2022

CASI Pharmaceuticals, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 38,704	$ 57,064
Investment in equity securities, at fair value	9,868	9,309
Accounts receivable, net of $0 allowance for doubtful accounts	9,803	4,645
Inventories	1,907	1,356
Prepaid expenses and other	1,688	1,651
Total current assets	61,970	74,025
Property, plant and equipment, net	12,712	2,062
Intangible assets, net	12,203	13,210
Long-term investments	40,128	29,442
Right of use assets	9,107	8,696
Other assets	2,178	299
Total assets	$ 138,298	$ 127,734
LIABILITIES, REDEEMABLE NONCONTROLLING INTEREST AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,789	$ 3,260
Accrued and other current liabilities	8,397	3,424
Bank borrowings	—	826
Notes payable	—	466
Total current liabilities	13,186	7,976
Deferred income	2,828	2,351
Other liabilities	14,325	13,834
Total liabilities	30,339	24,161
Commitments and contingencies (Note 21)		
Redeemable noncontrolling interest, at redemption value (Note 12)	23,457	22,033
Stockholders' equity:		
Preferred stock, $1.00 par value: 5,000,000 shares authorized and 0 shares issued and outstanding	—	—
Common stock, $0.01 par value:		
250,000,000 shares authorized at December 31, 2021 and December 31, 2020		
139,877,032 shares and 124,023,374 shares issued at December 31, 2021 and December 31, 2020, respectively;		
139,797,487 shares and 123,943,829 shares outstanding at December 31, 2021 and December 31, 2020, respectively	1,399	1,240
Additional paid-in capital	694,826	658,246
Treasury stock, at cost: 79,545 shares held at December 31, 2021 and December 31, 2020	(8,034)	(8,034)
Accumulated other comprehensive income	1,954	589
Accumulated deficit	(605,643)	(570,501)
Total stockholders' equity	84,502	81,540
Total liabilities, redeemable noncontrolling interest and stockholders' equity	$ 138,298	$ 127,734

The accompanying notes are an integral part of these consolidated financial statements.

CASI Pharmaceuticals, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Year Ended December 31	
	2021	2020
Revenues:		
Product sales	$ 30,020	$ 15,001
Lease income from a related party	148	140
Total revenues	30,168	15,141
Costs of revenues:		
Cost of goods sold	6,616	6,553
Royalty fee	5,941	2,955
Total costs of revenues	12,557	9,508
Gross Profit	17,611	5,633
Operating expenses:		
Research and development	14,422	11,470
General and administrative	23,766	19,661
Selling and marketing	14,705	7,815
Acquired in-process research and development	6,555	17,828
Gain on disposal of intangible assets	—	(1,152)
Impairment of intangible assets	—	1,537
Total operating expenses	59,448	57,159
Loss from operations	(41,837)	(51,526)
Non-operating income (expense):		
Interest income, net	321	866
Other income	558	82
Foreign exchange gain (losses)	321	(1,255)
Change in fair value of investments	5,660	4,322
Impairment loss of long-term investments	(865)	—
Loss before income tax expense	(35,842)	(47,511)
Income tax expense	—	—
Net loss	(35,842)	(47,511)
Less: loss attributable to redeemable noncontrolling interest	(700)	(918)
Accretion to redeemable noncontrolling interest redemption value	1,512	1,694
Net loss attributable to CASI Pharmaceuticals, Inc.	$ (36,654)	$ (48,287)
Net loss per share (basic and diluted)	$ (0.27)	$ (0.44)
Weighted average number of common stock outstanding (basic and diluted)	136,105,539	110,452,288
Comprehensive loss:		
Net loss	$ (35,842)	$ (47,511)
Foreign currency translation adjustment	1,977	3,904
Total comprehensive loss	$ (33,865)	$ (43,607)
Less: Comprehensive loss attributable to redeemable noncontrolling interest	(88)	(331)
Comprehensive loss attributable to common stockholders	$ (33,777)	$ (43,276)

The accompanying notes are an integral part of these consolidated financial statements.

CASI Pharmaceuticals, Inc.
Consolidated Statements of Stockholders' Equity
Years Ended December 31, 2021 and 2020
(In thousands, except share data)

	Preferred Stock		Common Stock		Additional Paid-in Capital	Treasury Stock	Accumulated Other Comprehensive Income/(Loss)	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount					
Balance at December 31, 2019	—	$ —	97,771,698	979	$ 606,686	$ (8,034)	$ (2,728)	$ (523,908)	$ 72,995
Issuance of common stock for options and warrants exercised	—	—	2,737,795	27	3,847	—	—	—	3,874
Repurchase of stock options to satisfy tax withholding obligations	—	—	—	—	(251)	—	—	—	(251)
Issuance of common stock pursuant to financing agreements	—	—	23,434,336	234	44,865	—	—	—	45,099
Stock issuance costs	—	—	—	—	(3,028)	—	—	—	(3,028)
Stock-based compensation expense, net of forfeitures	—	—	—	—	7,821	—	—	—	7,821
Foreign currency translation adjustment	—	—	—	—	—	—	3,317	—	3,317
Net loss attributable to CASI Pharmaceuticals, Inc.	—	—	—	—	(1,694)	—	—	(46,593)	(48,287)
Balance at December 31, 2020	—	$ —	123,943,829	$ 1,240	$ 658,246	$ (8,034)	$ 589	$ (570,501)	$ 81,540
Issuance of common stock pursuant to financing agreements	—	—	15,853,658	159	32,341	—	—	—	32,500
Stock issuance costs	—	—	—	—	(2,019)	—	—	—	(2,019)
Stock-based compensation expense, net of forfeitures	—	—	—	—	7,770	—	—	—	7,770
Foreign currency translation adjustment	—	—	—	—	—	—	1,365	—	1,365
Net loss attributable to CASI Pharmaceuticals, Inc.	—	—	—	—	(1,512)	—	—	(35,142)	(36,654)
Balance at December 31, 2021	—	$ —	139,797,487	$ 1,399	$ 694,826	$ (8,034)	$ 1,954	$ (605,643)	$ 84,502

The accompanying notes are an integral part of these consolidated financial statements.

CASI Pharmaceuticals, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended	
	December 31, 2021	December 31, 2020
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	$ (35,842)	(47,511)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation for property, plant and equipment	468	562
Loss on disposal of property, plant and equipment	65	—
Amortization of intangible assets and held-for-sale assets	1,347	1,397
Reduction in the carrying amount of the right-of-use assets	1,280	1,272
Gain on disposal of intangible assets	—	(1,152)
Impairment of intangible assets	—	1,537
Stock-based compensation expense	7,770	7,821
Acquired in-process research and development	6,555	17,828
Government grant as a result of loan forgiveness	(472)	—
Change in fair value of investments	(5,660)	(4,322)
Impairment loss of long-term investments	865	—
Changes in operating assets and liabilities:		
Accounts receivable	(5,158)	(3,352)
Inventories	(551)	3,186
Prepaid expenses and other assets	(1,303)	(184)
Accounts payable	1,491	(1,540)
Accrued liabilities and other liabilities	2,354	(1,393)
Deferred income	(51)	(35)
Net cash used in operating activities	(26,842)	(25,886)
CASH FLOWS FROM INVESTING ACTIVITIES		
Proceeds from disposal of intangible assets	—	2,700
Proceeds from disposal of property and equipment	10	—
Purchases of property, plant and equipment	(8,945)	(1,499)
Loan to a related party	—	(10,033)
Receipt of repayment of loan from a related party	—	10,033
Cash paid to acquire in-process research and development	(6,555)	(17,828)
Cash paid to acquire convertible loan in Black Belt Tx Limited	(86)	(83)
Receipt of repayment of Black Belt convertible note	172	—
Cash paid to acquire convertible loan in Alesta Tx	(261)	—
Cash paid to acquire convertible loan in Cleave	(5,500)	—
Cash paid to acquire equity securities in BioInvent International AB	—	(6,318)
Receipt of government grants related to land use right	474	2,309
Net cash used in investing activities	(20,691)	(20,719)
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from notes payable	—	466
Proceeds from bank borrowings	709	783
Repayment of bank borrowings	(1,548)	—
Stock issuance costs	(2,019)	(2,818)
Proceeds from sale of common stock	32,500	45,099
Proceeds from exercise of stock options	—	3,874
Repurchase of stock options to satisfy tax withholding obligations	—	(251)
Net cash provided by financing activities	29,642	47,153
Effect of exchange rate change on cash and cash equivalents	(469)	2,895
Net (decrease)/ increase in cash and cash equivalents	(18,360)	3,443
Cash and cash equivalents at beginning of year	57,064	53,621
Cash and cash equivalents at end of year	$ 38,704	$ 57,064
Supplemental disclosure of cash flow information:		
Interest paid	$ 42	$ —
Income taxes paid	$ —	$ —
Non-cash investing and financing activities:		
Purchases of property, plant and equipment in accrued and other current liabilities	$ 3,288	$ 467
Government grant as a result of loan forgiveness (Note 10)	$ 472	$ —

The accompanying notes are an integral part of these consolidated financial statements.

1. DESCRIPTION OF BUSINESS

CASI Pharmaceuticals, Inc. ("CASI" or the "Company") (Nasdaq: CASI) is a U.S. biopharmaceutical company focused on developing and commercializing innovative therapeutics and pharmaceutical products in China, the United States, and throughout the world. The Company was incorporated in 1991, and in 2012, with new leadership, the Company shifted its business strategy to China and has since built an infrastructure in China that includes sales and marketing, medical affairs, regulatory and clinical development and in the foreseeable future, manufacturing. In 2014, the Company changed its name to "CASI Pharmaceuticals, Inc." The majority of the Company's operations are now located in China. The Company is focused on acquiring, developing and commercializing products that augment its hematology/oncology therapeutic focus as well as other areas of unmet medical need. The Company is executing its plan to become a biopharmaceutical leader by launching medicines in the greater China market leveraging its China-based regulatory, clinical and commercial competencies and its global drug development expertise.

The Company launched its first commercial product, EVOMELA® (Melphalan for Injection) in China in August 2019. In China, EVOMELA® is approved for use as a conditioning treatment prior to stem cell transplantation and as a palliative treatment for patients with multiple myeloma. The other core hematology/oncology assets in the Company's pipeline include:

- *CNCT19* is an autologous CD19 CAR-T investigative product ("CNCT19") being developed by our partner Juventas Cell Therapy Ltd. ("Juventas") for which the Company has exclusive World-Wide co-commercial and profit-sharing rights. CNCT19 is being developed as a potential treatment for patients with hematological malignancies which express CD19 including, B-cell acute lymphoblastic leukemia ("B-ALL") and B-cell non-Hodgkin lymphoma ("B-NHL"). The CNCT19 Phase 1 studies in patients with B-ALL and B-NHL in China have been completed by Juventas, the Phase 2 B-ALL and B-NHL registration studies are both currently enrolling in China since the fourth quarter of 2020.

- *BI-1206* is an antibody which has a novel mode-of-action, blocking the inhibitory antibody checkpoint receptor FcγRIIB to unlock anti-cancer immunity and enhance the efficacy of antibody-based immunotherapy in both hematological malignancies and solid tumors for which the Company has licensed exclusive greater China rights from BioInvent International AB ("BioInvent"). BI-1206 is being investigated by BioInvent in a Phase 1/2 trial, in combination with anti-PD1 therapy Keytruda® (pembrolizumab), in patients with solid tumors, and in a Phase 1/2a trial in combination with MabThera® (rituximab) in patients with relapsed/refractory non-Hodgkin lymphoma (NHL). BI-1206 has the potential to restore the activity of rituximab in patients with relapsed/refractory non-Hodgkin lymphoma. Clinical Trial Application (CTA) was approved by China National Medical Products Administration (NMPA) in December 2021. The Company is planning Phase 1 trials of BI-1206 as a single agent to evaluate the PK/safety profile and in combination with rituximab in patients with NHL (mantle cell lymphoma, marginal zone lymphoma, and follicular lymphoma) to assess safety and tolerability, select the Recommended Phase 2 Dose and assess early signs of clinical efficacy as part of its development program for BI-1206 in China. The studies are expected to start in the first half of 2022.

- *CB-5339* is a novel VCP/p97 inhibitor focused on valosin-containing protein (VCP)/p97 as a novel target in protein homeostasis, DNA damage response and other cellular stress pathways for therapeutic use in the treatment of patients with various malignancies. The Company entered into an exclusive license on March 21, 2021 with Cleave Therapeutics, Inc. ("Cleave") for the development and commercialization of CB-5339 in Mainland China, Hong Kong, Macau and Taiwan. CB-5339, an oral second-generation, small molecule VCP/p97 inhibitor, is being evaluated in a Phase 1 clinical trial in patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). CB-5339 CTA application for the multiple myeloma indication is in preparation after receiving an acceptance letter for the CB-5339 IND package from the China Center of Drug Evaluation ("CDE").

- *CID-103* is a full human IgG1 anti-CD38 monoclonal antibody recognizing a unique epitope that has demonstrated encouraging preclinical efficacy and safety profile compared to other anti-CD38 monoclonal antibodies for which the Company has exclusive global rights. CID-103 is being developed for the treatment of patients with multiple myeloma. The Phase 1 dose escalation and expansion study of CID-103, in patients with previously treated, relapsed or refractory multiple myeloma is ongoing in France and the UK.

The Company also has greater China rights to Octreotide (Long Acting Injectable), a standard of care for the treatment of acromegaly and for the control of symptoms associated with certain neuroendocrine tumors; and Thiotepa, a cytotoxic agent which has a long history of established use in the hematology/oncology setting, the Company has an exclusive China license and distribution rights to a novel formulation of thiotepa, which has multiple indications including use as a conditioning treatment for certain allogeneic haemopoietic stem cell transplants. However, due to the evolving standard of care environment, the rare and niche indication for these products, potential US regulatory action and its commitment to prioritize resources, the Company is currently evaluating its potential opportunities for these products. In addition, the Company's assets include six FDA-approved ANDAs which it is evaluating due to generic drug pricing reforms by the Chinese government and its impact on the pricing and competitiveness of these products.

CASI has built a fully integrated, world class biopharmaceutical company dedicated to the successful development and commercialization of innovative and other therapeutic products. Its business development strategy is currently focused on acquiring additional targeted drugs and immuno-oncology therapeutics through licensing that will expand its hematology/oncology franchise. The Company uses a market-oriented approach to identify pharmaceutical/biotechnology candidates that it believes to have the potential for gaining widespread market acceptance, either globally or in China, and for which development can be accelerated under its global drug development strategy. In many cases its business development strategy includes direct equity investments in the licensor company. The Company intends for its pipeline to reflect a diversified and risk-balanced set of assets that include (1) late-stage clinical drug candidates in-licensed for China or global regional rights, (2) proprietary or licensed innovative drug candidates, and (3) select high quality pharmaceuticals that fit its therapeutic focus. The Company has focused on US/EU approved product candidates, and product candidates with proven targets or product candidates that have reduced clinical risk with a greater emphasis on innovative therapeutics. Although oncology with a focus on hematological malignancies is its principal clinical and commercial target, the Company is opportunistic about other therapeutic areas that can address unmet medical needs. The Company will continue to pursue building a robust pipeline of drug candidates for development and commercialization in China as its primary market, and if rights are available for the rest of the world.

The Company believes its China operations offer a significant market and growth potential due to the extraordinary increase in demand for high quality medicines coupled with regulatory reforms in China that facilitate the entry of new pharmaceutical products into the country. The Company will continue to in-license clinical-stage and late-stage drug candidates, and leverage its cross-border operations and expertise, and hope to be the partner of choice to provide access to the China market. The Company expects the implementation of its plans will include leveraging its resources and expertise in both the U.S. and China so that the Company can maximize regulatory, development and clinical strategies in both countries.

The Company's commercial product, EVOMELA®, was originally licensed from Spectrum Pharmaceuticals, Inc. ("Spectrum") and it had a supply agreement with Spectrum to support its application for import drug registration and for commercialization purposes. Spectrum completed the sale of its portfolio of FDA-approved hematology/oncology products including EVOMELA® to Acrotech Biopharma L.L.C. ("Acrotech") on March 1, 2019. The original supply agreement with Spectrum was assumed by Acrotech; Spectrum agreed to continue with a short-term supply agreement for EVOMELA® for the initial commercial product supply in connection with the launch, with the long-term supply assumed by Acrotech.

As part of the long-term strategy to support its future clinical and commercial manufacturing needs and to manage its supply chain for certain products, on December 26, 2018, the Company established CASI Pharmaceuticals (Wuxi) Co., Ltd.. ("CASI Wuxi") to develop a future GMP manufacturing facility that will be in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China. In November 2019, CASI Wuxi entered into a fifty-year lease agreement for the right to use state-owned land in China for the construction of a manufacturing facility. Pursuant to the agreement, CASI Wuxi has committed to invest land use right and property, plant and equipment of RMB 1 billion (equivalent to $143 million) by August 2022. In April 2020, CASI Wuxi received RMB 15.9 million (equivalent to $2.2 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as government grant for this development project which was recorded as deferred income in April 2020. In November 2021, CASI Wuxi received additional RMB 3.0 million (equivalent to $0.5 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as a government grant for this development project which was recorded as deferred income in November 2021. In 2020, for the design and construction work of the land, CASI Wuxi entered into several contracts for RMB 76.1 million ($12.0 million) to complete the phase 1 project of CASI Wuxi's research and development production base, the project was the estimated to be completed in October 2023. In February 2022, CASI Wuxi has reached an alignment with the Wuxi local government that it will collaborate with Wuxi LP to co-develop the land continuously in the future, and the development plan will be extended, details regarding the plan are under negotiation. Also in 2020, CASI Wuxi entered in to a lease agreement with local government for a manufactory building next to the leased land. Since then, the Company entered into a series of contracts for the remodeling and installation work of the building and warehouse, as well as purchase of equipments. The total contract amount entered into for this building is approximately RMB 92.9 million ($14.6 million).

Certain line item, as disclosed below, in the December 31, 2020 consolidated financial statements has been reclassified to conform to the December 31, 2021 presentation. Payables related to property and equipment in the amount of $0.5 million as of December 31, 2020, which was previously included in accounts payable, and has been reclassified as accrued and other current liabilities on the consolidated balance sheet as of December 31, 2020 (see Note 8).

Liquidity and Capital Resources

Since its inception in 1991, the Company has incurred significant losses from operations and, as of December 31, 2021, has incurred an accumulated deficit of $605.6 million.

Taking into consideration the cash and cash equivalents as of December 31, 2021, the Company believes that it has sufficient resources to fund its operations at least one year beyond the date that the consolidated financial statements are issued. As of December 31, 2021, the Company had a balance of cash and cash equivalents of $38.7 million, of which $19.3 million was held in the financial institutions in the PRC. The Company intends to continue to exercise tight controls over operating expenditures and will continue to pursue opportunities, as required, to raise additional capital and will also actively pursue non- or less-dilutive capital raising arrangements or opportunities.

Risks and Uncertainties

During the peak of the COVID-19 pandemic in 2020, the Company experienced disruptions to the EVOMELA® marketing and sales activities as well as to the supply chain for EVOMELA®. The COVID-19 pandemic also impacted the targeted start time of its CID-103 trial due to the lock down of many medical facilities in Europe. During 2021, the Company has experienced minimal disruption to its business activities or supply chain as a result of the COVID-19 pandemic. Furthermore, in June 2021, the Company achieved the First-Patient-In (FPI) in the Phase 1 dose escalation and expansion study of CID-103 in patients with previously treated, relapsed or refractory multiple myeloma. The study is designed to assess the safety, tolerability, pharmacology and clinical activity of CID-103.

The Company currently relies on a single source for the supply of EVOMELA®. The continuation of the COVID-19 pandemic or the emergence of new COVID-19 variants or new pandemics may affect the economies and financial markets of many countries, which may result in a period of economic slowdown or recessions. In such an event, its ability to continue to commercialize and expand distribution of EVOMELA® could be adversely affected if the supplier refuses or is unable to provide products for any reason (including the occurrence of an event like the COVID-19 pandemic that makes delivery impractical. The Company would have to work with Acrotech to negotiate an agreement with a substitute supplier, which, assuming a substitute supplier was available, would likely interrupt the manufacturing of EVOMELA®, cause supply chain delays and increase costs.

The COVID-19 pandemic has adversely affected, and may continue to adversely affect, the economies and financial markets of many countries, which may result in a period of regional, national, and global economic slowdown or regional, national, or global recessions that could affect the Company's ability to continue to commercialize and expand distribution of EVOMELA® (Melphalan

For Injection) or other drugs in its existing product pipeline. Early in the COVID-19 pandemic, the Company experienced a disruption to its supply chain for EVOMELA®, it has experienced no supply disruption in 2021; however, there can be no assurance that restrictions will not be imposed again. In addition, economic and other uncertainties may adversely affect other parties' willingness to negotiate and execute product licenses and thus hamper our ability to in-license clinical-stage and late-stage drug candidates in China or elsewhere.

License and Distribution Agreements

Acrotech License Arrangements

The Company has product rights and perpetual exclusive licenses from Acrotech Biopharma L.L.C. ("Acrotech") to develop and commercialize its commercial product EVOMELA® (Melphalan Hydrochloride For Injection) in the greater China region (which includes Mainland China, Taiwan, Hong Kong and Macau), as well as similar rights to assets ZEVALIN® (Ibritumomab Tiuxetan) and MARQIBO® (Vincristine Sulfate Liposome Injection). The exclusive licenses held by the Company were originally licensed from Spectrum Pharmaceuticals, and Spectrum completed the sale of its portfolio of FDA-approved hematology/oncology products including EVOMELA® to Acrotech on March 1, 2019. On December 3, 2018, the Company received NMPA's approval for importation, marketing and sales in China and in August 2019 the Company launched EVOMELA® in China. The NMPA required post-marketing study has completed and the clinical study report is being finalized for regulatory submission.

China Resources Pharmaceutical Commercial Group International Trading Co., Ltd.

In March 2019, the Company entered into a three-year exclusive distribution agreement with China Resources Pharmaceutical Commercial Group International Trading Co., Ltd. ("CRPCGIT") to appoint CRPCGIT on an exclusive basis as its distributor to distribute EVOMELA® in the territory of the People's Republic of China (excluding Hong Kong, Taiwan and Macau), subject to certain terms and conditions. The Company's internal marketing and sales team are responsible for commercial activities, including, for example, direct interaction with Key Opinion Leaders (KOL), physicians, hospital centers and the generating of sales. The agreement was renewed in March 2022 for another two years. Commercial sales of EVOMELA® were launched in August 2019. For the years ended December 31, 2021 and 2020, the Company recognized $30.0 million and $15.0 million, respectively, of revenues from sales of EVOMELA® under this arrangement.

Juventas Cell Therapy Ltd.

In June 2019, the Company entered into a license agreement for exclusive worldwide license to commercialize an autologous anti-CD19 T-cell therapy product (CNCT19) from Juventas (the "Juventas license agreement"). Juventas is a China-based company engaged in cell therapy. The terms of the agreement include RMB 70 million ($10 million) of milestone payments upon the registration of Phase II clinical trial of CNCT19 and sales royalty payments. The milestone was met during the quarter ended September 30, 2020. As a result, the Company paid the milestone payment of RMB 70 million to Juventas in September 2020 (see Note 3), which was expensed as acquired in-process research and development in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2020.

In September 2020, Juventas and its shareholders (including CASI Biopharmaceuticals) agreed to certain terms and conditions required by a new third-party investor to facilitate the Series B financing of Juventas, pursuant to which the Company agreed to amend and supplement the original licensing agreement (the "Supplementary Agreement") by agreeing to pay Juventas certain percentage of net profits generated from commercial sales of CNCT19 in addition to the royalty fee payment calculated as a percentage of net sales. The Supplementary Agreement also specifies a minimum annual target net profit to be distributed to Juventas and certain other terms and obligations. In return, the Company obtained additional equity interests in Juventas (see Note 3).

Under the Supplementary Agreement, Juventas and the Company will jointly market CNCT19, including, but not limited to, establishing medical teams, developing medical strategies, conducting post-marketing clinical studies, establishing Standardized Cell Therapy Centers, establishing and training providers with respect to cell therapy, testing for cell therapy, and monitoring quality controls (cell collection and transfusion, etc.), and patient management (adverse reactions treatment, patients' follow-up visits, and establishment of a database). The Company also will reimburse Juventas for a portion of Juventas' marketing expenses as reviewed and approved by a joint commercial committee to be constituted. The Company will continue to be responsible for recruiting and establishing a sales team to commercialize CNCT19.

BioInvent International AB

In October 2020, the Company entered into an exclusive licensing agreement with BioInvent International AB ("BioInvent") for the development and commercialization of novel anti-FcγRIIB antibody, BI-1206, in mainland China, Taiwan, Hong Kong and

Macau. BioInvent is a biotechnology company focused on the discovery and development of first-in-class immune-modulatory antibodies for cancer immunotherapy. BI-1206 is being investigated in a Phase 1/2 trial, in combination with anti-PD1 therapy Keytruda® (pembrolizumab), in patients with solid tumors, and in a Phase 1/2a trial in combination with MabThera® (rituximab) in patients with relapsed/refractory non-Hodgkin lymphoma (NHL). Clinical Trial Application (CTA) was approved by China National Medical Products Administration (NMPA) in December 2021. The Company is planning Phase 1 trials of BI-1206 as a single agent to evaluate the PK/safety profile and in combination with rituximab in NHL (mantle cell lymphoma, marginal zone lymphoma, and follicular lymphoma) to assess safety and tolerability, select the Recommended Phase 2 Dose and assess early signs of clinical efficacy as part of its development program for BI-1206 in China. The studies are expected to start in the first half of 2022.

Under the terms of the agreement, BioInvent and CASI will develop BI-1206 in both hematological malignancies and solid tumors, with CASI responsible for commercialization in China and associated markets. CASI made a $5.9 million upfront payment in November 2020 to BioInvent and will pay up to $83 million in development and commercial milestone payments plus tiered royalties in the high-single to mid-double-digit range on net sales of BI-1206. Because BI-1206 underlying the acquired rights has not reached technological feasibility and has no alternative future uses, the Company expensed $5.9 million as acquired in-process research and development in the accompanying consolidated statement of operations and comprehensive loss for the year ended December 31, 2020.

Black Belt Therapeutics Limited

In April 2019, the Company entered into a license agreement with Black Belt Therapeutics Limited ("Black Belt") for exclusive worldwide rights to CID-103, an investigational anti-CD38 monoclonal antibody (Mab) (formerly known as TSK011010). The Company expects that its clinical materials and commercial inventory will be supplied by one or more contract manufacturers with whom the Company has contracted with. Under the terms of the agreement, CASI obtained global rights to CID-103 for an upfront payment of 5 million euros ($5.7 million) and would pay up to $46.3 million in development milestone payments and certain royalties based on sales milestones. In June 2021, the Company achieved the First-Patient-In (FPI) in the Phase 1 dose escalation and expansion study of CID-103, and made $750,000 milestone payment in June 2021 and €250,000 ($305,000) payment in August 2021 under the terms of the agreement. Because CID-103 underlying the acquired rights has not yet reached technological feasibility and has no alternative uses, the Company expensed 5 million euros as acquired in-process research and development in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2019, and $1.1 million as acquired in-process research and development in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2021.

Cleave Therapeutics, Inc.

In March 2021, the Company entered into an exclusive license with Cleave Therapeutics, Inc. ("Cleave") for the development and commercialization of CB-5339, an oral novel VCP/p97 inhibitor, in both hematological malignancies and solid tumors, in Mainland China, Hong Kong, Macau and Taiwan. Cleave is a clinical-stage biopharmaceutical company focused on valosin-containing protein (VCP)/p97 as a novel target in protein homeostasis, DNA damage response and other cellular stress pathways for therapeutic use in the treatment of patients with cancer. Cleave and the Company will develop CB-5339 in both hematological malignancies and solid tumors, with CASI responsible for development and commercialization in China and associated markets. The Company paid a $5.5 million upfront payment to Cleave and will pay up to $74 million in development and commercial milestone payments plus tiered royalties in the high-single to mid-double-digit range on net sales of CB-5339.

CB-5339 is being evaluated by Cleave in a Phase 1 clinical trial in patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). Because CB-5339 has not yet reached technological feasibility and has no alternative future uses, the Company expensed the $5.5 million upfront payment as acquired in-process research and development in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2021.

Pharmathen Global BV

On October 29, 2019, the Company entered into an exclusive distribution agreement with Pharmathen Global BV ("Pharmathen") for the development and distribution of octreotide long acting injectable (Octreotide LAI) microsphere in China. Octreotide LAI formulations, which are approved in various European countries, are considered a standard of care for the treatment of acromegaly and the control of symptoms associated with certain neuroendocrine tumors. CASI intends to advance the development, import drug registration, and market approval of this product in China.

The terms of the agreement include an upfront payment of 1 million euros which was paid by the Company in 2019, and up to 2 million euros of additional milestone payments, of which 1.5 million euros ($1.7 million) was paid by the Company with achievements of certain milestones and was expensed as acquired in-process research and development in the accompanying consolidated statement

of operations and comprehensive loss for the year ended December 31, 2020. CASI is responsible for the development, import drug registration, product approval and commercialization in China. CASI has a 10-year non-royalty exclusive distribution period after the product launch at an agreed supply costs for the first three years.

Riemser Pharma GmbH

In August 2019, the Company entered into a distribution agreement in China with Riemser Pharma GmbH ("Riemser") to a novel formulation of thiotepa, a chemotherapeutic agent, which has multiple potential indications including use as a conditioning treatment for use prior to allogenic hematopoietic stem cell transplantation. Thiotepa has a long history of established use in the hematology/oncology setting. Pursuant to the distribution agreement, CASI obtained the exclusive distribution right of the products in China, and Riemser will be responsible for manufacturing and supplying CASI with clinical materials and commercial inventory. The Company is applying NADA registration and, subject to regulatory and marketing approvals, the Company intends to advance and commercialize this product in China. In January 2020, Riemser was acquired by Esteve Healthcare, S.L. ("ESTEVE"), an international pharmaceutical company headquartered in Barcelona. There is no contingent milestone payment due to Riemser under the agreement.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. The Company's significant accounting estimates relate to recoverability of operating lease right-of-use assets, intangible assets and long-term investments, net realizable value and obsolescence allowance for inventories, deferred tax assets and valuation allowance, allowance for doubtful accounts, stock-based arrangements and fair value of investments. Management bases its estimates on historical experience and on various other assumptions that it believes are reasonable under the circumstances. Actual results may differ from those estimates, and such differences may be material to the consolidated financial statements.

Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its subsidiaries, in which CASI, directly or indirectly, has a controlling financial interest.

These subsidiaries include Miikana Therapeutics, Inc. ("Miikana"), CASI China, CASI Wuxi, CASI Biopharmaceuticals (WUXI) Co., Ltd. ("CASI Biopharmaceuticals"), CASI Pharmaceuticals (Hainan) Co., Ltd. ("CASI Hainan") and ZhongBio (Beijing) Tech Co. Ltd. ("ZhongBio").

CASI China is a Chinese entity with 100% of its interest owned by CASI. CASI China received approval for a business license from the Beijing Industry and Commercial Administration in August 2012 and has operating facilities in Beijing. CASI Wuxi was established on December 26, 2018 in China to develop a manufacturing facility in China. CASI Biopharmaceuticals is a wholly owned subsidiary of CASI Wuxi and was established in April 2019. The Company controls CASI Wuxi through 80% voting rights. Accordingly, the financial statements of CASI Wuxi have been consolidated in the Company's consolidated financial statements since its inception. CASI Hainan and ZhongBio are wholly owned subsidiaries of CASI China and was established in June 2021 and September 2016, respectively.

All inter-company balances and transactions have been eliminated in consolidation. The Company currently operates in one operating segment, which is the development of innovative therapeutics addressing cancer and other unmet medical needs for the global market.

Foreign Currency Translation and Transactions

The accompanying consolidated financial statements of the Company are reported in US dollars. The financial position and results of operations of the Company's subsidiaries in the PRC are measured using the Renminbi (RMB), which is the local and functional currency of these entities. Assets and liabilities of the Company's PRC subsidiaries are translated into US$ using the exchange

rates in effect at the consolidated balance sheet date. The revenues and expenses of these entities are translated into US$ at the weighted average exchange rates for the period. The resulting translation gains (losses) are recorded in accumulated other comprehensive loss as a component of shareholders' equity.

Transactions denominated in foreign currencies are remeasured into the functional currency at the exchange rates prevailing on the transaction dates. Foreign currency denominated financial assets and liabilities are remeasured at the exchange rates prevailing at the balance sheet date. Net gains or losses resulting from foreign currency denominated transactions are recorded in foreign exchange gain (losses) in the consolidated statements of operations and comprehensive loss.

Revenue Recognition

Product sales recognized in the consolidated statements of operations and comprehensive loss are considered revenue from contracts with customers and, accordingly, the Company recognizes revenue using the following steps:

- Identification of the contract, or contracts, with a customer;
- Identification of the performance obligations in the contract;
- Determination of the transaction price, including the identification and estimation of variable consideration;
- Allocation of the transaction price to the performance obligations in the contract; and
- Recognition of revenue when the Company satisfies a performance obligation.

The Company recognizes revenue on sales of EVOMELA® when the control of the product is transferred to the distributor, which occurs upon delivery of the product to the carrier appointed by the distributor, in an amount that reflects the consideration to which the Company expects to be entitled to in exchange for the product, excluding amounts collected on behalf of third parties (e.g. value-added taxes). Payment terms for these sales are due within 90 days. The arrangement does not include any variable consideration. The Company recognizes accounts receivable when it recognizes revenues as its right to consideration is unconditional and only the passage of time is required before payment of that consideration is due.

The costs of assurance type warranties that provide the customer the right to exchange purchased product that does not meet appropriate quality standards are recognized when they are probable and are reasonably estimable. There was no product exchange during the years ended December 31, 2021 and 2020. As of December 31, 2021 and 2020, the Company did not incur, and therefore did not defer, any material costs to obtain or fulfill contracts. The Company did not have any contract assets or contract liabilities as of December 31, 2021 and 2020.

Concentrations Risks

Cash Concentration Risk

The Company maintains its U.S. and RMB cash in bank deposit accounts, which, at times, may exceed regulated insured limits. The Company believes it is not exposed to significant credit risk on cash and cash equivalents.

Vendor Concentration Risk

The Company has a sole supplier for its EVOMELA® product. Through the second quarter of 2020, it was sourced solely from Spectrum Pharmaceuticals, Inc. ("Spectrum") and its suppliers. Starting with the third quarter of 2020, and all future needs will be sourced from Acrotech and its suppliers. The Company's ability to select other providers of EVOMELA® is limited by FDA regulations.

Accounts Receivable and Credit Concentration

CRPCGIT is the sole customer of the Company's EVOMELA® product sales in China. All consolidated revenues for the years ended December 31, 2021 and 2020 were generated from sales to CRPCGIT in China, and all the Company's accounts receivable balance as of December 31, 2021 and 2020 were due from CRPCGIT.

The Company extends credit to CRPCGIT on an unsecured basis and maintains an allowance for doubtful accounts for estimated losses inherent in its accounts receivable. In establishing the required allowance, management considers the historical losses,

customer's financial condition, the amount of accounts receivables in dispute, the accounts receivables aging and the customer's payment pattern. The Company determined that no allowance for doubtful accounts were necessary as of December 31, 2021 and 2020. The balance of accounts receivable as of December 31, 2021 has been subsequently collected.

Fair Value of Financial Instruments

Fair value is the price that would be received from the sale of an asset or paid to transfer a liability assuming an orderly transaction in the most advantageous market at the measurement date. U.S. GAAP establishes a hierarchical disclosure framework which prioritizes and ranks the level of observability of inputs used in measuring fair value. These tiers include:

- Level 1—Quoted prices (unadjusted) in active markets that are accessible at the measurement date for identical assets or liabilities. The fair value hierarchy gives the highest priority to Level 1 inputs.

- Level 2—Observable market-based inputs other than quoted prices in active markets for identical assets or liabilities.

Level 3—Unobservable inputs are used when little or no market data is available. The fair value hierarchy gives the lowest priority to Level 3 inputs.

See Note 3 and Note 19 for additional fair value disclosures.

Cash and Cash Equivalents

Cash and cash equivalents include cash and highly liquid investments with original maturities of less than 90 days that are readily convertible to known amounts of cash.

Inventories

Inventories consist of EVOMELA® finished goods and raw materials to be used in production of ANDAs and are stated at the lower of cost or net realizable value. Cost is determined using a first-in, first-out method. Net realizable value is the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal, and transportation. Adjustments are recorded to write down the carrying amount of any obsolete and excess inventory to its estimated net realizable value based on historical and forecasted demand.

Property, Plant and Equipment

Property, plant and equipment are stated at cost, less accumulated depreciation and impairment, if any.

Costs incurred in the construction of property, plant and equipment, including down payments and progress payments, are initially capitalized as construction-in-progress and transferred into their respective asset categories when the assets are ready for their intended use, at which time depreciation commences. Furniture and equipment are depreciated over their estimated useful lives of 3 to 5 years. Leasehold improvements are amortized over the shorter of their useful lives or the lease term. Depreciation and amortization expense are determined on a straight-line basis.

Costs of Revenues

Costs of revenues consist primarily of the cost of inventories of EVOMELA® and sales-based royalties related to the sale of EVOMELA®.

Investments

The Company's investments consist of investments in equity securities with readily determinable fair value, equity securities without readily determinable fair value, and investments measured using fair value option.

Investment in equity securities with readily determinable fair value are measured at fair values, and any changes in fair value are recognized in earnings. Where the fair value of an investment in equity securities is not readily determinable, the Company recognizes such investment in long-term investments, and uses the measurement alternative of cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer.

For equity investments measured at fair value with changes in fair value recorded in earnings, the Company does not assess whether those securities are impaired. For equity investments without readily determinable fair value, at each reporting period, the Company makes a qualitative assessment considering impairment indicators to evaluate whether the investment is impaired. Impairment indicators that the Company considers include, but are not limited to, (i) the deterioration of earnings performance, credit rating, asset quality, or business prospects of the investee, (ii) a significant adverse change in the regulatory, economic, or technological environment of the investee, (iii) a significant adverse change in the general market condition of either the geographic area or the industry in which the investee operates. If a qualitative assessment indicates that the investment is impaired, the Company has to estimate the investment's fair value and if the fair value is less than the investment's carrying value, the Company recognizes an impairment loss in non-operating expenses equal to the difference between the carrying value and fair value.

Dividend income is recognized in other income when earned.

The Company elected to use fair value option to account for its investment in Cleave (see Note 3) as permitted under Accounting Standards Codification ("ASC") 825, *Financial Instruments* ("ASC 825"), which then refers to ASC 820, *Fair Value Measurement* ("ASC 820") to provide the fair value framework for valuing such investments. In accordance with ASC 820, the Company records such investment at fair value, with changes in fair value recorded in change in fair value of investments in the consolidated statements of operations and comprehensive loss.

Leases

At contract inception, the Company determines whether an arrangement is or contains a lease and whether the lease should be classified as an operating or a financing lease. A contract is or contains a lease if the contract conveys the right to control the use of the identified asset for a period of time in exchange for consideration. Control is determined based on the right to obtain all of the economic benefits from use of the identified asset and the right to direct the use of the identified asset. Right of use ("ROU") assets for operating leases represent the right to use an underlying asset for the lease term, and operating lease liabilities represent the obligation to make lease payments.

ROU assets and lease liabilities are recognized upon lease commencement for operating leases based on the present value of lease payments over the lease term. As the rate implicit in the lease cannot be readily determined, the Company uses incremental borrowing rate at the lease commencement date in determining the imputed interest and present value of lease payments. The incremental borrowing rate was determined based on the rate of interest that the Company would have to borrow an amount equal to the lease payments on a collateralized basis over a similar term. The incremental borrowing rate is primarily influenced by the risk-free interest rate of China and the US, the Company's credit rating and lease term, and is updated for measurement of new lease liabilities.

For operating leases, the Company recognizes a single lease cost on a straight-line basis over the remaining lease term.

The Company has elected not to recognize ROU assets or lease liabilities for leases with an initial term of 12 months or less; the Company recognizes lease expense for these leases on a straight-line basis over the lease term. In addition, the Company has elected not to separate non-lease components (e.g., common area maintenance fees) from the lease components.

Land use rights acquired are recognized in right-of-use assets if they meet the definition of lease.

Impairment of Long-Lived Assets

Long-lived assets, including property, plant and equipment, operating lease right-of-use ("ROU") assets and intangible assets subject to amortization, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Such events and circumstances include the use of the asset or asset group in current research and development projects and any potential alternative future uses of the asset or asset group. If circumstances require a long-lived asset or asset group be tested for possible impairment, the Company first compares undiscounted cash flows expected to be generated by that asset or asset group to its carrying value. If the carrying value of the long-lived asset or asset group is not recoverable on an undiscounted cash flow basis, an impairment is recognized to the extent that the carrying value exceeds its fair value. Fair value is determined through various valuation techniques including discounted cash flow models, quoted market values and third-party independent appraisals, as considered necessary. Impairment charges related to intangible assets were $0 and $1.5 million for the years ended December 31, 2021 and 2020, respectively.

Research and Development Expenses

Research and development expenses consist primarily of compensation and other expenses related to research and development personnel, research collaborations, costs associated with pre-clinical testing and clinical trials of the Company's product candidates, including the costs of manufacturing drug substance and drug product, regulatory maintenance costs, and facilities expenses, along with the amortization of acquired ANDAs. Research and development costs are expensed as incurred.

Acquired In-Process Research and Development Expense

The Company has acquired rights to develop and commercialize product candidates. Upfront payments that relate to the acquisition of a new drug compound, as well as pre-commercial milestone payments, are immediately expensed as acquired in-process research and development in the period in which they are incurred, provided that the new drug compound did not also include processes or activities that would constitute a "business" as defined under U.S. GAAP, the drug has not achieved regulatory approval for marketing and, absent obtaining such approval, has no established alternative future use.

The Company also pays contingent development milestone payments in accordance with agreements (see Note 1). The Company recognizes development milestone payments as acquired in-process research and development expenses when the milestones are reached.

Stock-Based Compensation

The Company records compensation expense associated with service and performance-based stock options in accordance with provisions of authoritative guidance. The estimated fair value of service-based awards is measured on the grant date and is generally recognized on a straight-line basis over the requisite service period and based on the proportionate amount of the requisite service period that has been rendered during each reporting period. The estimated fair value of performance-based awards is measured on the grant date and is recognized when it is determined that it is probable that the performance condition will be achieved. If the required vesting conditions are not met resulting in the forfeiture of the share-based awards, previously recognized compensation expense relating to those awards are reversed as occurred.

Grant date fair value was determined using an option pricing model which is affected by the fair value of underlying ordinary shares as well as assumptions regarding a number of complex and subjective variables, such as expected volitality, expected term of options, risk-free rate, and expected dividend yield.

Government Grants

Government grants are recognized when there is reasonable assurance that the Company will comply with required conditions and the grants will be received. Government grants related to assets are presented as deferred income that is recognized on a systematic basis over the useful life of the asset.

Income Taxes

Income tax expense is recognized using the asset and liability method. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities and operating loss and tax credit carryforwards as measured by the enacted tax rates that will be in effect when these differences reverse. A valuation allowance is provided to reduce the amount of deferred income tax assets if it is considered more likely than not that some portion or all of the deferred income tax assets will not be realized.

The Company recognizes in its consolidated financial statements the impact of a tax position if a tax return position or future tax position is "more likely-than-not" to be sustained upon examination, based on the technical merits of the position. Tax positions that meet the "more-likely-than-not" recognition threshold are measured at the largest amount of tax benefit that has a greater than fifty percent likelihood of being realized upon settlement. The Company recognizes interest and penalties related to uncertain tax positions, if any, in income tax expense.

Net Loss Per Share

Net loss per share (basic and diluted) was computed by dividing net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding.

New Accounting Pronouncements

Recently Adopted Pronouncements

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement. ASU 2018-13 eliminates, adds and modifies certain disclosure requirements for fair value measurements. The amendments applicable to the disclosures of changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial year of adoption. This ASU is effective for all entities for fiscal years beginning after December 15, 2019, including interim periods therein. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted, and an entity is also permitted to early adopt any removed or modified disclosures and delay adoption of the additional disclosures until their effective date. The Company adopted this guidance effective January 1, 2020. The adoption of this new accounting standard did not have a significant impact on the Company's consolidated financial statements.

Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13, Financial Instruments — Credit Losses (Topic 326) ("ASU 2016-13") and subsequent amendments to the initial guidance including ASU No. 2018-19, ASU No. 2019-04, and ASU No. 2019-05 (collectively, "Topic 326"). Topic 326 requires entities to measure all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. This replaces the existing incurred loss model and is applicable to the measurement of credit losses on financial assets measured at amortized cost. This standard is effective for public business entities, excluding entities eligible to be smaller reporting companies for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, this standard is effective for annual and interim periods beginning after December 15, 2022 and early adoption is permitted for annual and interim periods beginning after December 15, 2018. As a smaller reporting company, the Company expects to adopt this standard in fiscal year 2023. The Company is currently assessing the impact that the adoption of this ASU will have on the consolidated financial statements.

There are no other recently issued accounting pronouncements that are expected to have a material effect on the Company's financial position, results of operations or cash flows.

3. INVESTMENT IN EQUITY SECURITIES, AT FAIR VALUE AND LONG-TERM INVESTMENTS

Investment in equity securities, at fair value

MaxCyte Inc.

The Company has an equity investment in the common stock of MaxCyte, a publicly traded company. The Company's investment in this equity security is carried at its fair value, with changes in fair value reported in the consolidated statements of operations and comprehensive loss in each reporting period. The fair value of this security was measured using its quoted market price, a Level 1 input, and was $3.9 million as of December 31, 2021 and $2.7 million on December 31, 2020 (see Note 19).

BioInvent International AB

In October 2020, in conjunction with its license agreement entered into with BioInvent (see Note 1), a publicly traded company, CASI made a $6.3 million investment (equivalent to SEK 53.8 million) to acquire 1.2 million new shares (after 25:1 reverse stock split) of BioInvent, and 14,700,000 warrants, each warrant with a right to subscribe for 0.04 shares (after 25:1 reverse stock split) in BioInvent within a period of five years.

The investments in the ordinary shares and warrants of BioInvent are carried at fair value, with changes in fair value reported in the statement of operations each reporting period. The fair value of the ordinary shares was measured using its quoted market price, a Level 1 input, and was $6.0 million and $6.6 million as of December 31, 2021 and 2020 (see Note 19).

The fair value of the warrants was measured using observable market-based inputs other than quoted prices in active markets for identical assets, level 2 inputs. The Company uses the Black-Scholes-Merton valuation model to estimate the fair value of warrants. The fair value of the warrants was $591,000 as of December 31, 2021 (see Note 19), with assumptions including an expected life of 3.91 years, an assumed volatility of 46.32%, and a risk-free interest rate of 0.07%. The fair value of the warrants was $840,000 as of

December 31, 2020, with assumptions including an expected life of 4.91 years, an assumed volatility of 47.63%, and a risk-free interest rate of 0.36%. The Company recognized for such warrants unrealized loss of $0.25 million for the year ended December 31, 2021 and unrealized gain of $0.18 million for the year ended December 31, 2020, respectively.

The following table summarizes the Company's investments in equity securities at fair value as of December 31, 2021 and 2020, respectively:

(In thousands) As of December 31, 2021	Classification	Cost	Gross unrealized gains	Aggregate fair value
MaxCyte - equity interest	Investment	$ —	$ 3,866	$ 3,866
BioInvent - equity interest	Investment	$ 5,661	$ 341	$ 6,002
Total				$ 9,868

(In thousands) As of December 31, 2020	Classification	Cost	Gross unrealized gains	Aggregate fair value
MaxCyte - equity interest	Investment	$ —	$ 2,729	$ 2,729
BioInvent - equity interest	Investment	$ 5,661	$ 919	$ 6,580
Total				$ 9,309

Unrealized gains on the Company's equity investments for the years ended December 31, 2021 and 2020 were $1.1 million and $3.0 million, respectively. Unrealized lossess on the Company's equity investments for the years ended December 31, 2021 and 2020 were $0.6 million and nil, respectively.Unrealized gains (losses) on the Company's equity investments are recognized as change in fair value of investment in the consolidated statements of operations and comprehensive loss.

Long-term investments

Long-term investments as of December 31, 2021 and 2020 consisted of the following:

As of December 31, 2021 (In thousands)	Cost	Gross unrealized gains	Gross unrealized losses (including impairment)	Foreign currency translation adjustment	Aggregate fair value
Available-for-sale debt securities:					
Alesta Therapeutics B.V. - convertible loan	$ 261	$ 7	$ —	$ —	$ 268
Securities measured at fair value:					
BioInvent International AB - warrants	656	—	(65)	—	591
Cleave Therapeutics, Inc. - convertible loan	5,500	76	—	—	5,576
Equity securities without readily determinable fair value:					
Alesta Therapeutics B.V. - equity interests	2,250	—	(865)	—	1,385
Juventas Cell Therapy Ltd - equity interests	23,500	6,958	—	1,850	32,308
Juventas Cell Therapy Ltd - put option	491	—	(521)	30	—
Total	$ 32,658	$ 7,041	$ (1,451)	$ 1,880	$ 40,128

As of December 31, 2020 (In thousands)	Cost	Gross unrealized gains	Gross unrealized losses (including impairment)	Foreign currency translation adjustment	Aggregate fair value
Available-for-sale debt securities:					
Black Belt Tx Limited - convertible loan	$ 83	$ —	$ —	$ —	$ 83
Securities measured at fair value:					
BioInvent International AB - warrants	656	184	—	—	840
Equity securities without readily determinable fair value:					
Alesta Therapeutics B.V. - equity interests	2,250	—	—	—	2,250
Juventas Cell Therapy Ltd - equity interests	23,500	1,469	—	1,090	26,059
Juventas Cell Therapy Ltd - put option	491	—	(306)	25	210
Total	$ 26,980	$ 1,653	$ (306)	$ 1,115	$ 29,442

Alesta Therapeutics B.V. (previously Black Belt Tx Limited)

In April 2019, in conjunction with its license agreement the Company entered into with Black Belt (see Note 1), the Company made a 2 million euros ($2,249,600) equity investment in the ordinary shares of a newly established, privately held UK Company, Black Belt Tx Limited ("Black Belt Tx"), representing a 14.1% equity interest with the right to appoint a non-voting board observer.

Because the Company does not have significant influence over operating and financial policies of Black Belt Tx, and the equity interests do not yet have readily determinable fair value, the investment in Black Belt Tx is stated at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment.

In July 2021, Alesta Therapeutics B.V. ("Alesta Tx") was incorporated as the parent company holding all shares of Black Belt Tx with same ownership structure as Black Belt Tx. CASI obtained 14.1% equity interest in Alesta Tx in exchange for its 14.1% equity interest in Black Belt Tx. In July 2021, a new investor contributed 750,000 euros to Alesta Tx in exchange for 770,270 newly issued common stocks, representing 8.3% of the fully diluted capital. Upon the completion of the capital contribution, the Company's equity ownership in Alesta Tx was diluted from 14.1% to 12.9% with a fair value of $1,385,000, indicating an impairment of equity investment in Black Belt Tx. The Company recorded impairment of $865,000 representing the difference between the fair value of the investment and its carrying amount during the year ended December 31, 2021.

In July 2020, the Company entered into a three-year convertible loan agreement with Black Belt Tx (the "Black Belt Tx Loan") in the amount of 211,800 euros ($250,000) with a non-compounding annual interest rate of 6% payable, together with the principal balance at maturity.

The loan principal will be disbursed in three equal installments of 70,600 euros. The first tranche of 70,600 euros ($83,000) was disbursed upon execution of the loan agreement in August 2020. The second tranche of 70,600 euros ($86,000) was disbursed in February 2021, upon Black Belt Tx's achievement of certain operational targets as stipulated in the loan agreement and approved by the Black Belt Tx's Board of Directors. The third tranche would have been disbursed if Black Belt Tx reaches certain additional operational targets as stipulated in the loan agreement and approved by Black Belt Tx's Board of Directors.

In the event that Black Belt Tx, on or prior to the maturity date, completes an equity financing round of at least 5,000,000 euros ($5.9 million), then the outstanding principal amount shall be automatically converted into such shares at 80% of the price per share issued divided by a compensating factor based on the number of years that the Black Belt Tx Loan has been outstanding. The investment in convertible loan is accounted for as investment in debt securities as available-for-sale instrument.

In July 2021, Black Belt Tx repaid the convertible loan of 146,566 ($172,000) euros to the Company, including 1st tranche of 70,600 euros ($83,000), 2nd tranche of 70,600 euros ($83,000)and interest of 5,366 euros ($6,000). Concurrently, the Company entered into a three-year convertible loan agreement with Alesta Tx (the "Alesta Tx Loan") in the amount of 217,166 euros ($261,000) with a non-compounding annual interest rate of 6% payable, together with the principal balance, at maturity.

Juventas Cell Therapy Ltd.

In June 2019, in conjunction with its license agreement entered into with Juventas (see Note 1), the Company, through CASI Biopharmaceuticals, made an RMB 80 million ($11,788,000) investment in Juventas, a privately held, China-based company, in Juventas' Series A plus equity, which represented a 16.327% equity interests on a fully diluted basis, and the right to appoint a non-voting board observer. The Company is entitled to substantive liquidation preference over the founding shareholders of Juventas. In addition, the Juventas' founding shareholders provided a put option to the Company pursuant to which the Company can put the equity investment to the founding shareholders at a fixed return of 8% per annum upon occurrence of certain events. The investment in the equity interests of the Juventas and the investment in put option to the founding shareholders were accounted for as investments in equity securities using the measurement alternative at its cost, minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer, as the fair value of the equity securities of Juventas is not readily determinable. The consideration of RMB 80 million ($11,788,000) was allocated into investment in equity interests and investment in put option based on their relative fair value on the transaction date.

In September 2020, in conjunction with the Supplementary Agreement entered into with Juventas (see Note 1), the Company obtained additional Series A plus equity interests in Juventas with substantive liquidation preference over Juventas' founding shareholders, resulting in the Company's equity ownership increasing to 16.45% (post-Juventas Series B financing) on a fully diluted basis. CASI Biopharmaceuticals is also entitled to appoint a director to Juventas' board of directors. Juventas' founding shareholders also provided a put option to the Company pursuant to which the Company can put the additional equity investment to the founding shareholders at RMB 70 million plus a fixed return of 8% per annum upon occurrence of certain events. The transaction closed on September 29, 2020. The fair value of the Company's additional equity interests in Juventas and the new put option was RMB 83.7 million ($12.3 million) and RMB 0.4 million ($64,000) on September 29, 2020, respectively.

Since the equity interests with substantive liquidation preference is not in-substance common stock, the investment in the additional equity interests of Juventas was accounted for as an investment in equity securities at transaction date fair value with a corresponding credit to Other Liabilities. The profit-sharing liability represents the Company's obligation to pay an increased share of future profits pursuant to the Supplementary Agreement (see Note 1) which was conveyed by the Company in exchange for the additional equity interests in Juventas. The Company views this as a payment from a vendor that should reduce cost of revenues over the period of royalty payments. The long-term liability will be derecognized as payments are made on a systematic and rational basis representing the pattern in which the Company expects to settle the profit-sharing payment during the commercialization period of CNCT19.

The investments are measured using the measurement alternative at its cost, minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer, as the fair value of the equity securities of Juventas is not readily determinable. In addition, the changes in the fair value of the original investment in equity interests and put option in the amount of $1,116,000 resulting from the observable price in this transaction was recognized during the year ended December 31, 2020.

On October 26, 2021, Juventas completed its Series C financing through which it raised capital of RMB 410 million ($63 million). Upon the completion of Juventas Series C financing, the Company's equity ownership in Juventas decreased to 12.01% on a fully diluted basis. The Company determined the Series C financing represented an orderly transaction for a similar investment of the same issuer. The fair value of the Company's equity interests in Juventas and the put option was RMB 205.6 million ($32.3 million)

and nil on October 26, 2021, respectively. The Company recognized gain of fair value change for equity interests of RMB 35.2 million ($5.5 million) and loss of fair value change for put option of RMB1.4 million ($0.2 million), respectively, in its consolidated statements of operations and comprehensive loss for the year ended December 31, 2021, based on the price in the orderly transaction for newly issued equity interests of Juventas, which is further adjusted to reflect the differences between the newly issued equity interests of Juventas and the Company's investment.

In June 2020, the Company entered into a one-year loan agreement with Juventas in the amount of RMB 30,000,000 ($4,243,000) with an annual interest rate of 20%. In August 2020, the Company entered into another one-year loan with Juventas in the amount of RMB 40 million ($5,790,000) for one year with an annual interest rate of 20%. In September 2020, the Company received early repayments for both principals and accrued interest from Juventas. For the year ended December 31, 2020, the Company recognized interest income of $351,000 and $375,000, respectively, for these two loans.

Cleave Therapeutics, Inc.

In March 2021, in conjunction with its license agreement entered into with Cleave (see Note 1), CASI made a $5.5 million investment in Cleave through a three-year convertible note with an annual interest rate of 3% payable at maturity. The principal balance is also due at maturity. The proceeds will support and advance Cleave's programs and general operations.

In the event that Cleave, on or prior to the maturity date, completes an equity financing round of preferred stock of at least $10.0 million, then the outstanding principal amount and accrued interest shall be automatically converted into such shares at 80% of the price per share issued. The investment in the convertible loan is designated an investment measured at fair value through profit or loss. The Company recognized fair value change of $76,000 for the year ended December 31, 2021.

4. INVENTORIES

The Company's inventories consist of finished goods amounted to $1.9 million and $1.4 million, as of December 31, 2021 and 2020, respectively. No provisions to write down the carrying amount of inventory have been recorded in the year ended December 31, 2021 and December 31, 2020.

5. LEASES

Operating lease ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. Rent expense is recognized on a straight-line basis over the lease term.

Operating lease liabilities are included in accrued and other current liabilities and other liabilities (noncurrent) in the consolidated balance sheets as of December 31, 2021 and 2020. As of December 31, 2021 and 2020, the Company did not have any finance leases.

In November 2019, CASI Wuxi entered into a fifty-year lease agreement for the right to use state-owned land in China for the construction of a manufacturing facility. The land parcel is 74,028.40 square meters. The Company classifies this lease as an operating lease. The Company prepaid all of the lease payments for the land use right in 2019 in the amount of RMB45 million (equivalent to $6.5 million).

Rent expense for the years ended December 31, 2021 and 2020 was $1,452,000 and $1,600,000, respectively. There were no variable lease costs or sublease income for leased assets for the years ended December 31, 2021 and 2020.

Right of use assets and liabilities as of December 31, 2021 and 2020 were classified on the consolidated balance sheets as follows:

(In thousands)	December 31, 2021	December 31, 2020
Right of use assets	$ 9,107	$ 8,696
Accrued and other current liabilities	$ 1,061	$ 939
Other liabilities	1,105	965
Total lease liabilities	$ 2,166	$ 1,904

Supplemental cash flow information related to leases was as follows:

	Year Ended December 31,	
(In thousands)	2021	2020
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows	$ 1,354	$ 1,375
Right of use assets obtained in exchange for lease obligations:	$ 1,525	$ 1,196

All of the Company's existing leases as of December 31, 2021 and 2020 are classified as operating leases. As of December 31, 2021 and 2020, the Company had eight and seven, respectively, material operating leases for land and facilities with remaining terms expiring from 2022 through 2069 and a weighted average remaining lease term of 36.47 years and 38.37 years, respectively. The Company has fair value renewal options for many of the Company's existing leases, none of which are considered reasonably certain of being exercised or included in the minimum lease term. Weighted average discount rates used in the calculation of the lease liability for 2021 and 2020 is 3.56% and 3.72%, respectively. The discount rates reflect the estimated incremental borrowing rate, which includes an assessment of the credit rating to determine the rate that the Company would have to pay to borrow, on a collateralized basis for a similar term, an amount equal to the lease payments in a similar economic environment.

A maturity analysis representing the future undiscounted cash flow of the Company's operating leases liabilitiesas of December 31, 2021 is as follows:

(In thousands)	
2022	$ 1,122
2023	774
2024	359
Total	2,255
Discount factor	(89)
Lease liability	2,166
Amounts due within 12 months	1,061
Non-current lease liability	$ 1,105

6. PROPERTY, PLANT AND EQUIPMENT

The Company's property, plant and equipment ("PP&E") mainly includes construction in progress ("CIP"), furniture and equipment, and leasehold improvements.

Construction in progress ("CIP") is stated at cost and includes costs incurred to acquire, construct, or install PP&E. CIP overhead is expensed as incurred. Construction in progress is not depreciated until such time when the asset is substantially completed and ready for its intended use. Furniture and equipment are stated at cost and are depreciated over their estimated useful lives of 3 to 5 years. Leasehold improvements are stated at cost and are amortized over the shorter of their useful lives or the lease term. Depreciation and amortization expense are determined on a straight-line basis.

In November 2019, CASI Wuxi entered into a lease agreement for the right to use state-owned land in China for the construction of a manufacturing facility. In 2020 and 2021, CASI Wuxi entered into a series of construction contracts for the building, remodeling and installation of Wuxi Project. As of December 31, 2021, the project was still under construction and the ending balance of CIP is $12.1 million.

Property, plant and equipment consist of the following:

(In thousands)	December 31, 2021	December 31, 2020
Furniture and equipment	$ 1,728	$ 1,622
Leasehold improvements	1,133	985
Construction in progress	12,095	1,193
Total property, plant and equipment, gross	14,956	3,800
Accumulated depreciation and amortization	(1,817)	(1,322)
Impairment of property, plant and equipment	(427)	(416)
	$ 12,712	$ 2,062

Depreciation expense were $468,000 and $562,000 in 2021 and 2020, respectively. The Company recognized no impairment during the years ended December 31, 2021 and 2020.

7. INTANGIBLE ASSETS

Intangible assets include ANDAs that were acquired as part of 2018 asset acquisitions of U.S. marketed generic products, as well as capitalized costs related to a cloud computing arrangement ("CCA"). These intangible assets were originally recorded at relative estimated fair values based on the purchase price for the asset acquisitions and are stated net of accumulated amortization and impairment, if any.

The ANDAs are amortized over their estimated useful lives of 13 years, using the straight-line method. The CCA is being amortized over its useful life of 5 years.

In February 2020, the Company entered into an agreement with Chartwell Rx Sciences, LLC ("Chartwell") in which the Company sold and transferred the control of seven U.S. FDA-approved ANDAs to Chartwell in exchange for $450,000 in cash, which the Company received in March 2020. These ANDAs had a net book value of $0 at the time of sale. The Company is entitled to an additional $1 million, contingent upon Chartwell receiving certain FDA approvals relating to certain of these ANDAs. The Company recognized a gain on disposal of intangible assets in the amount of $450,000 in the accompanying consolidated statement of operations and comprehensive loss for the year ended December 31, 2020. The additional $1 million is treated as variable consideration. Because the amount of variable consideration is highly susceptible to factors outside the Company's influence and the Company's experience with similar types of contracts is limited, the Company did not include the amount of variable consideration in recognition of gain on disposal of intangible assets for the year ended December 31, 2021. The Company will recognize the variable consideration and additional gain on disposal of intangible assets when the constraint on variable consideration is resolved, i.e., Chartwell receives relevant FDA approvals. As of December 31, 2021, no FDA approvals have been obtained by Chartwell on those products.

Intangible assets at December 31, 2021 and 2020 consists of the following:

(In thousands) Asset as of December 31, 2021	Purchase Price	Accumulated Amortization	Estimated useful lives
ANDAs	$ 15,832	$ (3,688)	13 years
Others	197	(138)	5 years
Total	$ 16,029	$ (3,826)	

(In thousands) Asset as of December 31, 2020	Purchase Price	Accumulated Amortization	Estimated useful lives
ANDAs	$ 15,832	$ (2,721)	13 years
Others	197	(98)	5 years
Total	$ 16,029	$ (2,819)	

The changes in intangible assets for the years ended December 31, 2021 and 2020 are as follows:

(In thousands)	2021	2020
Balance at the beginning of the year	$ 13,210	$ 13,674
Amortization expense	(1,347)	(1,289)
Foreign currency translation adjustment	340	825
Balance at the ending of the year	$ 12,203	$ 13,210

Expected future amortization expense is as follows as of December 31, 2021:

(In thousands)	
2022	$ 1,351
2023	1,351
2024	1,323
2025	1,323
2026	1,323
2027 and thereafter	5,532

8. ACCRUED AND OTHER CURRENT LIABILITIES, AND OTHER LIABILITIES

	Year Ended December 31,	
(In thousands)	2021	2020
Accrued and other current liabilities:		
Payroll and welfare payable	$ 3,336	$ 1,535
Payables related to property and equipment	3,288	467
Lease liabilities-current (Note 5)	1,061	939
Value-added tax and other tax payable	652	434
Other	60	49
	$ 8,397	$ 3,424
Other Liabilites		
Profit-sharing liability to Juventas (Note 3)	$ 13,220	$ 12,869
Lease liabilities-noncurrent (Note 5)	1,105	965
	$ 14,325	$ 13,834

9. BANK BORROWINGS

On November 3, 2020, Beijing Branch of China CITIC Bank Corporation Limited approved a guaranteed line of credit ("Bank Borrowings") to the Company with maximum borrowings of RMB 10.0 million ($1.5 million). The joint and several liability guarantee was provided by Beijing Capital Financing Guarantee Co, Ltd.. At December 31, 2020, the Company had outstanding borrowings under the Bank Borrowings of RMB 5.4 million ($0.8 million), which matured and was repaid in on November 7, 2021, and beared interest at a fixed rate of 3.35% per annum.

On February 3, 2021, the Company obtained an additional borrowings of RMB 4.6 million ($0.7 million) under the Bank Borrowing which also matured and was repaid in 2021, and beared a fixed interest rate of 3.72% per annum.

Interest expense of $41,000 and $1,000 was recorded for the years ended December 31, 2021 and 2020, respectively.

10. NOTES PAYABLE

On April 27, 2020, M&T Bank approved a $465,595 loan to the Company under the Paycheck Protection Program (PPP) pursuant to the Coronavirus Aid, Relief and Economic Security (CARES) Act that was signed into law on March 27, 2020. The loan, evidenced by a promissory note to M&T Bank as lender and dated April 29, 2020, has a term of two years, is unsecured, and is guaranteed

by the Small Business Administration (SBA). The loan bears interest at a fixed rate of one percent per annum. Some or all of the loan may be forgiven if the Company complies with certain relevant conditions. In June 2020, the PPP was amended through enactment of the Paycheck Protection Program Flexibility Act of 2020 (PPPFA). Under the PPPFA, the Company's payments of principal and interest were deferred until October 2021. In September 2021, the loan principal of $465,595 and outstanding interest of $6,212 were forgiven and recorded in other income in the Company's consolidated statements of operations and comprehensive loss.

Interest expense of $2,900 and $3,100 was recorded for the years ended December 31, 2021 and 2020, respectively.

11. GRANTS

In November 2019, CASI Wuxi entered into a fifty-year lease agreement for the right to use state-owned land in China for the construction of a manufacturing facility (see Note 5). In November 2019, the Company entered into a grant agreement with the Administrative Committee of Wuxi Huishan Economic Development Zone, under which, the Company is eligible for grants up to RMB 25 million (equivalent to $3.6 million) to support the development of CASI Wuxi's manufacturing site.

In April 2020, CASI Wuxi received RMB 15.9 million (equivalent to $2.2 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as a government grant for this development project which was recorded as deferred income in April 2020. In November 2021, CASI Wuxi received additional RMB 3.0 million (equivalent to $0.5 million) from the Jiangsu Province Wuxi Huishan Economic Development Zone as a government grant for this development project which was recorded as deferred income in November 2021.

As of December 31, 2021 and 2020, deferred income balance represents the grants related to the lease of the land and will be amortized over the remaining term of the lease of the land. The Company recognized $51,000 and $35,000 of other income during the years ended December 31, 2021 and 2020, respectively.

12. REDEEMABLE NONCONTROLLING INTEREST

On December 26, 2018, the Company, together with Wuxi Jintou Huicun Investment Enterprise, a limited partnership organized under Chinese law ("Wuxi LP") established CASI Wuxi to build and operate a manufacturing facility in the Wuxi Huishan Economic Development Zone in Jiangsu Province, China. The Company holds 80% of the equity interests in CASI Wuxi and will invest, over time, $80 million in CASI Wuxi. The Company's investment will consist of (i) $21 million in cash (paid in February 2019), (ii) a transfer of selected ANDAs valued at $30 million (transferred in May 2019), and (iii) an additional $29 million cash payment within three years from the date of establishment of CASI Wuxi. The payment schedule has been changed into three installments of $10 million paid in July 2021, $10 million and $9 million to be paid in 2022 and 2023, respectively. Wuxi LP holds 20% of the equity interest in CASI Wuxi through its investment in RMB of $20 million in cash (paid in March 2019). As the transfer of ANDAs, valued at $30 million, was to the Company's consolidated subsidiary (CASI Wuxi), the Company recognized the transfer of the ANDAs at their carrying value and did not recognize a gain on the transfer.

Pursuant to the investment contract between the Company and Wuxi LP and Articles of Association of CASI Wuxi, the Company has the call option to purchase the 20% equity interest in CASI Wuxi held by Wuxi LP at any time within 5 years from the date of establishment of CASI Wuxi (i.e. up to December 26, 2023). Wuxi LP has the put option to require the Company to redeem the 20% equity interest in CASI Wuxi at any time after December 26, 2023. The redemption value under both the Company's embedded put option and Wuxi LP's embedded call option is equal to $20 million plus interest at the bank loan interest rate issued by the People's Bank of China for the period beginning with the initial capital contribution by Wuxi LP to the date of redemption. In addition, Wuxi LP has the put option to require the Company to redeem the 20% equity interest in CASI Wuxi at $20 million upon the occurrence of any of the following conditions: (i) the Company fails to fulfill its investment obligation to CASI Wuxi; (ii) CASI Wuxi suffers serious losses, discontinued operation, dissolution, goes into process of bankruptcy liquidation; or (iii) the Company substantially violates the investment contract and Articles of Association of CASI Wuxi.

The investment of Wuxi LP in CASI Wuxi is treated as redeemable noncontrolling interest and is classified outside of permanent equity on the consolidated balance sheets because (1) the noncontrolling interest is not mandatorily redeemable financial instruments, and (2) it is redeemable at the option of the holder, or upon the occurrence of an event that is not solely within the control of the Company. The Company initially recorded the redeemable noncontrolling interest at its fair value of $20 million. The carrying amount of the redeemable noncontrolling interest is subsequently recorded at the greater of the amount of (1) the initial carrying amount, increased or decreased for the redeemable noncontrolling interest's share of net income or loss in CASI Wuxi or (2) the redemption

value, assuming the noncontrolling interest is redeemable at the balance sheet date. Accretion of the carrying amount of redeemable noncontrolling interest to the redemption value is recorded in additional paid-in capital.

Changes in redeemable noncontrolling interest during the years ended December 31, 2021 and 2020 are as follows:

	Year Ended December 31,	
(In thousands)	2021	2020
Balance at beginning of period	$ 22,033	$ 20,670
Share of CASI Wuxi net loss	(700)	(918)
Accretion of redeemable noncontrolling interest	1,512	1,694
Foreign currency translation adjustment	612	587
Balance at end of period	$ 23,457	$ 22,033

13. STOCKHOLDERS' EQUITY

The Company had 250 million of authorized common stock at December 31, 2021 and 2020, respectively. The Company had 5 million of authorized preferred stock as of December 31, 2021 and 2020. The Company held 79,545 of shares of common stock in treasury at its acquisition cost at December 31, 2021 and 2020.

Stock Repurchase Program

On December 15, 2021, the board of directors of CASI Pharmaceuticals, Inc. (the "Company") approved a stock repurchase program for the repurchase of up to USD 10 million of the Company's common stock (and no more than 12,500,000 shares of the Company's common stock) through open market purchases in compliance with Rule 10b-18 under the Securities Exchange Act of 1934 and through trading plans established pursuant to Rule 10b5-1 of the Securities Exchange Act. Under any Rule 10b5-1 trading plan the Company might adopt, the Company's third-party broker, subject to Securities and Exchange Commission regulations regarding certain price, market, volume and timing constraints, would have authority to purchase the Company's common stock in accordance with the terms of the plan. The actual timing, number and value of shares repurchased under the stock repurchase program will depend on a number of factors, including constraints specified in any Rule 10b5-1 trading plans, price, general business and market conditions, and alternative investment opportunities. The stock repurchase program does not obligate the Company to acquire any specific number of shares in any period, and may be expanded, extended, modified or discontinued at any time. The Company anticipates funding for stock repurchase program to come from available corporate funds, including cash on hand and future cash flow. As of March 18, 2022, the Company has repurchased 3,207,661 shares of common stock amounted to $2.5 million under a Rule 10b5-1 trading plan that will terminate on March 31, 2022.

March 2021 Underwritten Public Offering

On March 24, 2021, the Company closed an underwritten public offering of 15,853,658 shares of the Company's common stock (the "Offering") at a price to the public of $2.05 per share. The gross proceeds to CASI from the Offering were $32.5 million before deducting the underwriting discounts and commissions and offering expenses payable by CASI.

The Company is using the net proceeds of this offering for working capital and general corporate purposes, which include, but are not limited to advancing the Company's product portfolio, acquiring the rights to new product candidates and general and administrative expenses.

July 2020 Underwritten Public Offering

On July 24, 2020, the Company closed an underwritten public offering of 23 million shares of common stock (the "Offering") and received gross proceeds of $43.7 million before deducting the underwriting discounts and commissions and offering expenses payable by CASI. Certain insiders, including CASI's Chairman and CEO, and CASI's President, purchased shares of common stock in the Offering at the public offering price and on the same terms as the other purchasers in this Offering. CASI's Chairman and CEO purchased 2,952,426 shares directly and ETP Global Fund LP purchased 1,200,000 shares. CASI's President purchased 20,152 shares.

Common Stock Sales Agreements

On February 23, 2018, the Company entered a Common Stock Sales Agreement (the "Sales Agreement"), as amended, with H.C. Wainwright & Co., LLC ("HCW") that would allow the Company to sell up to $20 million of shares of common stock in "at-the-

market" transactions, subject to compliance with the terms and conditions of the Sales Agreement. In 2018, the Company issued 143,248 shares under the Sales Agreement resulting in net proceeds to the Company of $475,000. During the year ended December 31, 2021, the Company has not offered and sold any shares of common stock under the Sales Agreement. Concurrently with and upon the execution of the new Stock Sales Agreement mentioned below, the Sales Agreement dated as of February 23, 2018, between CASI and HCW, was terminated by mutual agreement of the parties.

On July 19, 2019, the Company entered into an Open Market Sale Agreement℠ with Jefferies LLC , as sales agent (the "Open Market Agreement") pursuant to which the Company may elect to sell from time to time, at its option, up to $30 million in shares of the Company's common stock, subject to the terms and conditions of the Open Market Agreement. In 2019, the Company issued 59,000 shares under the Open Market Agreement resulting in net proceeds to the Company of $182,000. In 2020, the Company issued 434,000 shares under the Open Market Agreement with net proceeds of $1,357,000. During the year ended December 31, 2021, the Company has not offered and sold any shares of common stock under the Open Market Agreement. As of December 31, 2021, the Company issued 493,000 shares with net proceeds of $1,539,000. As of December 31, 2021, $28.5 million remained available under the Open Market Agreement.

On October 29, 2021, the Company has entered into a common stock sales agreement ("Stock Sales Agreement"), with H.C. Wainwright & Co., LLC, relating to shares of common stock of the Company. In accordance with the terms of the sales agreement, the Company may offer and sell shares of common stock in "at-the-market" transactions, subject to compliance with the terms and conditions of the Stock Sales Agreement, with an aggregate offering price of not more than $20,000,000. As of December 31, 2021, the Company has not offered or sold any shares of common stock under the sales agreement.

Stock Purchase Warrants

In history, the Company issued shares of its common stock with accompanying warrants to certain institutional investors, accredited investors and existing stockholders.

Stock purchase warrants activity for the years ended December 31, 2021 and 2020 is as follows:

	Number of Warrants	Weighted Average Exercise Price
Outstanding at December 31, 2019	9,843,720	$ 4.43
Exercised	(82,304)	$ 1.69
Expired	(1,489,707)	$ 3.75
Outstanding at December 31, 2020	8,271,709	$ 4.58
Expired	(2,098,877)	$ 7.19
Outstanding at December 31, 2021	6,172,832	$ 3.69
Exercisable at December 31, 2021	6,172,832	$ 3.69

All outstanding warrants are equity classified and will expire by March 2023.

14. COSTS OF REVENUES

Costs of revenues consists primarily of the cost of inventories of EVOMELA® and sales-based royalties related to the sale of EVOMELA®. The Company is obligated to pay 20% of the Company's revenue from EVOMELA® sales as royalties for a period of 10 years after the commercial launch of the products in 2019.

15. NET LOSS PER SHARE

Net loss per share (basic and diluted) was computed by dividing net loss attributable to common stockholders, considering the accretions to redemption value of the redeemable noncontrolling interest, by the weighted average number of shares of common stock outstanding. As of December 31, 2021, and 2020, outstanding stock options totaling 33,243,790 and 16,746,238, respectively, and outstanding warrants totaling 6,172,832 and 8,271,709, respectively, were anti-dilutive, and therefore, were not included in the computation of weighted average shares used in computing diluted loss per share.

The following table sets forth the basic and diluted net loss per share computation and provides a reconciliation of the numerator and denominator for the periods presented:

(In thousands, except share and per share data)	Year Ended December 31, 2021	2020
Numerator:		
Net loss attributable to CASI Pharmaceuticals, Inc.	$ (36,654)	$ (48,287)
Denominator:		
Weighted average number of common stock	136,105,539	110,452,288
Denominator for basic and diluted net loss per share calculation	136,105,539	110,452,288
Net loss per share		
— Basic and diluted	$ (0.27)	$ (0.44)

16. EMPLOYEE BENEFIT PLAN

The Company sponsors the CASI Pharmaceuticals, Inc. 401(k) Plan and Trust. The plan covers substantially all U.S. employees and enables participants to contribute a portion of salary and wages on a tax-deferred basis. Contributions to the plan by the Company are discretionary. Contributions by the Company totaled $187,000 and $250,000 for the years ended December 31, 2021 and 2020, respectively.

Full time employees of the Company in the PRC participate in a government mandated defined contribution plan, pursuant to which certain pension benefits, medical care, employee housing fund and other welfare benefits are provided to employees. Chinese labor regulations require that the PRC subsidiaries of the Company make contributions to the government for these benefits based on certain percentages of the employees' salaries. The Company has no legal obligation for the benefits beyond the contributions made. The total amounts for such employee benefits, which were expensed as incurred, were $3,137,000 and $1,542,000 for the years ended December 31, 2021 and 2020, respectively.

17. STOCK-BASED COMPENSATION

The Company has adopted various stock compensation plans for executive, scientific and administrative personnel of the Company, as well as outside directors and consultants.

In June 2019, the Company's stockholders approved an amendment to the 2011 Long-Term Incentive Plan (the "2011 Plan"), increasing the number of shares of common stock reserved for issuance from 20,230,000 to 25,230,000 to be available for grants and awards.

On June 15, 2021, the 2021 Long-Term Incentive Plan (the "2021 Plan") was approved by the Company's stockholders. The maximum number of shares of common stock that are available for grants and awards equals to 20,000,000 shares of stock, which includes 10,726,673 shares of common stock remaining under the 2011 Plan as of April 12, 2021. Currently, the 2021 Plan is administered by the Company's compensation committee.

As of December 31, 2021, a total of 10,515,448 shares remained available for grant under the Company's 2021 Long-Term Incentive Plan.

In addition to the 2011 Plan and the 2021 Plan, the Company also granted stock options to Dr. He, the Company's Chairman and CEO. On June 20, 2019, the Company's stockholders approved a grant of stock options to Dr. He at the 2019 Annual Meeting. Under the terms of the grant, Dr. He received a stock option covering 4 million shares of common stock, at an exercise price of $2.85, vesting upon the earlier of (i) the completion of a transformative event by the Company as determined at the discretion of the Company's compensation committee and (ii) April 2, 2021, the second anniversary of the date of his appointment as CEO. On June 15, 2021, the Board approved a grant of stock options to Dr. He which consists of 4 million shares time-based and 4 million shares performance-based stock options.

The share-based compensation expenses are recorded as components of general and administrative expense, selling and marketing expense, and research and development expense, as follows:

	Year Ended December 31,	
(In thousands)	2021	2020
Research and development	$ 361	$ 245
Sales and Marketing	449	39
General and administrative	6,960	7,537
Share-based compensation expense	$ 7,770	$ 7,821

Compensation expense related to stock options with service conditions is recognized over the requisite service period, which is generally the option vesting term of up to five years. Compensation expense related to stock options with performance conditions are recognized when it is probable that the performance condition will be achieved. For the years ended December 31, 2021 and 2020, $2,319,000 and $49,000 was expensed for stock option awards with performance conditions that were probable during the year, respectively.

The Company uses the Black-Scholes-Merton valuation model to estimate the fair value of service based and performance-based stock options granted to employees. Option valuation models, including Black-Scholes-Merton, require the input of highly subjective assumptions, and changes in the assumptions used can materially affect the grant date fair value of an award.

Expected Volatility—Volatility is a measure of the amount by which a financial variable such as a share price has fluctuated (historical volatility) or is expected to fluctuate (expected volatility) during a period. The Company uses the historical volatility based on the daily price observations of its common stock during the period immediately preceding the share-based award grant that is equal in length to the award's expected term. The Company believes that historical volatility represents the best estimate of future long term volatility.

Risk-Free Interest Rate—This is the average interest rate consistent with the yield available on a U.S. Treasury note (with a term equal to the expected term of the underlying grants) at the date the option was granted.

Expected Term of Options—This is the period of time that the options granted are expected to remain outstanding. The Company uses a simplified method for estimating the expected term of service based awards granted. For performance based awards, the expected term of service is based on the derived service period.

Expected Dividend Yield—The Company has never declared or paid dividends on its common stock and does not anticipate paying any dividends in the foreseeable future. As such, the dividend yield percentage is assumed to be zero.

Following are the weighted-average assumptions used in valuing the stock options granted to employees during the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
Expected volatility	79.68 %	78.70 %
Range of expected volatility	75.69%-81.50 %	75.84% to 81.63 %
Range of risk free interest rate	0.72%-1.38 %	0.31% to 1.77 %
Expected term of option	6.17 years	6.10 years
Expected dividend yield	0.00 %	0.00 %

The weighted average fair value of stock options granted during the years ended December 31, 2021 and 2020 were $1.0 and $1.85, respectively.

A summary of the Company's stock option plans and changes in options outstanding under the plans during the years ended December 31, 2021 and 2020 is as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term In Years	Aggregate Intrinsic Value
Outstanding at December 31, 2019	18,268,372	$ 2.58		
Exercised	(2,789,473)	$ 1.39		$ 1,856,978
Granted	2,380,686	$ 2.71		
Expired	(117,722)	$ 5.06		
Forfeited	(995,625)	$ 3.78		
Cancelled	—	$ —		
Outstanding at December 31, 2020	16,746,238	$ 2.71		
Exercised	—	$ —		$ —
Granted	17,939,552	$ 1.49		
Expired	(387,000)	$ 4.56		
Forfeited	(1,055,000)	$ 2.64		
Cancelled	—	$ —		
Outstanding at December 31, 2021	33,243,790	$ 2.04	7.71	$ —
Vested and expected to vest at December 31, 2021	33,243,790	$ 2.04	7.71	$ —
Exercisable at December 31, 2021	15,294,016	$ 2.44	5.81	$ —

The aggregate intrinsic value is calculated as the difference between (i) the closing price of the common stock at December 31, 2021 and (ii) the exercise price of the underlying awards, multiplied by the number of options that had an exercise price less than the closing price on the last trading day of the year. Cash received from option exercises under all share-based payment arrangements for the twelve months ended December 31, 2021 and 2020 was $0 and $3.9 million, respectively.

The following summarizes information about stock options that are outstanding at December 31, 2021:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding at December 31, 2021	Weighted Average Remaining Contractual Life in Years	Weighted Average Exercise Price	Number Exercisable at December 31, 2021	Weighted Average Exercise Price
$0.00 - $1.00	3,223,853	7.66	$ 0.87	1,373,853	$ 0.87
$1.01 - $2.00	20,495,481	7.98	$ 1.52	6,158,707	$ 1.47
$2.01 - $4.00	8,209,456	7.25	$ 2.99	6,746,456	$ 2.94
$4.01 - $7.00	1,110,000	6.65	$ 6.82	810,000	$ 6.89
$7.01 - $9.00	205,000	6.50	$ 8.23	205,000	$ 8.23
	33,243,790	7.71	$ 2.04	15,294,016	$ 2.44

As of December 31, 2021, there was $16,148,000 of total unrecognized compensation cost related to non-vested stock options, excluding not-probable performance condition options. That cost is expected to be recognized over a weighted-average period of 2.7 years.

18. INCOME TAXES

For financial reporting purposes, loss before income taxes includes the following components:

(In thousands)	2021	2020
United States	$ (32,169)	$ (40,626)
PRC	(3,673)	(6,885)
Total	$ (35,842)	$ (47,511)

Significant components of the Company's deferred income tax assets and liabilities as of December 31, 2021 and 2020 are as follows:

(In thousands)	December 31, 2021	2020
Deferred income tax assets:		
Net operating loss carryforwards	$ 69,684	$ 78,790
Research and development credit carryforwards	4,259	6,244
Intangible assets	8,051	8,049
Stock-based compensation	5,336	5,126
Impairment loss of long-term investments	182	—
Others	540	394
Valuation allowance for deferred income tax assets	(83,651)	(94,986)
	$ 4,401	$ 3,617
Deferred income tax liabilities:		
Deferred Royalty Income	(2,342)	(2,823)
Change in fair value of investments	(1,865)	(690)
Others	(194)	(104)
	$ (4,401)	$ (3,617)

The Company has U.S. federal and state net operating loss (NOL) carryforwards of $302.1 million at December 31, 2021. Federal and certain state NOLs generated after 2017, have indefinite lives. Certain NOLs generated prior to 2018 begin to expire in years 2022 through 2037. The Company also has People's Republic of China ("PRC") NOLs carryforward of $24.2 million at December 31, 2021 that begin to expire in years 2022 through 2026. The Company also has research and experimentation ("R&E") tax credit carryforwards of $4.3 million as of December 31, 2021 that begin to expire in years 2022 through 2038. Unused R&E tax credit carryforwards expire after a period of 20 years.

Under the provisions of the Internal Revenue Code, the NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986, respectively, as well as similar state tax provisions. This could limit the amount of tax attributes that the Company can utilize annually to offset future taxable income or tax liabilities. The amount of the annual limitation, if any, will be determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. For financial reporting purposes, a 100% valuation allowance has been recognized to reduce the net deferred tax assets to zero because it is more likely than not that the Company could not generate sufficient taxable income in the future to realize the benefit of deferred income tax assets.

A reconciliation of the provision for income taxes to the federal statutory rate is as follows:

(In thousands)	2021	2020
Tax benefit at statutory rate of 21%	$ (7,526)	$ (9,977)
State taxes	—	(732)
Attribute expiration	10,676	13,707
Change in applicable tax rates	7,117	11,612
Nondeductible expenses	1,059	358
Deemed royalty	—	4,220
Others	9	(54)
Change in valuation allowance	(11,335)	(19,134)
	$ —	**$ —**

Note (1) Change in applicable tax rates represents the difference between the US federal statutory tax rate and the PRC statutory tax rate applied to the entities that operate in PRC. Additionally, change in applicable tax rates reflects the reduction of the Company's deferred tax assets related to the change in the Company's activities in and the tax laws of certain states.

A reconciliation of the beginning and ending amount of gross unrecognized tax benefits is as follows:

(In thousands)	2021	2020
Unrecognized tax benefits balance at January 1	$ 2,082	$ 2,581
Reductions for tax positions of prior periods	(642)	(499)
Additions for tax positions of current period	—	—
Unrecognized tax benefits balance at December 31	$ 1,440	$ 2,082

The Company had $1.4 million of unrecognized tax benefits as of December 31, 2021 related to net R&E tax credit. For the year ended December 31, 2021, there was a net reduction of unrecognized tax benefits of $0.6 million related to R&E tax credits. The Company has a full valuation allowance at December 31, 2021 and 2020 against the full amount of its net deferred tax assets and, therefore, there was no impact on the Company's financial position. The Company does not expect significant changes to the unrecognized benefit during 2020. As of December 31, 2021 and 2020, the Company did not accrue any interest related to uncertain tax positions. To date, there have been no interest or penalties charged to the Company related to income taxes.

The Company and each of its PRC subsidiaries file income tax returns in the United States and the PRC, respectively. Due to the existence of tax attribute carryforwards (which are currently offset by a full valuation allowance), all of the Company's tax returns since 1999 are open to examination by the taxing authorities. According to the PRC Tax Administration and Collection Law, the statute of limitations is three years if the underpayment of taxes is due to computational errors made by the taxpayer or the withholding agent. The statute of limitations is extended to five years under special circumstances where the underpayment of taxes is more than RMB100,000 ($14,334). In the case of transfer pricing issues, the statute of limitations is ten years. There is no statute of limitations in the case of tax evasion. In the US, the Company is no longer subject ot income tax examinations by authorities for years ended on or before December 31, 2017 except for certain states where the open periods are one year longer.

19. FAIR VALUE MEASUREMENTS

Financial instruments of the Company primarily consist of cash and cash equivalents, investment in equity securities, accounts receivable, long-term investments, accounts payable, accrued liabilities, notes payable and bank borrowings. As of December 31, 2021 and 2020, the carrying amount of cash and cash equivalents, accounts receivable, accounts payable, accrued liabilities, notes payable and bank borrowings are carried at cost which approximates their fair values due to the short-term nature of the instruments.

Financial Assets and Liabilities Measured at Fair Value on a Recurring Basis

The Company evaluates financial assets and liabilities subject to fair value measurements on a recurring basis to determine the appropriate level at which to classify them each reporting period. This determination requires the Company to make subjective judgments as to the significance of inputs used in determining fair value and where such inputs lie within the hierarchy.

The Company has equity investments in the common stock of two publicly traded companies. The Company's investments in these equity securities are carried at their estimated fair value, with changes in fair value reported in the consolidated statement of operations and comprehensive loss each reporting period (see Note 3). The fair value of the common stock is based on quoted market price for the investees' common stock, a Level 1 input.

The Company has an equity investment in the warrants of a publicly traded company. The Company's investment is carried at its estimated fair value, with changes in fair value reported in the consolidated statement of operations and comprehensive loss each reporting period (see Note 3). The fair value of the warrants was measured using observable market-based inputs other than quoted prices in active markets for identical assets, level 2 inputs. The Company uses the Black-Scholes-Merton valuation model to estimate the fair value of warrants. Option valuation models, including Black-Scholes-Merton, require the input of highly subjective assumptions, and changes in the assumptions used can materially affect the fair value determination of a warrant.

The Company has an investment in the convertible debt of Black Belt Tx. The Company's investment is carried at its estimated fair value, with changes in fair value reported in the consolidated statement of operations and comprehensive loss each reporting period (see Note 3) using Level 3 input.

The Company has an investment in the convertible debt of Cleave. The Company's investment is carried at its estimated fair value, with changes in fair value reported in the consolidated statement of operations and comprehensive loss each reporting period (see Note 3) using Level 3 input.

The following tables present the Company's financial assets accounted for at fair value on a recurring basis as of December 31, 2021 and December 31, 2020, by level within the fair value hierarchy:

(In thousands) Description	Fair Value at December 31, 2021	Level 1	Level 2	Level 3
Investments classified as Current and non-Current Assets				
Investments in common stock	$ 9,868	$ 9,868	$ —	$ —
Investment in warrants - Designated as investment measured at FVTPL	$ 591	$ —	$ 591	$ —
Investment in convertible loan - AFS	$ 268	$ —	$ —	$ 268
Investment in convertible loan - Designated as investment measured at FVTPL	$ 5,576	$ —	$ —	$ 5,576

	Quantitative Information about Level 3 Fair Value Measurements			
Description	Fair Value at December 31, 2021	Valuation Techniques	Unobservable Input	Average/Median
Investment in convertible loan - Designated as investment measured at FVTPL	$ 5,576	Discounted cash flow	Discount rate	20%/20%

(In thousands) Description	Fair Value at December 31, 2020	Level 1	Level 2	Level 3
Investments classified as Current and non-Current Assets				
Investments in common stock	$ 9,309	$ 9,309	$ —	$ —
Investment in warrants - Designated as investment measured at FVTPL	$ 840	$ —	$ 840	$ —
Investment in convertible loan - AFS	$ 83	$ —	$ —	$ 83

Financial Assets and Liabilities Measured at Fair Value on a Non-Recurring Basis

The Company measures equity investments without readily determinable fair values at its cost, minus impairment, if any, plus or minus changes resulting from observable transactions of identical or similar securities of the same issuer.

On September 29, 2020 and October 23, 2021, respectively, the Company remeasured the investments in equity securities in Juventas to the fair value (see Note 3). The Company estimated the fair value of these securities based on the transaction price of similar securities issued by the investee.

	Quantitative Information about Level 3 Fair Value Measurements			
Description	Fair Value at September 29, 2020 (remeasurement date)	Valuation Techniques	Unobservable Input	Average/Median
Investment in equity securities using measurement alternative	$ 26,059	Market approach	Multiples of selected comparable companies	5.3/1.1

	Quantitative Information about Level 3 Fair Value Measurements			
Description	Fair Value at October 23, 2021 (remeasurement date)	Valuation Techniques	Unobservable Input	Average/Median
Investment in equity securities using measurement alternative	$ 32,308	Market approach	Expected volatility	59%/58%

On June 30, 2021, the Company remeasured the investment in equity securities in Alesta to the fair value of $1,385,000 (see Note 3). The Company estimated the fair value of the securities using Level 2 inputs based on the transaction price of identical securities issued by the investee.

Non-Financial Assets and Liabilities Measured at Fair Value on a Recurring Basis

The Company has no non-financial assets and liabilities that are measured at fair value on a recurring basis.

Non-Financial Assets and Liabilities Measured at Fair Value on a Non-Recurring Basis

As of June 30, 2020, the intangible assets and assets held for sale with a total carrying amount of $3,087,000 were written down to their fair value of $1,550,000, resulting in an impairment charge of $1,537,000, which represents the difference between the carrying value of the intangible asset and assets held for sale and its fair value. The Company estimated the fair value using Level 2 inputs based on quoted price. Assets held for sale were subsequently sold in July 2020 and October 2020, respectively.

No impairment was recorded for the year ended December 31, 2021. The Company has no non-financial assets and liabilities that are measured at fair value on a non- recurring basis as of December 31, 2021.

20. RELATED PARTY TRANSACTIONS

Juventas. On July 1, 2019, the Company entered into a one-year equipment lease with Juventas in the amount of RMB 80,000 ($15,000) a month, which is classified as an operating lease. Transactions with Juventas are considered to be related party transactions as the Company's CEO and Chairman is the chairman and one of the founding shareholders of Juventas. The lease was renewed for another year in July 2020 and in June 2021 with the same monthly lease income. During the years ended December 31, 2021 and 2020, the Company recognized lease income of $148,000 and $140,000, respectively.

BioCheck. In June 2019, the Company entered into a one-year agreement primarily for the sublease of certain office and lab space with BioCheck Inc. ("BioCheck") in the amount of $60,000 ($5,000 a month), which is classified as an operating lease. Transactions with BioCheck are considered to be related party transactions because Dr. Wei-Wu He, the Company's Chairman and CEO is also the Chairman of BioCheck. Transactions with ETP, parent of BioCheck, and a more than 5% shareholder of the Company, are also considered to be related party transactions as Dr. Wei-Wu He, the Company's CEO and Chairman is also the founder and managing partner of ETP.

Because the Company required additional office space, in January 2020, the agreement was amended for annualized rents in the amount of $144,000 ($12,000 a month) with a stipulation that the new rent was retroactive to October 1, 2019. The lease expired on June 9, 2021 and was not renewed. During the years ended December 31, 2021 and 2020, the Company recognized rent expense of $60,000 and $144,000, respectively.

March 2021 Underwritten Public Offering Transactions. On March 24, 2021, the Company closed an underwritten public offering of 15,853,658 shares of the Company's common stock (the "Offering") at a price to the public of $2.05 per share. The gross proceeds to CASI from the Offering were $32.5 million before deducting the underwriting discounts and commissions and offering expenses payable by CASI.

ETP BioHealth III Fund LP ("ETP BioHealth"), in which CASI's Chairman and CEO is the founder and managing partner of ETP BioHealth's general partner (Emerging Technology Partners, LLC ("ETP")), purchased shares of common stock in the Offering at the public offering price and on the same terms as the other purchasers in the Offering. ETP BioHealth purchased 3,000,000 shares at the public offering price of $2.05 per share for a total of $6.15 million.

21. COMMITMENTS AND CONTINGENCIES

In conjunction with the Cleave agreement entered into during 2021 (see Note 1), the Company is responsible for certain milestone and royalty payments. As of December 31, 2021, no milestones have been achieved.

In conjunction with the BioInvent agreement entered into during 2020 (see Note 1), the Company is responsible for certain milestone and royalty payments. As of December 31, 2021, no milestones have been achieved.

In conjunction with the Black Belt agreement entered into during 2019 (see Note 1), the Company is responsible for certain milestone and royalty payments. In June 2021, the Company achieved the First-Patient-In (FPI) in the Phase 1 dose escalation and expansion study of CID-103, and made $750,000 milestone payment in June 2021 and 250,000 euros ($305,000) in August 2021. As of December 31, 2021, no other milestones have been achieved.

In conjunction with the Pharmathen agreement entered into during 2019 (see Note 1), the Company is responsible for one remaining milestone payment. As of December 31, 2021, the remaining milestone has not been achieved.

In November 2019, CASI Wuxi entered into a lease agreement for the right to use state-owned land in China for the construction of a manufacturing facility. Pursuant to the agreement, CASI Wuxi has committed to invest land use right and property, plant and

equipment of RMB1 billion (equivalent to $143 million) by August 2022. In 2020, for the design and construction work of the land, CASI Wuxi entered into several contracts for RMB 76.1 million ($12.0 million) to complete the phase 1 project of CASI Wuxi's research and development production base, the project was the estimated to be completed in October 2023. In February 2022, the Company has reached an alignment with the Wuxi local government that it will collaborate with Wuxi LP to co-develop the land continuously in the future, and the original three-year investment plan will be extended, details regarding the plan are under negotiation. The commitment under these contracts was RMB 54.5 million ($8.5 million).

Also in 2020, CASI Wuxi entered in to a lease agreement with local government for a manufactory building next to the leased land. Since then, the Company entered into a series of contracts for the remodeling and installation work of the building and warehouse, as well as purchase of equipments. The total contract amount entered into for this building is approximately RMB 92.9 million ($14.6 million), and the commitment under these contracts was RMB 14.6 million ($2.3 million).

The Company is subject in the normal course of business to various legal proceedings in which claims for monetary or other damages may be asserted. Management does not believe such legal proceedings, unless otherwise disclosed herein, are material.

22. SUBSEQUENT EVENTS

Renewal of Agreement with CRPCGIT

In March 2019, the Company entered into a three-year exclusive distribution agreement with CRPCGIT to appoint CRPCGIT on an exclusive basis as its distributor to distribute EVOMELA® in the territory of the People's Republic of China (excluding Hong Kong, Taiwan and Macau), subject to certain terms and conditions. The Company's internal marketing and sales team are responsible for commercial activities, including, for example, direct interaction with Key Opinion Leaders (KOL), physicians, hospital centers and the generating of sales. The agreement was renewed in March 2022 for another two years.

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