Zentalis Pharmaceuticals Reports Third Quarter 2022 Financial Results and Operational Updates

November 9, 2022

Six sponsored studies with potentially first-in-class Wee1 inhibitor, ZN-c3, ongoing and continuing dose optimization work, as drug continues to show improved tolerability in initial safety data from monotherapy Phase 2 USC trial announced today

Identified Cyclin E driven high-grade serous ovarian cancer patients as initial expansion population for ZN-c3 biomarker monotherapy trial

Announced first ZN-c3 clinical development collaboration with Pfizer in BRAF mutant mCRC; Expanded ZN-c3 clinical development collaboration with GSK in PARP resistant ovarian cancer

Declared BCL-xL protein degrader candidate and initiated IND-enabling studies; Molecule has broad potential across multiple tumor types and in combination

Strengthened Board and management team with appointments of Chief Medical Officer, Chief Scientific Officer and Chief Translational Officer

$422 million cash balance as of September 30, 2022, with projected cash runway into 2025

NEW YORK and SAN DIEGO, Nov. 09, 2022 (GLOBE NEWSWIRE) -- Zentalis™ Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical-stage biopharmaceutical company focused on discovering and developing clinically differentiated small molecule therapeutics targeting fundamental biological pathways of cancers, today announced financial results for the third quarter ended September 30, 2022 and highlighted recent corporate accomplishments.

“During the third quarter, we made tremendous progress advancing our clinical strategy and corporate capabilities. We have established a three-pronged development plan for ZN-c3, our potentially first-in-class Wee1 inhibitor—investigation as a monotherapy, in combination with chemotherapy, and in combination with targeted therapies,” said Kimberly Blackwell, MD, Chief Executive Officer of Zentalis. “Building on ZN-c3’s favorable safety profile in the monotherapy setting across tumor types, we are pleased to announce Cyclin E gene amplification and protein overexpression as our biomarker strategy in high-grade serous ovarian cancer. This biomarker defined trial in ovarian cancer will allow us to demonstrate potential efficacy in an enriched patient population that has shown evidence of clinical sensitivity to Wee1 inhibition. This trial also has the potential to show initial proof of concept for Wee1 inhibition in Cyclin E driven cancers, which have higher levels of chemotherapy and targeted therapy resistance. On the combination front, there is strong data demonstrating Wee1 inhibition’s synergy with DNA-damaging therapies, such as PARP inhibitors, and with targeted agents in mutationally driven cancers. There is significant interest in these approaches, and we currently have collaborations with Pfizer, GSK and the Dana-Farber Cancer Institute to explore these combinations in the clinic.”

Dr. Blackwell continued, “Our development of ZN-c3 includes ongoing dose optimization activities across the clinical program. Although we have demonstrated a favorable safety profile and monotherapy efficacy when ZN-c3 was given on a continuous daily dosing schedule, data show that higher doses delivered on an intermittent schedule have the potential to lead to higher pharmacokinetic exposures and a more favorable therapeutic index. We believe our dose optimization work will allow us to benefit the broadest range of cancer patients and maximize value for all of our stakeholders. With our strong cash position and strengthened management team, we believe we are well-positioned to execute on our clinical development plans and further our mission to improve the lives of cancer patients.”

Wee1 Inhibitor (ZN-c3) Program Highlights

- **Monotherapy in USC safety and enrollment update**: As of a data cutoff on September 14, 2022, a total of 43 patients were enrolled and dosed in the Phase 2 monotherapy uterine serous carcinoma (USC) trial. ZN-c3 was well tolerated and the safety profile was similar or improved relative to previously disclosed data, exhibiting a better hematological and gastrointestinal tolerability profile. The U.S. Food and Drug Administration has granted Fast Track designation to ZN-c3 in this setting.

- **Cyclin E biomarker strategy in high-grade serous ovarian cancer**: The Company announced that Cyclin E overexpression and/or amplification in high-grade serous ovarian cancer will become the focus of its ongoing Phase 1/2 clinical study examining biomarker-driven enrichment strategies for ZN-c3. Cyclin E overexpression acts at the G1-S checkpoint by driving premature entry into S-phase resulting in replicative stress and significantly increases sensitivity to ZN-c3. The Company has generated preclinical data showing that Cyclin E overexpression sensitizes cancer cells to the anti-tumor effects of ZN-c3 as well as preliminary retrospective clinical data that Cyclin E protein levels may be associated with clinical benefit from ZN-c3. The Company plans to present the preclinical data in the first half of 2023. The two new cohorts of patients will be given monotherapy, which will potentially generate meaningful data sets in patients with Cyclin E gene amplification and patients with Cyclin E protein overexpression independent of gene amplification.

- **Dose optimization**: The Company highlighted that it continues to optimize dosing across the ZN-c3 clinical portfolio to maximize exposure, improve normal tissue tolerability and enable maximum probability of success. The Company anticipates that the Phase 2 USC trial dose will be modified based on these ongoing dose optimization studies and that, as

a result, the timeline of the USC study will be extended. The Company anticipates providing an update on ZN-c3 dosing in the first half of 2023, including expected program timelines and potential paths to registration.

- **Pfizer collaboration in mCRC**: Zentalis and Pfizer are collaborating on a Phase 1/2 dose escalation study of ZN-c3 in combination with encorafenib and cetuximab (BEACON regimen) in BRAF V600E-mutated metastatic colorectal cancer (mCRC) patients. In preclinical studies, Wee1 inhibition has shown synergy with many targeted agents in mutationally driven cancers, and the addition of ZN-c3 to the BEACON regimen enhanced anti-tumor activity in a cell-line-derived xenograft model. Additional information on this clinical development collaboration is available here.

- **GSK collaboration in ovarian cancer**: Zentalis and GSK are expanding their ongoing collaboration looking at the clinical synergy of ZN-c3 and niraparib in PARP resistant ovarian cancer. The Phase 1/2 dose escalation study, currently enrolling with concurrent dosing of the two drugs, will be expanded to include a cohort that will be given ZN-c3 and niraparib on a dose escalating, alternating schedule of one week of ZN-c3 followed by one week of niraparib.

- **Chemotherapy combination in platinum-resistant ovarian cancer**: The Company continues to enroll its dose escalation trial of standard chemotherapy (paclitaxel, gemcitabine, and carboplatin) in platinum-resistant ovarian cancer.

- **Chemotherapy combination in osteosarcoma**: The Company will be presenting initial data from its Phase 1/2 combination trial of ZN-c3 and chemotherapy in osteosarcoma in a poster session at the upcoming Connective Tissue Oncology Society (CTOS) 2022 Annual Meeting, being held November 16-19 in Vancouver. Details for the CTOS poster presentation are as follows:
    - **Title:** Preliminary Data from a Phase 1 Dose Escalation Study of ZN-c3 Plus Gemcitabine in Relapsed/Refractory Osteosarcoma (NCT04833582)
    - **Session:** Medical & Pediatric Oncology and Trials
    - **Date/Time:** November 17, 2022 from 5:00pm to 7:00pm ET
    - **Presenter:** Viswatej Avutu, MD, Assistant Attending Physician at Memorial Sloan Kettering Cancer Center

- **Dana-Farber combination study in platinum-resistant pancreatic cancer**: Zentalis announced an investigator-initiated trial with Dana-Farber Cancer Institute, funded by Stand Up To Cancer and the Lustgarten Foundation, to explore the combination of ZN-c3 with gemcitabine in platinum-resistant advanced pancreatic adenocarcinoma. James Cleary, MD, PhD, Director, Clinical Research, Division of Gastrointestinal Oncology at the Dana-Farber Cancer Institute, and Brandon Huffman, MD, Adult Medical Oncology Fellow at the Dana-Farber Cancer Institute, will be running this trial. “We are pleased to announce this important trial which builds on the growing body of clinical evidence supporting the use of ZN-c3 across a range of tumor types,” said Dr. Cleary. “Pancreatic cancer continues to be an area of high unmet patient need, and we look forward to understanding the potential role of ZN-c3 in helping these patients.”

BCL-2 Inhibitor (ZN-d5) Update

- **Monotherapy dose optimization continues in NHL and amyloidosis**: Dosing with food is ongoing in patients in non-Hodgkin lymphoma (NHL) and amyloidosis, and the combination study of ZN-d5 and ZN-c3 in acute myeloid leukemia (AML) is scheduled to initiate in the fourth quarter of 2022.

BCL-xL Degrader Update

- **Declared candidate and initiated IND-enabling studies**: BCL-xL degrader candidate demonstrates potent anti-cancer activity in several preclinical models and has the potential to have platelet sparing benefits over clinical-stage BCL-xL targeted inhibitors.

Corporate Highlights

- In September, Zentalis appointed Jan Skvarka, PhD, MBA, to its Board of Directors. Dr. Skvarka is an accomplished biopharmaceutical executive bringing over three decades of extensive operational, strategic and financial expertise to Zentalis. Dr. Skvarka was formerly Chief Executive Officer of Trillium Therapeutics, Inc., which was acquired by Pfizer under his leadership.

- In October, the Company promoted co-founder Kevin Bunker, PhD, to Chief Scientific Officer. In this new role, Dr. Bunker will focus on leading Research and Development and advancing the preclinical pipeline with the Company’s Integrated Discovery Engine.

- In October, Zentalis appointed Carrie Brownstein, MD, as Chief Medical Officer. Dr. Brownstein, a leading oncologist and hematologist, joins Zentalis with over two decades of medical and biopharmaceutical experience, successfully executing clinical program strategies across all phases of product development.

- In October, the Company appointed Mark Lackner, PhD, as Chief Translational Officer, Head of Biomarker Strategy. Dr.

Lackner, a recognized and respected cancer biologist, joins Zentalis with over two decades of oncology-focused drug development expertise, including significant experience in biomarker discovery and clinical biomarker strategies.

Third Quarter 2022 Financial Results

- **Cash and Marketable Securities Position**: As of September 30, 2022, Zentalis had cash, cash equivalents and marketable securities of $421.7 million. The Company believes that its existing cash, cash equivalents and marketable securities as of September 30, 2022 will be sufficient to fund its operating expenses and capital expenditure requirements into the first quarter of 2025.
- **Research and Development Expenses**: Research and development (R&D) expenses for the three months ended September 30, 2022 were $42.2 million, compared to $54.0 million for the three months ended September 30, 2021. The decrease of $11.8 million was primarily due to non-recurring R&D impairments and licensing milestones of $8.8 million and $5.0 million, respectively, recorded during the three months ended September 30, 2021. Other decreases in R&D expenses included $4.6 million in decreased manufacturing and collaborative expenses, and $0.3 million of additional reimbursement from Zentera under our cost sharing arrangement. These decreases were offset by increases of $3.4 million, $3.1 million and $0.4 million of clinical trial related costs, personnel and consulting costs, and overhead allocations, respectively.
- **General and Administrative Expenses**: General and administrative expenses for the three months ended September 30, 2022 were $12.0 million, compared to $8.9 million during the three months ended September 30, 2021. This increase of $3.1 million was primarily attributable to an increase in non-cash, stock-based compensation expense of $1.8 million and $0.3 million related to other compensation expense. Increases of $1.9 million, $0.6 million and $0.5 million were seen in rent and depreciation expense, external consulting expense and legal expense, respectively. These amounts were partially offset by a decrease in permits and fees and allocation of overhead expenditures to R&D of $1.6 million and $0.4 million, respectively.

About Zentalis Pharmaceuticals

Zentalis Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company focused on discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers. The Company is developing a focused pipeline of potentially best-in-class oncology candidates, all internally discovered, which include ZN-c3, a potentially first-in-class Wee1 inhibitor for advanced solid and liquid tumors, ZN-d5, a BCL-2 inhibitor for hematologic malignancies and related disorders, and a heterobifunctional degrader of BCL-xL for solid and hematological malignancies. The Company has licensed ZN-c3 and ZN-d5 to its joint venture, Zentera Therapeutics, Ltd. to develop and commercialize these candidates in Greater China, but otherwise retains full economic ownership and control of ZN-c3 and ZN-d5. Zentalis has operations in both New York and San Diego.

For more information, please visit www.zentalis.com. Follow Zentalis on Twitter at @ZentalisP and on LinkedIn at www.linkedin.com/company/zentalis-pharmaceuticals.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements relating to the potential for a product candidate to be first-in-class and/or best-in-class; the potential benefits of our dose optimization work, including the potential benefit of higher doses delivered on an intermittent schedule; projected cash runway; potential benefits of our product candidates; potential benefits of the Cyclin E biomarker defined trial; our belief we are well-position to execute on our clinical development plans and further our mission to improve the lives of cancer patients; plans to expand our clinical trials, including our Phase 1/2 dose escalation study in ovarian cancer in collaboration with GSK; plans to present preclinical data relating to Cyclin E and the timing thereof; potentially modifying the Phase 2 USC trial dose and the impact of that modification on the timeline of the Phase 2 USC trial; the timing of providing an update on ZN-c3 dosing and the content of that update; the timing of initiation of our clinical trials; and the potential of ZN-c3 to help pancreatic cancer patients. The terms “believe,” “look forward,” “may,” “opportunity,” “optimize,” “plans,” “potential,” “scheduled,” “will” and similar references are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: our limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability; we have and expect to continue to incur significant losses; our need for additional funding, which may not be available; our substantial dependence on the success of our lead product candidates; the outcome of preclinical testing and early trials may not be predictive of the success of later clinical trials; failure to identify additional product candidates and develop or commercialize marketable products; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process or ongoing regulatory obligations; failure to obtain U.S. or international marketing approval; our product candidates may cause serious adverse side effects; inability to maintain our collaborations, or the failure of these collaborations; our reliance on third parties; effects of significant competition; the possibility of system failures or security breaches; risks relating to intellectual property; our ability to attract, retain and motivate qualified personnel, and risks relating to management transitions; significant costs as a result of operating as a public company; the COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials; and the other important factors discussed under the caption “Risk Factors” in our most recently filed periodic report on Form 10-K or 10-Q and subsequent filings with the U.S. Securities and Exchange Commission (SEC) and our other filings with the SEC. Any such forward-looking statements represent management’s estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

ZENTALIS™ and its associated logos are trademarks of Zentalis and/or its affiliates. All website addresses and other links in this press release are for information only and are not intended to be an active link or to incorporate any website or other information into this press release.

Investor Contacts:
Adam D. Levy, PhD, MBA
alevy@zentalis.com

Alexandra Roy
Solebury Strategic Communications
aroy@soleburystrat.com

Media Contact:
Julia Deutsch
Solebury Strategic Communications
jdeutsch@soleburystrat.com

Zentalis Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating Expenses				
Research and development	$ 42,181	$ 53,998	$ 132,118	$ 137,162
General and administrative	12,012	8,872	43,415	31,187
Total operating expenses	54,193	62,870	175,533	168,349
Operating loss	(54,193)	(62,870)	(175,533)	(168,349)
Other Income (Expense)				
Investment and other income, net	1,905	99	2,755	313
Gain on deconsolidation of Zentera	—	51,582	—	51,582
Net loss before income taxes	(52,288)	(11,189)	(172,778)	(116,454)
Income tax expense (benefit)	(159)	(697)	(109)	(456)
Loss on equity method investment	2,371	—	9,460	—
Net loss	(54,500)	(10,492)	(182,129)	(115,998)
Net loss attributable to noncontrolling interests	(99)	(6,301)	(294)	(7,332)
Net loss attributable to Zentalis	$ (54,401)	$ (4,191)	$ (181,835)	$ (108,666)
Net loss per common share outstanding, basic and diluted	$ (0.96)	$ (0.09)	$ (3.56)	$ (2.59)
Common shares used in computing net loss per share, basic and diluted	56,807	44,609	51,098	41,918

Zentalis Pharmaceuticals, Inc.
Selected Condensed Consolidated Balance Sheet Data
(Unaudited)
(In thousands)

	As of June 30,	As of December 31,
	2022	2021
Cash, cash equivalents and marketable securities	$ 421,726	$ 339,887
Working capital [(1)]	379,829	306,826
Total assets	529,193	454,507
Total liabilities	100,455	90,025
Total Zentalis equity	$ 428,738	$ 364,482

[(1)] The Company defines working capital as current assets less current liabilities.