Modernas flu vaccine, mRNA-1010, met its primary endpoint in Phase 3 trial; separate Phase 1/2 data demonstrated higher HAI titers than Fluzone HD.

Vaccine pipeline advancing rapidly with Company announcing the completion of RSV BLA filing (mRNA-1345), completion of adult enrollment in the Phase 3 trial of mRNA-1647, a first-in-class vaccine against CMV, and the Phase 3 trial of mRNA-1283, a next-generation COVID-19 vaccine.

With its partner Merck, the Company plans to begin a second Phase 3 trial of mRNA-4157, its individualized neoantigen therapy (INT), in combination with Keytruda®, for non-small cell lung cancer later this year; updated efficacy follow-up from the ongoing Phase 2 study in adjuvant melanoma expected in Q4.

With positive clinical data announced in mRNA-3705, a treatment for methylmalonic acidemia, the Company has three chronic rare disease medicines that have demonstrated potential for clinical benefit in patients.

Over the next five years, the Company expects to launch up to 15 new products addressing high unmet needs, to bring up to 50 new candidates into clinical trials and to continue expanding the field of mRNA into new applications.

CAMBRIDGE, MA / ACCESSWIRE / September 13, 2023 / Moderna, Inc. (NASDAQ:MRNA) today announced business and clinical updates across its franchises and introduced several new development programs at the Company's annual R&D Day.
"Our mRNA platform is working. With today’s positive Phase 3 flu results, along with previous results in COVID and RSV, we are now three for three on advancing respiratory disease programs to positive Phase 3 data," said Stéphane Bancel, Chief Executive Officer of Moderna. "In the near term, we look forward to product launches in our oncology, latent, rare and infectious disease franchises. In the fourth quarter of this year, we also expect to provide data on our next-generation COVID and flu combination, mRNA-1083, and additional efficacy analysis on our Phase 2 INT study. With significant momentum across the business and our pipeline, we are excited by the near future and focused on execution."

Expanding the Field of mRNA Medicine
Moderna was founded and built to use nature’s information molecule, mRNA, to treat and prevent disease. The premise has always been that an mRNA-based approach to making medicine could advance at the pace of information, leveraging common science, technology, and infrastructure to create medicines addressing high unmet needs at unprecedented speed and efficiency.

Through more than a decade of investment in science, the Company has created the field of mRNA medicine. The Company has advanced a diverse pipeline and demonstrated the potential for clinical benefit in cancer (mRNA-4157), in three different rare diseases (mRNA-3705, mRNA-3927, mRNA-3745), and multiple infectious disease vaccines (mRNA-1273, mRNA-1345, mRNA-1010). The Company has advanced six programs into late-stage development, including two approved or filed for approval, and three more that have completed Phase 3 enrollment. The Company expects to double the number of programs in Phase 3 by 2025 and launch up to 15 products in five years across cancer, rare disease, and infectious disease. Up to four of those launches could come by 2025.

Staying true to its mission, over the next five years the Company will continue to invest in science to expand the field of mRNA medicine into new frontiers and expects to advance up to 50 new candidate medicines into clinical trials across established and new modalities.

Updates and recent progress include:

RESPIRATORY FRANCHISE
Moderna’s respiratory pipeline continues to exhibit consistent efficacy in older adults and immunocompromised individuals. The Company is also advancing its efforts to develop multiple generations of single-virus and combination respiratory vaccines that address significant public health needs.

The respiratory franchise, now a seasonal business with an annual recurring revenue stream, is targeting an approximately $30 billion annual market, comprised of an approximately $15 billion COVID-19 market, a $10 billion
RSV market, and a $6 billion flu market, with the potential for growth with more effective vaccines. Respiratory products sales in 2027 are expected to be in the range of $8 billion to $15 billion, depending on vaccination rates, efficacy and Company market share, as previously communicated at Vaccines Day.

COVID-19 Vaccine Update
Following the June FDA VRBPAC meeting, the Company demonstrated potent neutralization and cross-reactivity with its monovalent XBB.1.5 vaccine, mRNA-1273.815, with similar neutralization for XBB.1.5, XBB.1.16, and XBB.2.3.2 sub-variants. Clinical trial data from research assays also confirmed mRNA-1273.815 showed an 8.7 to 11-fold increase in neutralizing antibodies against circulating variants, including BA.2.86, EG.5, and FL.1.5.1. With these data, Moderna has confirmed an antibody response against current strains of concern, suggesting that the updated vaccine is well-matched for the upcoming vaccination season.

On September 11, 2023, the U.S. Food and Drug Administration (FDA) approved the supplemental Biologics License Application (sBLA) for Spikevax® for ages 12 years and above. Emergency Use Authorization (EUA) for the Moderna COVID-19 Vaccine was also received for individuals 6 months through 11 years of age. Moderna's updated COVID-19 vaccine contains spike proteins for the XBB.1.5 sublineage of SARS-CoV-2 to help prevent COVID-19 in individuals 6 months of age and older. Clinical trial data confirm mRNA-1273.815 showed a strong immune response in humans against BA.2.86, EG.5 and FL.1.5.1 variants. With the U.S. FDA's decision, Moderna has begun shipping doses to vaccination sites across the U.S., with updated vaccines expected to be available in the coming days.

In addition, the Company's next-generation, refrigerator-stable COVID-19 vaccine, mRNA-1283, demonstrated encouraging results in multiple clinical studies and has now completed enrollment of its Phase 3 trial.

Seasonal Influenza Vaccine
mRNA-1010 demonstrated an acceptable safety and tolerability profile across all clinical trials to date, including three Phase 3 trials (P301, P302, P303), and independent data and safety monitoring boards (DSMBs) have raised no safety concerns.

Enrollment is complete in the Company's Phase 3 safety and immunogenicity trial for the updated formulation of mRNA-1010 (P303). In an interim analysis of the P303 study, mRNA-1010 met all co-primary endpoints across all four A and B strains (A/H1N1, A/H3N2, influenza B/Yamagata, B/Victoria). Higher HAI geometric mean titers and seroconversion rates were observed for all four strains compared to a licensed comparator (Fluarix). Local and systemic solicited adverse reactions were similar to those reported in previous mRNA-1010 studies.

Improved immunogenicity was observed across age groups, and importantly, was seen in older adults. mRNA-1010 also elicited higher HAI titers against A/H1N1, A/H3N2, B/Victoria, and comparable titers to B/Yamagata compared to Fluzone HD in a separate Phase 1/2 head-to-head study. Consultations with regulators on a potential licensing
package are currently ongoing based on these data.

As the previous P302 efficacy study has not accrued its target case numbers by the end of the most recent season, the Company would need to enroll a second season to accrue enough cases. In light of P303 meeting all its primary endpoints, the Company has decided not to enroll a second season in the P302 study.

The Company continues to advance a portfolio of influenza vaccine candidates that include additional HA antigens for broader coverage of circulating influenza A strains (mRNA-1011 and mRNA-1012) and candidates that incorporate both HA and neuraminidase (NA) antigens to target multiple proteins involved in the influenza virus lifecycle to reduce the potential of viral antigenic escape (mRNA-1020 and mRNA-1030).

Respiratory Syncytial Virus (RSV) Vaccine
Moderna has submitted marketing authorization applications globally for mRNA-1345, a vaccine for the prevention of RSV-associated lower respiratory tract disease (RSV-LRTD) and acute respiratory disease (ARD) in adults aged 60 years or older. The Company filed for a Biologics License Application (BLA) with the FDA and used a Priority Review Voucher (PRV). The Company expects an April 2024 PDUFA date. Regulatory applications were also submitted in Europe (EMA), Switzerland (Swissmedic), Australia (TGA), Canada (Health Canada), and United Kingdom (MHRA).

The regulatory applications are based on positive data from the pivotal ConquerRSV study, a randomized, double-blind, placebo-controlled study of approximately 37,000 adults 60 years or older. The trial met both its primary efficacy endpoints, with a vaccine efficacy (VE) of 83.7% (95.88% CI: 66.1%, 92.2%; p<0.0001) against RSV-LRTD as defined by two or more symptoms, and a VE of 82.4% (96.36% CI: 34.8%, 95.3%; p=0.0078) against RSV-LRTD defined by three or more symptoms. No cases of Guillain-Barre Syndrome (GBS) have been reported with mRNA-1345 in the Phase 3 RSV trial. In addition to older adults, mRNA-1345 is being investigated in a fully enrolled, ongoing Phase 1 trial in pediatric populations.

Combination Respiratory Vaccines
Moderna's development strategy for combination vaccines can provide substantial public health benefits. The Company's combination vaccine candidates address respiratory viruses associated with the largest disease burden in the category and are designed for higher compliance, increased uptake, consumer convenience and benefits to healthcare systems. Enrollment is now complete in the following combination trials:

- Flu/COVID-19 (mRNA-1073: mRNA-1010 + mRNA-1273) Phase 1/2
- Flu/RSV (mRNA-1045: mRNA-1010 + mRNA-1345) Phase 1
- Flu/COVID-19/ RSV (mRNA-1230: mRNA-1010 + mRNA-1273 +mRNA-1345) Phase 1
- Flu/COVID-19 (mRNA-1083: mRNA-1010 + mRNA-1283) Phase 1/2
The Company intends to have a combination vaccine available as early as 2025 and expects to regularly update combinations with improved next-generation vaccine candidates as appropriate. The Company further expects to provide an investor update in Q4 of this year.

LATENT and OTHER VIRUSES FRANCHISE
Modern is currently developing vaccines against six latent and other viruses with unmet or underserved needs, including cytomegalovirus, Epstein Barr virus, herpes simplex virus, varicella zoster virus, norovirus, and HIV. The latent and other vaccine market is a large unaddressed market estimated at approximately $10 billion to $25 billion.

Cytomegalovirus (CMV) Vaccine
The pivotal Phase 3 study of Moderna's CMV vaccine candidate (mRNA-1647), known as CMVictory, is fully enrolled with adults. The trial evaluates the efficacy, safety and immunogenicity of mRNA-1647 in the prevention of primary infection in women of childbearing age.

Norovirus (NoV)
Enteric viruses, including norovirus, are a leading cause of global acute gastroenteritis (AGE), resulting in significant morbidity and mortality worldwide, particularly among young children and older adults. Norovirus is highly contagious and the leading cause of diarrheal disease globally, associated with 18% of all diarrheal diseases worldwide, resulting in approximately 200,000 deaths per year and substantial healthcare costs.

Moderna is developing two multi-valent virus-like particle (VLP) vaccines to tackle norovirus diversity, mRNA-1403 (trivalent) and mRNA-1405 (pentavalent) for the prevention of acute gastroenteritis (AGE) from the most prevalent norovirus genotypes in young children and older adults. The Phase 1 trial of norovirus vaccine candidate, mRNA-1403, is currently enrolling participants.

ONCOLOGY FRANCHISE
The oncology franchise includes the individualized neoantigen therapy being developed in partnership with Merck, as well as Moderna's checkpoint and triplet vaccines. The announced adjuvant indications for Phase 3 represent estimated eligible population sizes in the U.S. and E.U. of approximately 30,000 patients for melanoma and 101,000 eligible patients for non-small cell lung cancer.

Individualized Neoantigen Therapy (INT)

Melanoma: Phase 2b in patients with resected high-risk melanoma (stage III/IV)
In April 2023, Moderna and Merck reported the results from the Phase 2b KEYNOTE-942/mRNA-4157-P201 trial evaluating mRNA-4157 (V940), an investigational individualized neoantigen therapy (INT), in combination with
KEYTRUDA, Merck’s anti-PD-1 therapy, in patients with resected high-risk melanoma (stage III/IV). In the overall intention-to-treat population, adjuvant treatment with mRNA-4157 (V940) in combination with KEYTRUDA demonstrated a statistically significant and clinically meaningful improvement in recurrence-free survival (RFS) and reduced the risk of recurrence or death by 44% (HR=0.56 [95% CI, 0.309-1.017]; one-sided p value=0.0266) compared with KEYTRUDA alone. In June, the Company announced a statistically significant and clinically meaningful improvement in distant metastasis-free survival (DMFS) from the Phase 2b KEYNOTE-942/mRNA-4157-P201 trial. mRNA-4157-P201/KEYNOTE-942 is the first randomized trial to demonstrate improvement in recurrence-free survival and distant metastasis-free survival with an individualized neoantigen therapy approach.

The Company expects to provide additional data from the Phase 2 study in Q4.

Melanoma: Phase 3 in patients with resected high-risk melanoma (Stage IIB-IV)
Merck and Moderna announced the initiation of a pivotal Phase 3 study (V940-001) to evaluate the safety and efficacy of mRNA-4157 (V940) in combination with KEYTRUDA in people with resected high-risk (Stage IIB-IV) melanoma compared to KEYTRUDA alone. The primary endpoint of the study is recurrence-free survival (RFS), and secondary endpoints include distant metastasis-free survival (DFMS), overall survival (OS) and safety.

Non-small cell lung cancer (NSCLC)
The Company presented plans to partner with Merck in an upcoming Phase 3 trial in NSCLC in patients with resected stage II-IIIB NSCLC patients who have received adjuvant chemotherapy, with no recurrence. The companies expect to initiate that trial later this year.

Moderna and Merck plan to expand the INT development program to additional tumor types.

Checkpoint Vaccine
Moderna’s checkpoint vaccine, mRNA-4359, aims to stimulate effector T cells that target and kill suppressive immune and cancer cells that express high levels of target checkpoint antigens. mRNA-4359 is being evaluated in an ongoing Phase 1/2 study as monotherapy and in combination with pembrolizumab. Eligible tumors included in the trial include cutaneous melanoma, NSCLC, non-muscle invasive bladder cancer, head and neck squamous cell carcinoma, microsatellite stable colorectal cancer, basal cell carcinoma, and triple-negative breast cancer.

Triplet
Moderna’s Triplet (mRNA-2752) is being evaluated in an ongoing Phase 1 study to evaluate safety and tolerability of mRNA-2752 administered alone and in combination with durvalumab, as well as an ongoing study evaluating mRNA-2752 in patients with ductal carcinoma in situ (DCIS). The dose escalation and confirmation arms enroll participants with accessible solid tumors and lymphomas, and dose expansion enrolls participants with CPI refractory melanoma. The DCIS study is currently enrolling patients with mRNA-2752 administered as
monotherapy.

**RARE DISEASE FRANCHISE**
Modernia’s rare disease portfolio, which includes therapies targeting methylmalonic acidemia (MMA), propionic acidemia (PA), glycogen storage disease (GSD1A) and Phenylketonuria (PKU) may represent a $10 billion market while also addressing significant unmet medical needs. The Company is expecting up to four rare disease product launches in the next five years.

**Methylmalonic acidemia (MMA)**
MMA therapy candidate, mRNA-3705, encodes for a missing or deficient hepatic enzyme. In the Phase 1/2 study, eleven participants have been dosed, with a total of 221 doses administered. Thus far, all participants have opted to participate in the Open-Label Extension study. To date, mRNA-3705 has generally been well-tolerated with no discontinuations due to safety or meeting protocol defined dose limiting toxicity criteria.

Interim results from the global Phase 1/2 clinical trial of mRNA-3705 demonstrated encouraging initial pharmacodynamic data, with dose-dependent reductions in methylmalonic acid in Cohorts 2 and 3. Early results suggest potential decreases in annualized metabolic decompensation events (MDEs), frequency and MMA-related hospitalizations compared to pre-treatment.

**Propionic Acidemia (PA)**
Propionic acidemia is a rare, serious, inherited metabolic disorder with significant morbidity and mortality. Currently, there are no effective therapies for PA that target the underlying root cause of the disease. The global Phase 1/2 clinical trial of mRNA-3927 is enrolling patients in the dose confirmation arm. Sixteen patients have been dosed with more than 280 intravenous doses of mRNA-3927 and twelve patients have received more than a year of dosing. mRNA-3927 is generally well-tolerated to date with no discontinuations due to safety and no events meeting protocol-defined dose-limiting toxicity criteria. Enrollment is ongoing in the Phase 1/2 study with a goal to identify an optimal dose. All participants who have completed the treatment period of the main study have opted enter a long-term extension study.

**PKU**
Phenylketonuria (PKU) is a rare and serious metabolic disease, affecting approximately 40,000 patients in the US and EU5 (France, Germany, Italy, Spain, and the United Kingdom). Mutations in the phenylalanine hydroxylase (PAH) gene encoding the PAH enzyme, result in the inability to metabolize the essential amino acid Phe to Tyr in the liver. There is a high unmet medical need for patients with PKU with early and continuous treatment throughout life being fundamental to prevent the development of irreversible neuropsychiatric outcomes. mRNA-3210 is an mRNA encoding the PAH enzyme encapsulated in the same LNP as that used in MMA and PA development candidates, with the potential to address the unmet need in patients with PKU.
The Company has opened an Investigational New Drug Application (IND) for mRNA-3210.

FINANCIAL UPDATE

Moderna expects to add $10 billion to $15 billion in annual sales five years after launching new products in Oncology, Rare and Latent diseases by 2028. This is in addition to the previously announced $8 billion to $15 billion of expected sales from the Respiratory Franchise in 2027.

The Company expects to support this organic growth framework by investing approximately $25 billion in research and development from 2024 through 2028.

Additionally, the Company continues to expect 2023 COVID-19 sales of $6 billion to $8 billion, dependent on U.S. vaccination rates. While 2023 cost of sales remain elevated, the Company is currently resizing its manufacturing footprint and supply base to accelerate gross margin expansion towards its longer-term target of 75-80%.

About Moderna

In over 10 years since its inception, Moderna has transformed from a research-stage company advancing programs in the field of messenger RNA (mRNA), to an enterprise with a diverse clinical portfolio of vaccines and therapeutics across seven modalities, a broad intellectual property portfolio in areas including mRNA and lipid nanoparticle formulation, and an integrated manufacturing plant that allows for rapid clinical and commercial production at scale. Moderna maintains alliances with a broad range of domestic and overseas government and commercial collaborators, which has allowed for the pursuit of both groundbreaking science and rapid scaling of manufacturing. Most recently, Moderna's capabilities have come together to allow the authorized use and approval of one of the earliest and most effective vaccines against the COVID-19 pandemic.

Moderna's mRNA platform builds on continuous advances in basic and applied mRNA science, delivery technology and manufacturing, and has allowed the development of therapeutics and vaccines for infectious diseases, immuno-oncology, rare diseases, cardiovascular diseases and auto-immune diseases. Moderna has been named a top biopharmaceutical employer by Science for the past eight years. To learn more, visit www.modernatx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding: the potential for Moderna to launch up to 15 products in the next five years, and advancement of new products into clinical studies; Moderna's discussions with regulators and the potential for accelerated, conditional or other product approvals in certain markets; the expectation that INT will begin a Phase 3 study in NSCLC in 2023; clinical trial progress and results from Moderna's programs; Moderna's ability to develop combination vaccines and the benefits of those vaccines; the ability of
Moderna's XBB.1.5 monovalent COVID-19 vaccine (mRNA-1283.815) to provide protection during the fall 2023/2024 season; Moderna's ability to develop updated vaccines to provide protection against evolving SARS-CoV-2 variants of concern; the safety and tolerability profile for Moderna's products; and the size of the addressable markets being targeted by Moderna's pipeline, Moderna's estimated future revenue from sales in those markets and its anticipated future margins. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties, and other factors include, among others, those risks and uncertainties described under the heading "Risk Factors" in Moderna's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, filed with the U.S. Securities and Exchange Commission (SEC), and in subsequent filings made by Moderna with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date of this press release.

Moderna Contacts

Media:
Chris Ridley
Vice President, Communications
617-800-3651
Chris.Ridley@modernatx.com

Investors:
Lavina Talukdar
Senior Vice President & Head of Investor Relations
617-209-5834
Lavina.Talukdar@modernatx.com

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