INTERNATIONAL SOS WEEKLY SCIENTIFIC UPDATE
Focussing on immunity and vaccine development

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In this edition:

VACCINE DEVELOPMENT & APPROVAL

1. Moderna vaccine prevents 94% of COVID-19 – including severe disease

The independent Data Safety Monitoring Board (DSMB) for the Phase 3 study of Moderna vaccine has announced a vaccine efficacy of 94.5%.

"This first interim analysis was based on 95 cases, of which 90 cases of COVID-19 were observed in the placebo group versus 5 cases observed in the mRNA-1273 group, resulting in a point estimate of vaccine efficacy of 94.5% (p <0.0001).

"By the end of 2020, the Company expects to have approximately 20 million doses of its vaccine ready to ship in the US and remains on track to manufacture 500 million to 1 billion doses globally in 2021."

2. Cuba leads race for Latin American coronavirus vaccine

Reuters reports that Cuba has two vaccines – "Sovereign 1" and "Sovereign 2" - in clinical trials.

If the vaccine/s succeed, Cuba could become an important supplier to neighbouring countries, who may struggle to access vaccine as wealthy Western nations have secured much of the early supply. The vaccines would be available through the Pan American Health Organisation (PAHO)

Cuba's vaccines are being tracked by COVAX but are not included in the nine vaccines being supported.

3. Is two months long enough to monitor for vaccine safety concerns?

The US Food and Drug Administration (FDA) has stipulated that prior to applying for a Emergency Use Authorisation (EUA), vaccine manufacturers must follow volunteers for at least two months after their second shot. But is two months enough to assess the safety of the vaccines?

"We have to balance the safety we get upfront with the need to try to save lives with a vaccine that's helping to prevent a virus that's killing 1000 or more people a day in the United States," Dr Peter Marks, director of the FDA division that approves vaccines, said last month. "We picked two months as something that was reasonably aggressive, yet also somewhat, kind of in the middle. Not too aggressive, not too conservative."

Professor Dale Godfrey, Immunology Theme Leader at the Doherty Institute, said that the idea of whether two months represents an adequate period is "not a straightforward question", but things are more likely to "go wrong" earlier in the monitoring phase than towards the end. "Ordinarily, two months is way shorter than it would normally take to assess phase 3 trial results," he said. "But no one is going to be happy if we say, 'Yes, we'll get a vaccine to you in five years.' So, it's a risk–benefit analysis."

4. Pfizer / BioNTech concludes Phase 3 study

The Pfizer Phase 3 vaccine trial is now complete.

Efficacy: 95%

Of 43,661 participants, the 170 events, 162 were in the placebo group and eight were in the vaccine group giving ac 95% efficacy – up from 90% in their first readout! That is approximately the same efficacy as Moderna reported earlier this week (94.5%).

Safety: no serious concerns

Pfizer also reported no serious safety concerns in its study, which included 43,661 volunteers. Data on common side effects was tracked in an 8,000-patient portion of the study. The only severe side effects to

occur in more than 2% of people were fatigue, which occurred in 3.7% of patients after the second dose, and headache, which occurred in 2%. Older adults had fewer and milder side effects than younger participants. Approximately 19,000 participants in the study have been followed for at least two months since their second dose of the vaccine.

Pfizer may apply to the Food and Drug Administration (FDA) for an Emergency Use Authorization for its COVID-19 vaccine within days.

5. Johnson & Johnson launches two-dose Phase 3 vaccine trials

The Johnson & Johnson "Ensemble 1" Phase 3 of a single dose of its vaccine, which began in late September, continues to enroll and vaccinate up to 60,000 participants worldwide.

The company has just announced "Ensemble 2", a Phase 3 trial of two doses of its vaccine; this will be a multi-country large-scale trial enrolling up to 30,000 participants in Belgium, Colombia, France, Germany, the Philippines, South Africa, Spain, the United Kingdom and the United States. The two trials will run in parallel.

The Johnson & Johnson vaccine uses viral vector technology. Advantages of this vaccine:

- It may require only one dose
- It only needs refrigeration, not deep freeze

6. FDA to make Emergency Use Authorization data public for vaccine authorization

The U.S. Food and Drug Administration (FDA) said on 17 November that it would make reviews of all data and information regarding the Emergency Use Authorization (EUA) granted to COVID-19 drugs and vaccines public.

"Today's transparency action is just one of a number of steps we are taking to ensure public confidence in our EUA review process for drugs and biological products, especially any potential COVID-19 vaccines," FDA Commissioner Stephen Hahn said in a statement.

VACCINE DISTRIBUTION

1. Namibia joins the COVAX facility

GAVI (the Global Vaccine Alliance) has announced that Namibia has joined the WHO-supported COVAX facility – the 187th country to do so.

2. Pfizer to start pilot delivery program for its COVID-19 vaccine in four US States

The Guardian reports that Pfizer has launched a pilot delivery program for its experimental COVID-19 vaccine in four US states: Rhode Island, Texas, New Mexico, and Tennessee as the US drug maker seeks to address distribution challenges facing its ultra-cold storage requirements.

Pfizer's vaccine must be shipped and stored at -70 degrees Celsius (minus 94°F).

The four states will not receive vaccine doses earlier than other states by virtue of the pilot.

3. Sinopharm JV to supply 10,000 doses of COVID-19 vaccine for Malaysian “frontliners”

The Edge Markets reports that Chinese pharmaceutical group Sinopharm, through a joint venture with GI Healthcare Resources, has agreed to supply 10,000 doses of COVID-19 vaccine for Malaysian ‘frontliners’, especially medical officers and the police.
The Edge Markets continues, “According to GI Healthcare Resources, Sinopharm is currently carrying out Phase III trials on its two vaccine candidates in 10 countries, including the United Arab Emirates (UAE), Bahrain, Egypt, and Morocco, involving over 55,000 subjects. The company said none of the trial participants reported any adverse reactions or side effects.

“Its vaccines have also been approved for emergency use in China, the UAE and Bahrain.
“More than 60,000 personnel who have been vaccinated have gone to work in more than 180 countries overseas without a single reported case of COVID-19 infection.

“GI Healthcare Resources claimed that based on the examples above, Sinopharm's vaccine effectiveness is close to 100%.

"Of the 99 employees in Huawei's Mexico office, 81 were vaccinated and 18 were not vaccinated. After the outbreak, none of the 81 vaccinated employees were infected, whereas 10 out of the 18 employees who were not vaccinated were diagnosed to be COVID-19 positive.”

4. The differing storage requirements of mRNA vaccines

With both Pfizer and Moderna having reported vaccine efficacy of more than 90%, the logistics of storing, distributing, and administering these vaccines becomes vitally important.
Curevac, an mRNA vaccine candidate developed in Germany, has the advantage of being stable for up to three months at refrigerator temperatures.

Pfizer storage requirements

Pfizer's vaccine requires storage at a minus 70 degrees C (minus 94 degrees F) and can be stored for five days at refrigerated temperatures between 2-8 degrees C (35.6 and 46.4 degrees F).

To facilitate distribution, Pfizer has developed specially built deep-freeze "suitcases" that can be tightly sealed and shipped in non-refrigerated trucks.

However, looking forward, Pfizer is working on a powdered formulation do be delivered to market next year.

“For mass distribution of the Pfizer vaccine, the most practical solution may be setting up large, centralized vaccination centers that could rapidly go through doses, rather than trying to get the jab into every doctor’s office and pharmacy,” Paula Cannon, an associate professor of molecular microbiology and immunology at the University of Southern California’s Keck School of Medicine, told Time

On 11 November Pfizer/BioNTech announced an agreement to supply 200 million doses of their vaccine to the European Commission.

Moderna storage requirements

The Moderna COVID-19 vaccine remains stable at -20° C for up to six months, at the temperature of a standard home or medical refrigerator 2° to 8°C for 30 days, and at room temperature for up to 12 hours.

“We believe… our manufacturing process development will allow us to store and ship our COVID-19 vaccine candidate at temperatures commonly found in readily available pharmaceutical freezers and refrigerators,” said Juan Andres, Chief Technical Operations and Quality Officer at Moderna.

Curevac storage requirements

The Curevac mRNA candidate vaccine, being developed in Germany, is reported to be stable for up to three months at refrigerator temperatures. It can also be kept for up to 24 hours at room temperature.

Curevac, which began Phase 2a testing in late September, "has the potential both to enable decentralized storage and to significantly facilitate large-scale vaccination efforts during the current pandemic," Chief Production officer Florian von der Mülbe said in a statement reported by fiercepharma.

On 16 November, the President of the European Commission (EC), Ursula von der Leyen, announced a contract to purchase 405 million doses of Curevac, if proven safe and effective. This is the fifth vaccine contract for the EC. The EC is currently also negotiating with Moderna.

Non-mRNA vaccines that can be stored at refrigerator temperatures

Outside the mRNA class, other vaccine manufacturers such as AstraZeneca, Sanofi, Johnson & Johnson and Novavax are developing vaccine candidates that can be stored at standard refrigerator temperatures.

IMMUNE RESPONSE

1. Immunity to the coronavirus might last years, perhaps even decades

One of the worries about vaccination plans is that we are unsure of the duration of protection that vaccination may provide.

A new study, so far not peer-reviewed, found that eight months after people had recovered from COVID-19 infection, the vast majority have robust levels of B cells (which can make antibodies as needed), as well as the types of T cells needed to fight the virus, and they have a very slow rate of decline. This slow rate of decline is consistent with many years of protection. This research sits well with the finding that the survivors of SARS, caused by another coronavirus, still have immunity 17 years after recovering from the disease.

As vaccines generally provide stronger, longer lasting protection than natural infection, we may not need annual COVID-19 vaccination boosters as has been assumed. We await further information on this topic.

2. AstraZeneca vaccine produces strong response in elderly

The University of Oxford has confirmed that the COVID-19 vaccine it is developing with AstraZeneca produced strong immune responses in older adults.
The data published in The Lancet on 19 November suggest that those aged over 70, who are at higher risk of serious illness and death from COVID-19, build robust immunity.

3. Sinovac vaccine triggers “quick” antibody response – good for “Emergency Use”

A Lancet article (17 November 2020) indicates that data, based on the Phase 1 & 2 trials conducted in April and May of this year, show that Sinovac Biotech's “CoronaVac” triggered a “quick immune response.” The article discusses that this property may make the vaccine "suitable for emergency use".

Trials of the Sinovac Biotech vaccine in Brazil were briefly halted last week but resumed after the reported death of a volunteer was found to have no links to the vaccine.

COVID TESTING

1. Tourists are buying fake COVID-19 test results on the black market to travel

Forging or purchasing of COVID test results for the purposes of travel has been identified in Brazil, France and the United Kingdom.

Recent instances:

- An alleged forgery ring has been selling false test certificates at Charles de Gaulle Airport
- Brazilian police recently arrested four domestic travellers who forged negative coronavirus tests
- The Lancashire Telegraph contacted a man who had altered a friend’s negative test and travelled internationally

However, test results are becoming more high-tech, and soon travellers will find it much harder to travel with falsified documents.

The Safe Travels Program in Hawaii, for example, requires visitors to preregister using their online testing program, use an approved testing partner, and upload results to a digital portal. Paper copies are not accepted.

Another example is the ICC / International SOS AOKpass mobile app, which provides trusted recognition of COVID-19 compliance status.

2. American, British Airways, Oneworld to Trial COVID-19 Tests

Reuters reports that “American Airlines, British Airways (BA), and the Oneworld alliance will launch a COVID testing trial aimed at convincing the US and UK governments to introduce testing so that transatlantic travel can restart.

“Alongside its partners, BA plans to collect data from at least 500 passengers on flights from three US cities to London Heathrow by asking them to take three free COVID-19 tests as part of their journey: one before departure, one on landing, and one three days after their arrival.”

COVID TREATMENT

1. Early treatment with fluvoxamine may prevent serious respiratory problems

Early treatment with the antidepressant fluvoxamine (Luvox) may help prevent respiratory deterioration in patients with mild symptomatic COVID-19, results of a small and preliminary randomized controlled trial published in JAMA suggest.

In the trial, none of the patients who took fluvoxamine within 7 days of first symptoms developed serious breathing difficulties or required hospitalization for respiratory deterioration.
The authors caution that the study was small and with short follow-up, and that the findings "need to be interpreted as hypothesis generating rather than as a demonstration of efficacy."

SPECIAL REPORT: GLOBAL COVID VACCINE ORDER AND SUPPLY

Contents

1. A billion doses of COVID-19 vaccine are already reserved

- Higher-income countries have pre-ordered half of projected COVID-19 vaccine supply
- Less-well-off countries may have to wait years to vaccinate their population

Advance Market Commitments (AMCs) is the term used for orders of vaccines (or other medications) prior to them becoming available on the market.

Data collected by researchers at Duke University's Global Health Innovation Center shows that higher-income countries account for more than half of all AMCs.

- The US has ordered more than one billion doses from at least six drug makers, accounting for nearly 1/6th of all AMCs

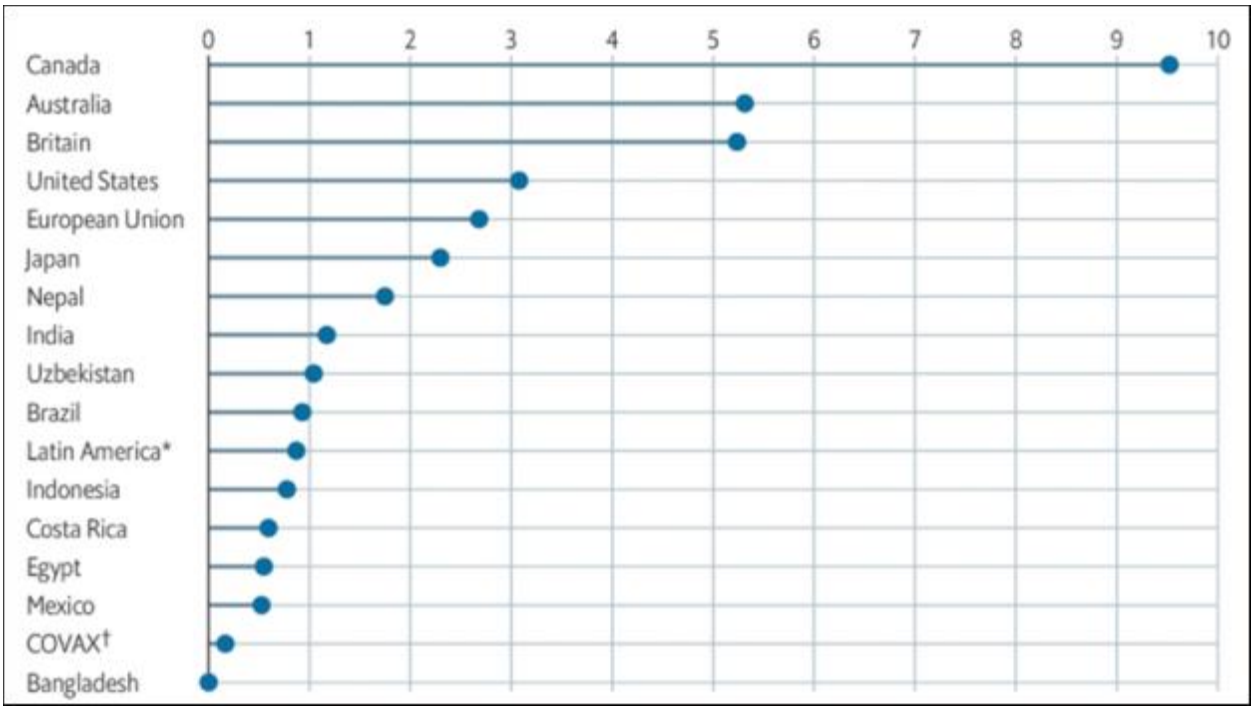
- Canada has purchased ten doses for each of its citizens, the most for any country or alliance on a per person basis (see chart)

- Higher-income countries have already contracted to buy approximately 600 million doses of the Pfizer-BioNTech vaccine; this is nearly half of the total that Pfizer can produce by the end of 2021

At present, even before any vaccine candidates have been approved for market, there are confirmed purchases of 6.4 billion doses, with another 3.2 billion doses currently under negotiation or reserved as optional expansions of existing deals.

Table 1: Confirmed orders of COVID-19 vaccine dose per person

(Note: most COVID-19 vaccines required two doses for the primary vaccination course)

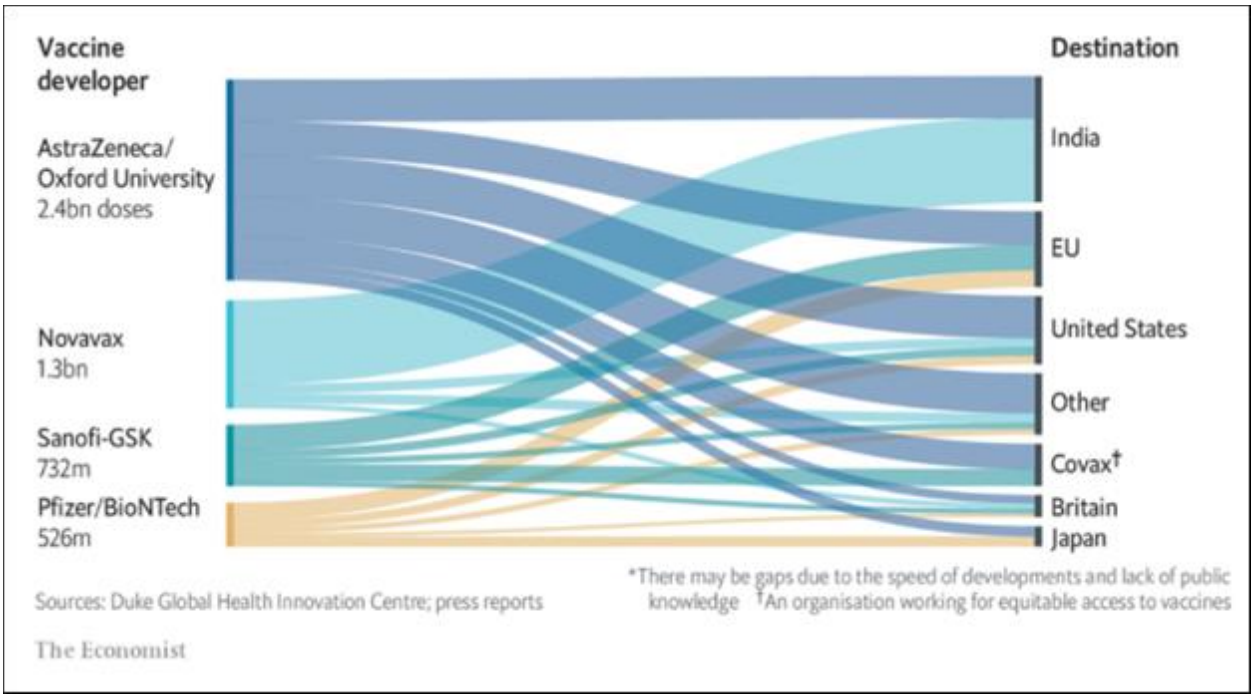


Source: [The Economist] (see lower for a lower resolution chart listing many more countries)

2. The world is betting big on AstraZeneca

Of the 4.95 billion doses of COVID-19 vaccinations with firm orders from the four vaccine manufacturers listed in the table below, 48% (2.4 billion doses) have been ordered from AstraZeneca

Table 2: top four COVID-19 vaccines confirmed number of doses ordered



Source: The Economist

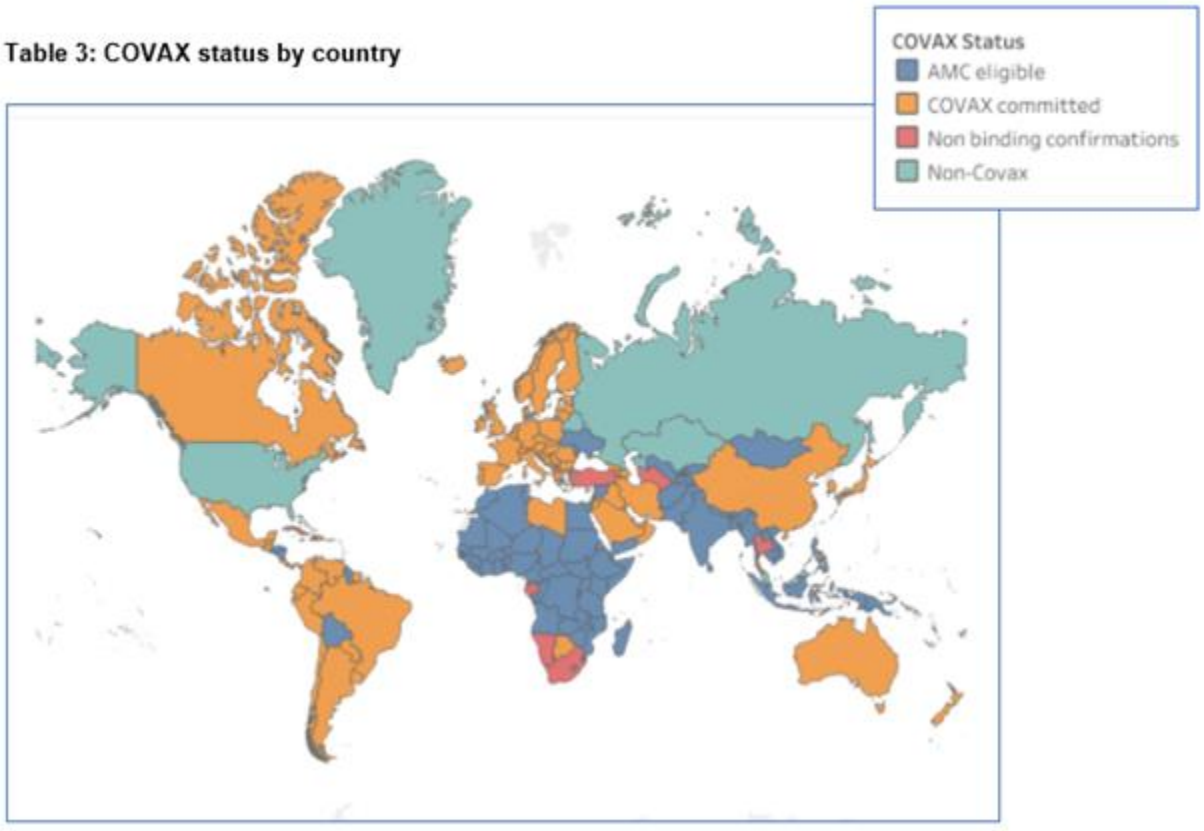
3. Manufacturing capacity limits the total number of doses available until 2024

The Launch and Scale Speedometer is led by the Duke Global Health Innovation Center, with support from the Bill & Melinda Gates Foundation.

“Current models predict that there will not be enough vaccine to cover the world's population until 2024. Manufacturing capacity can be expanded with targeted investment but only to an extent and it will remain a rate limiter.

“COVAX ** aims to provide two billion doses by the end of 2021 to protect high-risk populations around the world. In the longer term, the goal is to provide funded countries with enough doses to cover 20% of their population, while self-financing countries can purchase different levels of population coverage.”

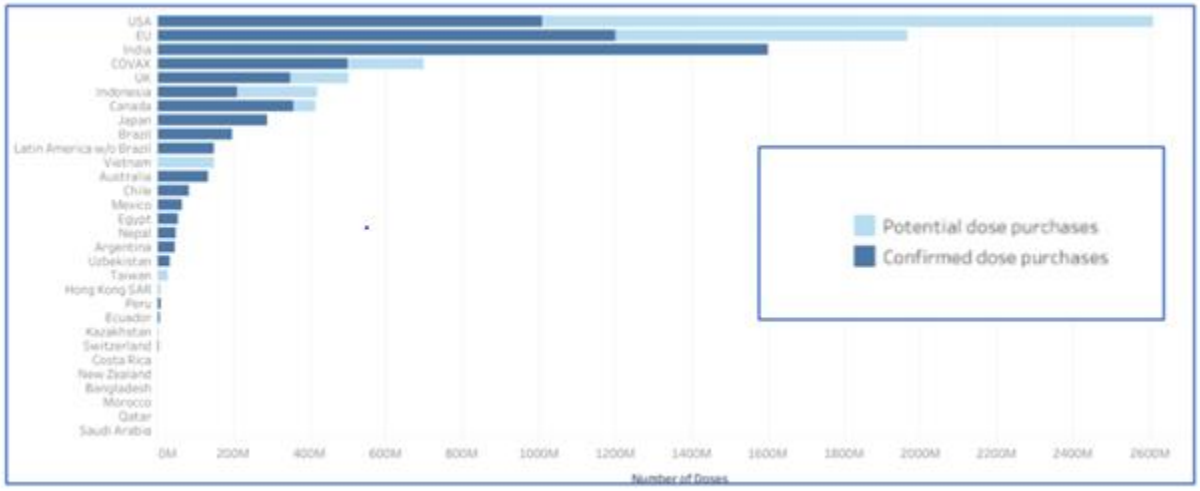
Table 3: COVAX status by country



Source: launchandscalefaster.org

** COVAX: A partnership between GAVI, the World Health Organization, and the Coalition for Epidemic Preparedness Innovations (CEPI). COVAX is a global mechanism that invests in the development, manufacture, and procurement of a portfolio of COVID-19 vaccine candidates, offering member countries equal access to successful vaccines as they become available. The majority of high- and middle-income countries (shown in gold) have committed funding to COVAX, joining lower-income countries (shown in blue) that will be covered as funded countries. There are still a few (in red) who have confirmed their interest in joining but have not yet made a binding financial commitment. The vast majority of the world's population lives in COVAX-participating countries.

Table 4: Higher detail of COVID-19 vaccine Advance Market Commitments by country



Source: launchandscalefaster.org