COVID–19 Treatments Weekly Report IFPMA

12 April 2022

Contents

→ Pipeline Overview:

18 candidates have been approved as COVID-19 treatments in the U.K., U.S. and E.U.

A total of 6 new candidates added to the platform this week

Pipeline overview by Airfinity priority groupings and development status for COVID-19 treatments

Approved (36 candidates):
Candidates that have received emergency use or full use approval by a regulatory body.

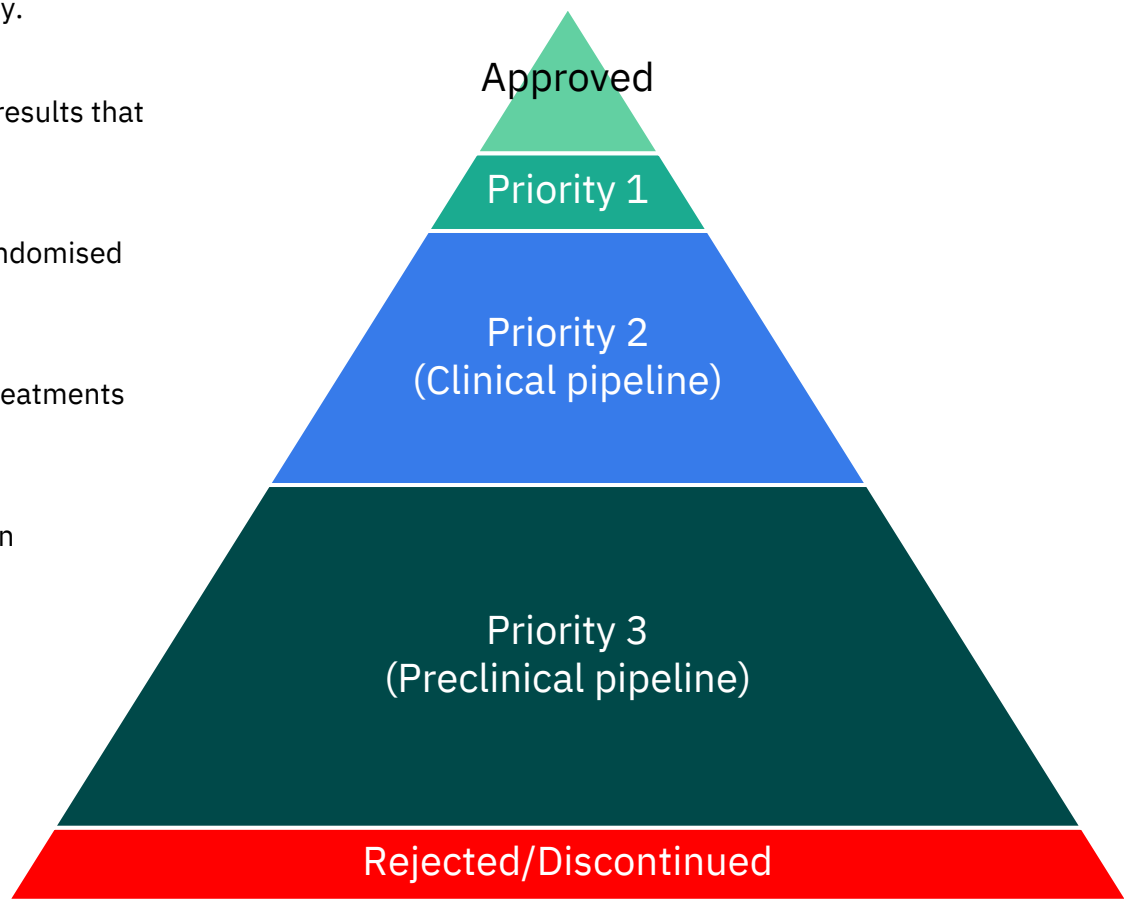
Airfinity Priority 1 (34 candidates):
Candidates that have/expected to report positive late phase randomised clinical trial results that have **not** received regulatory approval.

Airfinity Priority 2 (clinical development pipeline) (840 candidates): +4 new
Candidates, not in priority 1, that have undergone or are undergoing well-designed randomised control clinical trials and have a progress score.

Airfinity Priority 3 (preclinical development pipeline) (813 candidates): +2 new
All remaining treatment candidates that have been identified as possible COVID-19 treatments (all of which are preclinical candidates).

Rejected/Discontinued/Failed (46 candidates):
Candidates that have been proven to be ineffective at treating COVID-19, or have been discontinued as viable treatment candidates.

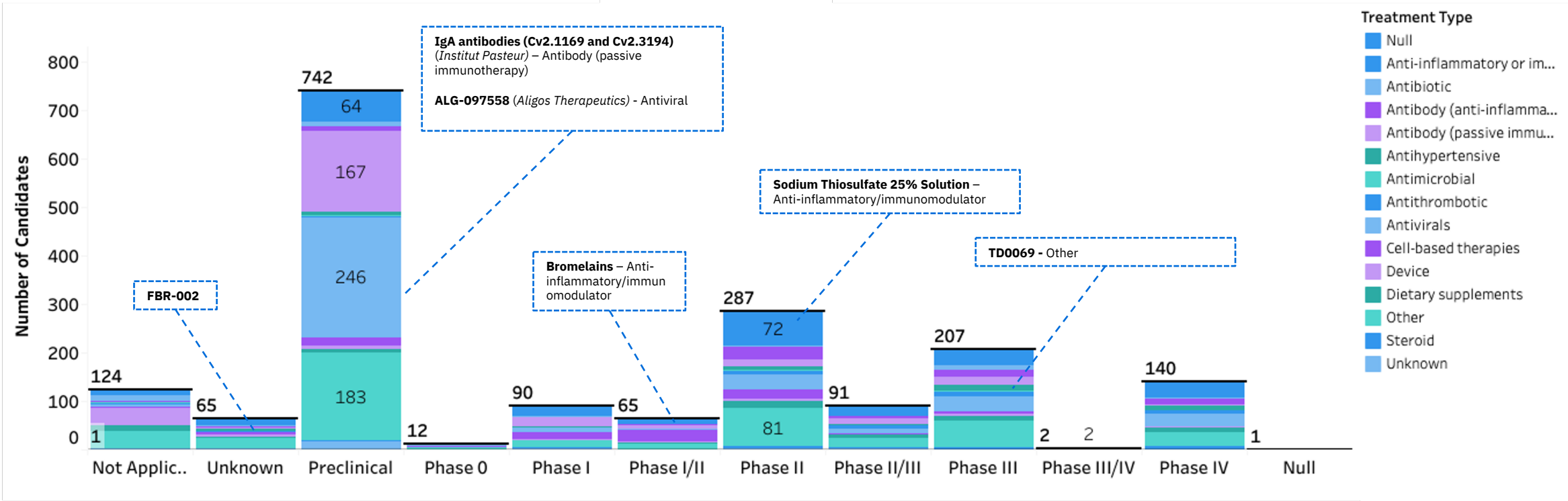
Total number of candidates: 1769 +6 new



18 candidates have been approved for COVID-19 treatments in the U.K., U.S. and E.U.

Pipeline overview by development status for COVID-19 treatments

Six candidates were added to the group platform this week, including two pre-clinical candidates, two anti-inflammatory/immunomodulators in Phase I/II and Phase II clinical trials, and a Phase III oral agent (TD0069). Candidates have been marked as inactive if there have been no developments over the last 12 months.



→ Candidate Progression:

Camostat Mesylate progresses as Phase III trial results are published

Camostat Mesylate progresses as phase 3 trial results are published

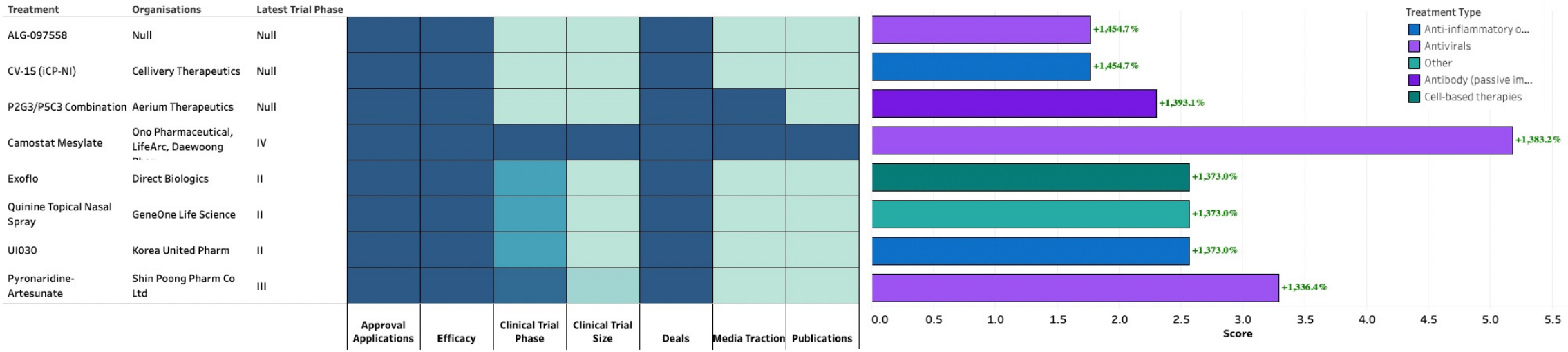
Overview of the candidates with the greatest changes in progress scores

This week, Camostat Mesylate has seen progression due to the publication of Phase III trial results as a press release. The small trial, funded by Ono Pharmaceutical, investigated Camostat Mesylate as a treatment for mild to moderate COVID-19 in 155 participants; the results demonstrated that the treatment was no more effective than placebo at improving viral clearance. Elsewhere, Exoflo progressed this week due to increased media traction. This came after Direct Biologics announced top-line results from a Phase II trial as a press release. ExoFlo demonstrated a reduction in 60-day mortality rate of 37.6% in comparison to placebo as well as a robust safety profile, warranting further clinical investigation with a pivotal Phase III study.

Limitations:

→ We use a range of sources, some of which are not peer reviewed, so we cannot guarantee their reliability.

→ Unable to differentiate between positive or negative media traction.



Data and Visualisation: Airfinity

The Shionogi oral antiviral candidate, S-217622, is the highest ranked candidate in our progress tool

Overview of the candidates with the highest progress scores

The candidate progress tool scores COVID-19 treatment and prophylaxis candidates based on a range of metrics to indicate its progression towards an approval.

Limitations:

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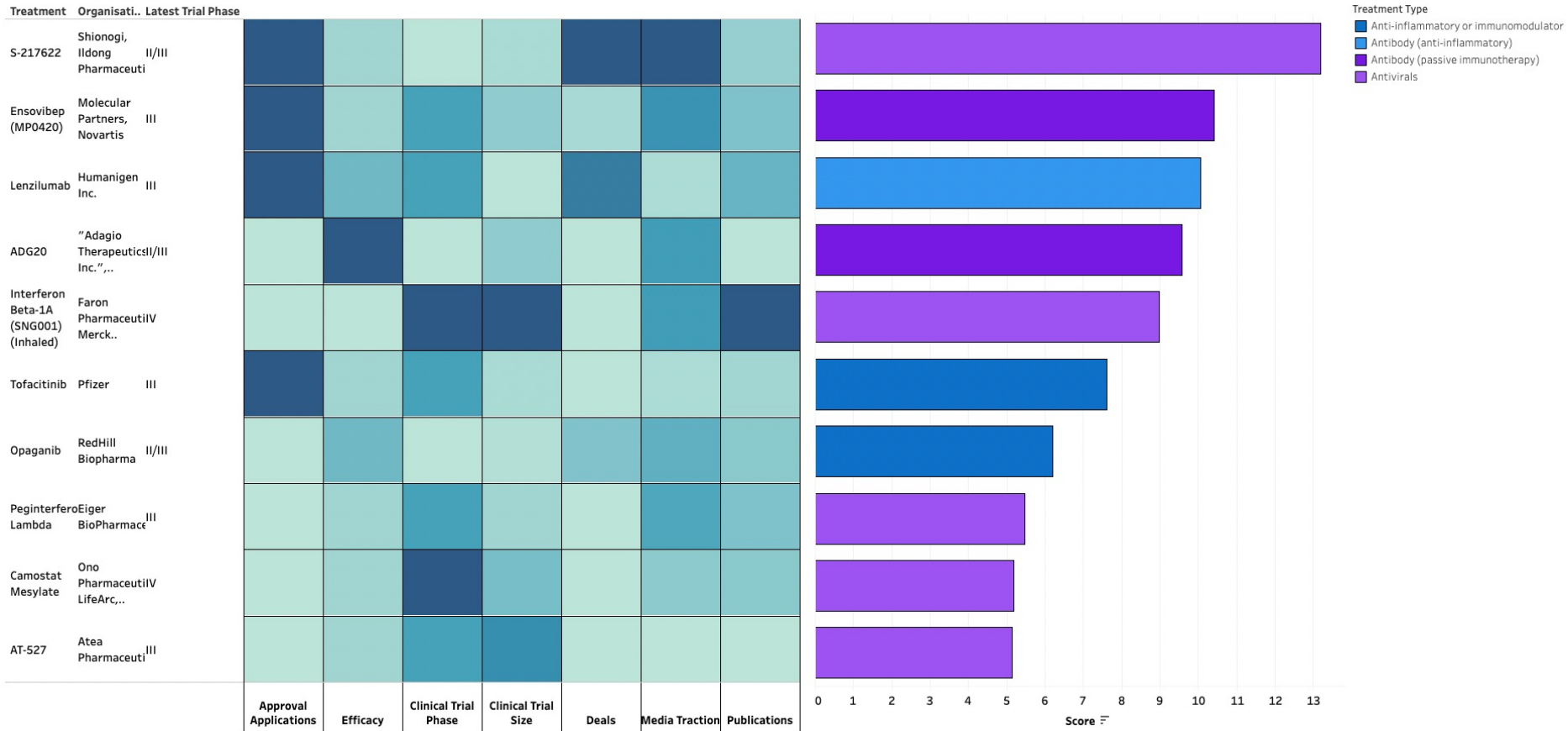
→ Unable to differentiate between positive or negative media traction.



Data and Visualisation: Airfinity

→ Efficacy and Safety:

Hydroxychloroquine and Remdesivir post neutral results from large Phase III trials

Monoclonal antibodies: Published pseudovirus assay demonstrates Brii Biosciences mAb combo has a moderate loss in efficacy against the Omicron Variant

Summary of new findings this week on the functional impact of variants on COVID-19 monoclonal antibody treatments

Complete loss of neutralisation	>1000 fold decrease compared to WT
High	50-1000 fold decrease
Moderate	20-50 fold decrease
Minimal	2-20 fold decrease
None	0-2 fold decrease

Brii Biosciences Result
Visualisation: Airfinity efficacy against variants page

Antivirals: No updates

Summary of new findings this week on the functional impact of variants on COVID-19 antiviral treatments

Complete loss of neutralisation	>1000 fold decrease compared to WT
High	50-1000 fold decrease
Moderate	20-50 fold decrease
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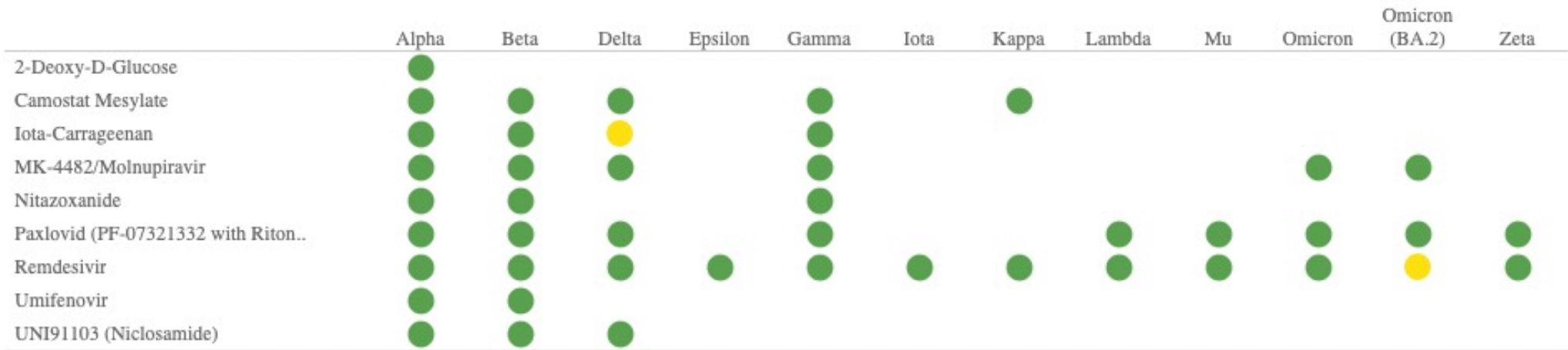


Visualisation: Airfinity efficacy against variants page

→ Deep Dive: Outpatient Treatment Expiry

COVID-19 therapeutics shelf lives range from 12 to 36 months

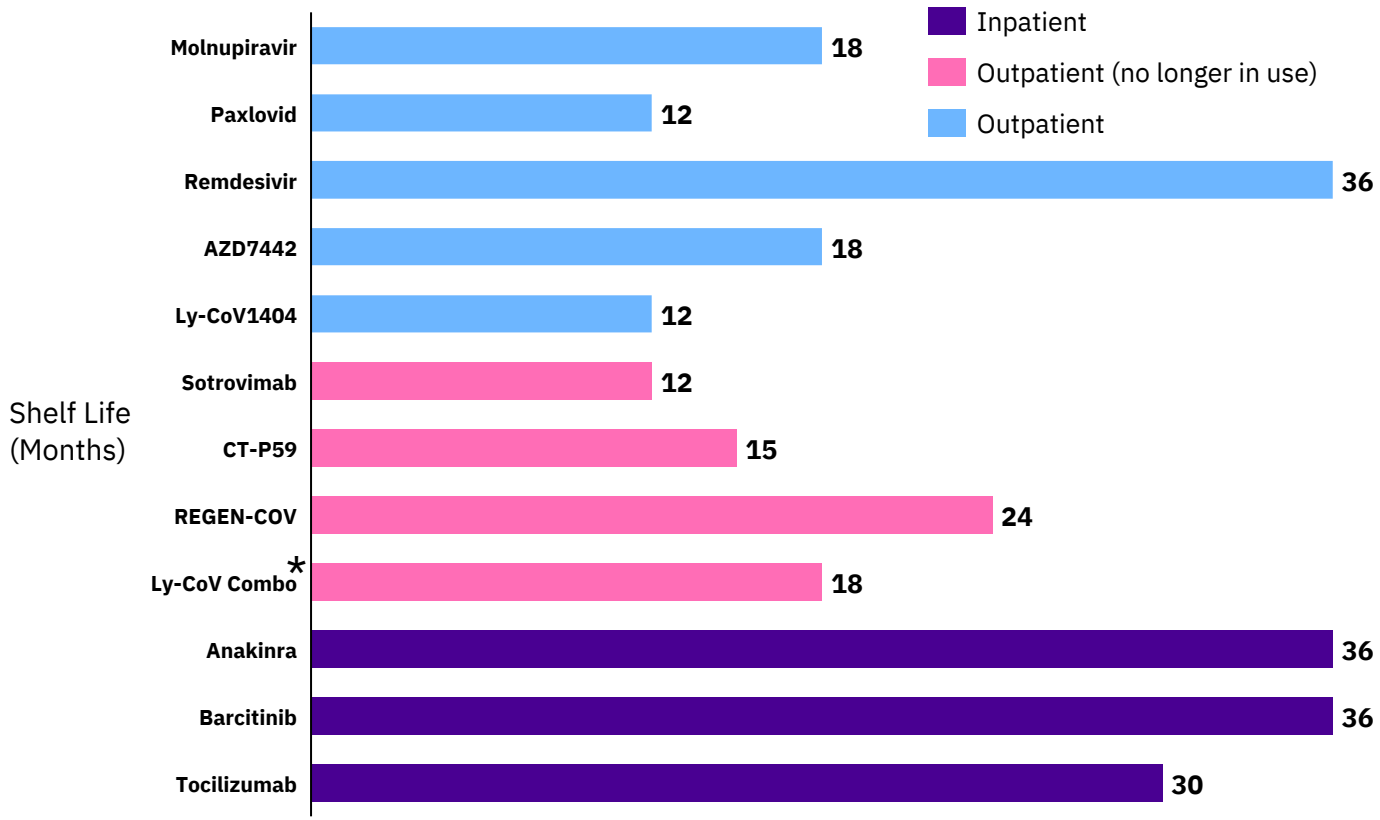
LY-CoV1404 uptake will need to increase 1500% from current rates to utilise supplies before doses expire

COVID-19 therapeutics shelf lives range from 12 to 36 months

COVID-19 therapeutics shelf life overview

A drug's shelf life, or expiry date, is defined as 'the date at which the manufacturer can still guarantee the full potency and safety of the drug'. Novel COVID-19 therapeutics that are now approved for use have been exclusively manufactured in the last 2 years, however some may be approaching their company stated shelf life if they have not yet been administered to patients.

Limitations:
→ LY-CoV1404 shelf life unknown, estimated from shelf life of LY-CoV Combo.



*The U.S. FDA extended the shelf life of the LY-CoV combo from 12 to 18 months in December 2021

The Fate of Currently Unused Treatments

The monoclonal antibodies REGEN-COV, CT-P59 and the LY-CoV Combo all had complete loss of neutralisation against the Omicron variant so usage was halted in early 2022. Additionally, in April 2022, the U.S. halted use of Sotrovimab due to the prevalence of the BA.2 sublineage.
Courses of these treatments will have already been produced, and could potentially be used in future to combat a new variant which may arise, if they demonstrate neutralising efficacy
The table below highlights the latest date that already produced monoclonal antibodies would need to be used by, if the treatments are not efficacious by this point then remaining doses will be wasted.

Treatment	Estimated use by date
CT-P59	Q1 2023
Sotrovimab	Q1 2023
LY-CoV Combo	Q2 2023
REGEN-COV	Q1 2024

Treatment Shelf Lives, shelf life definition
Visualisations: Airfinity

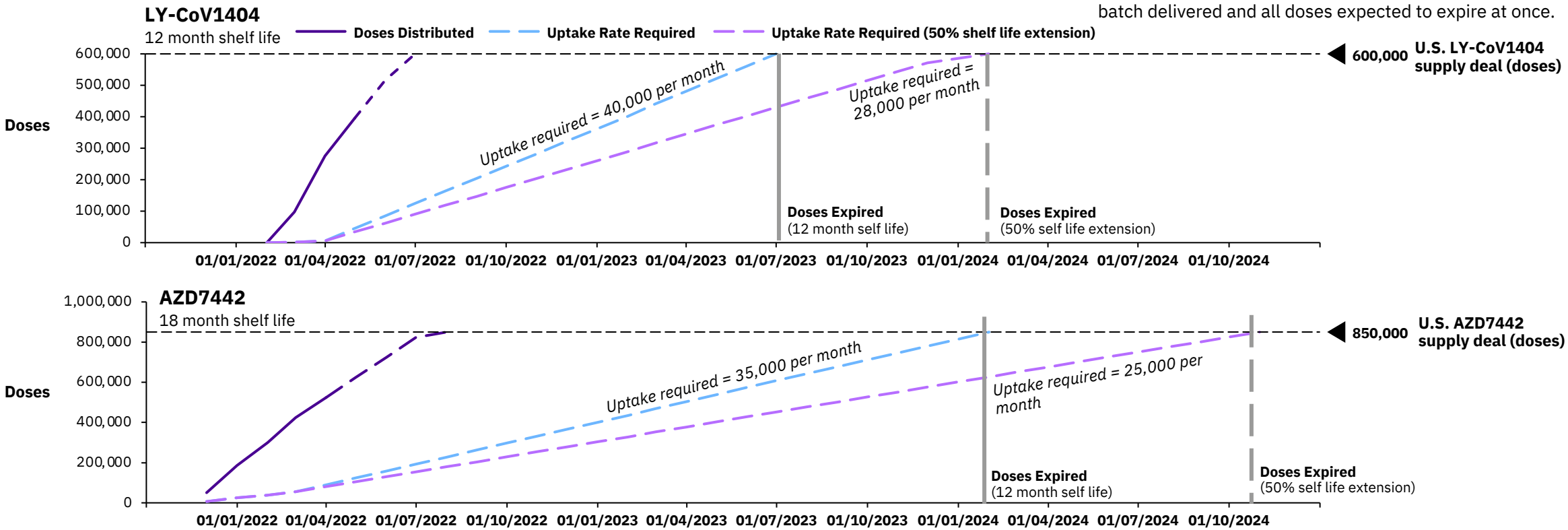
LY-CoV1404 uptake will need to increase 1500% from current rates to utilise supplies before doses expire

U.S. monoclonal treatment distribution, shelf life and uptake

After the halting of Sotrovimab distribution this week, the U.S. has two monoclonal candidates remain in use; Ly-CoV1404 and AZD7442. Using their published shelf lives, an estimate can be made for the treatment uptake required to ensure all doses are utilised before their expiry date. Additionally, based on the U.S. FDA extending the shelf life of the LY-CoV Combo from 12 to 18 months (50% increase) we have estimated the required uptake rate with the shelf life extension. Even to meet this later expiry date, uptake required to prevent waste would be 28,000 and 25,000 courses per month for LY-CoV1404 and AZD7442, respectively.

Limitations:

- → AZD7442 supply deal and distribution doses halved to account for the doubling of its dosage.
- → Future doses distributed are estimated using previous months distribution data.
- → Uptake is plotted linearly and does not take into account case rates.
- → Expiry date taken to be X months from the estimated final batch delivered and all doses expected to expire at once.



Treatment Distribution, Treatment Uptake
Visualisations: Airfinity

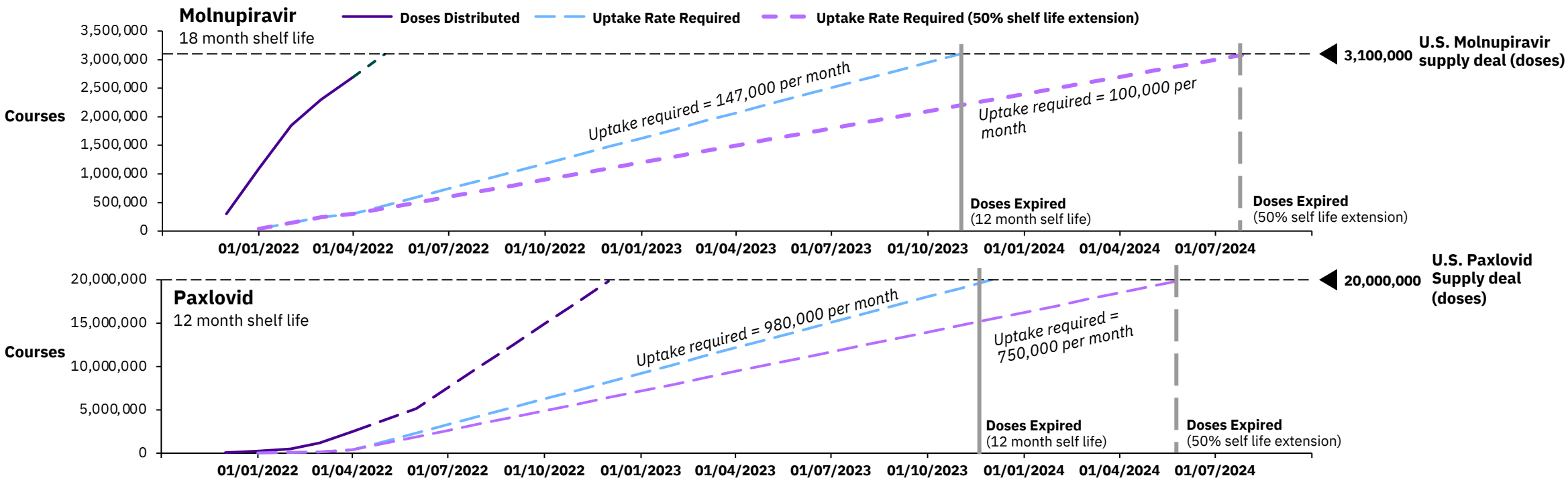
Paxlovid uptake will need to increase 4 fold from current rates to utilise supplies before doses expire

U.S. antiviral treatment distribution, shelf life and uptake

Similarly to the monoclonal antibodies, if we apply a 6 month shelf life extension to the oral antivirals uptake required to prevent waste would be 100,000 and 750,000 courses per month for Molnupiravir and Paxlovid, respectively. However, given that Tamiflu, an Influenza oral antiviral, has a shelf life of 10 years (with some reports suggesting this can be extended 5 more years), it is likely shelf lives for Molnupiravir and Paxlovid will be extended, meaning there may be less pressure to utilise current supplies.

Limitations:

- → Future doses distributed are estimated using previous months distribution data.
- → Uptake is plotted linearly and does not take into account case rates.
- → Expiry date taken to be X months from the estimated final batch delivered and all doses expected to expire at once.



Treatment Distribution, Treatment Uptake, Tamiflu Shelf Life
Visualisations: Airfinity

Market & Production Contents

→ Supply:

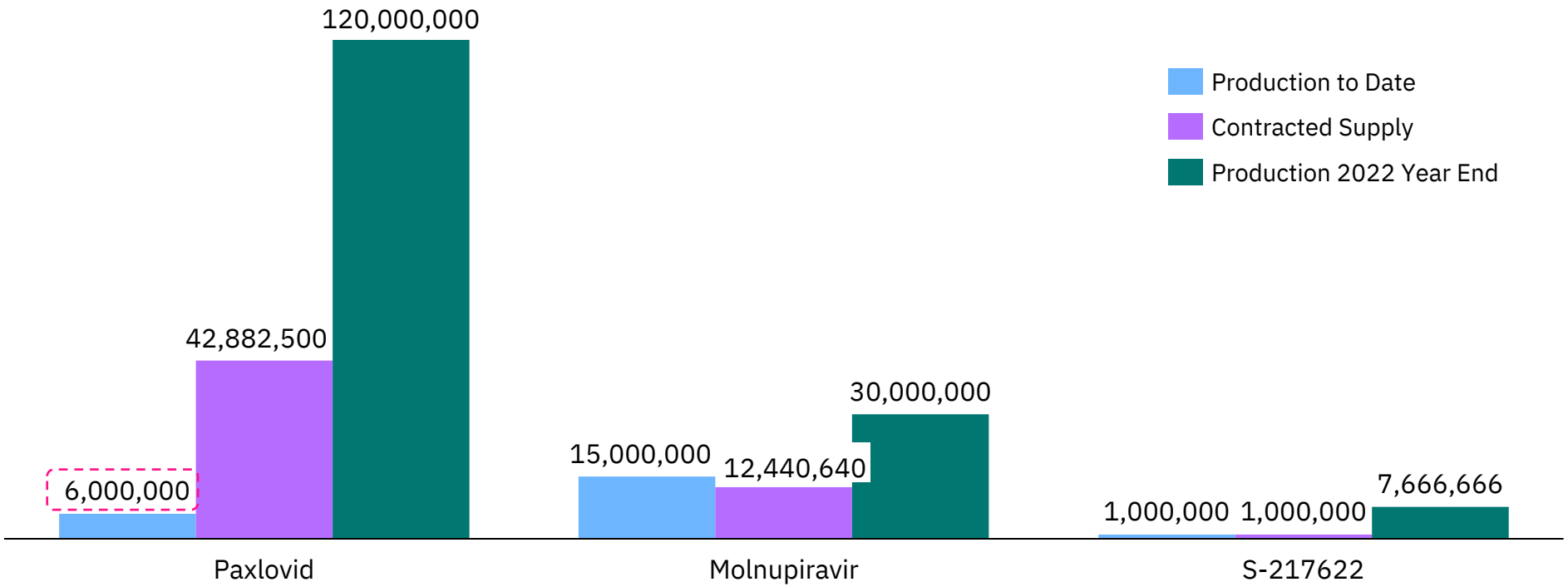
Pfizer meets production target for Paxlovid in Q1 2022

Pfizer confirms Q1 2022 production target of 6 million Paxlovid courses was met

Oral antiviral production to date and total contracted supply

Pfizer stated a production target of 6 million Paxlovid courses in Q1 2022. It was confirmed this week that this target was met[1], and that Pfizer had shipped courses to over 26 countries. Pfizer's production estimate for Q2 2022 is 24 million courses. However, if the Q2 target is met, bringing the total to 30 million, this would still fall short of the total number of courses agreed upon in supply deals by nearly 13 million courses.

Limitations:
→ Based on publicly announced production and supply contracts.



Data: Airfinity [1] Pfizer Announcement
Visualisation: Airfinity

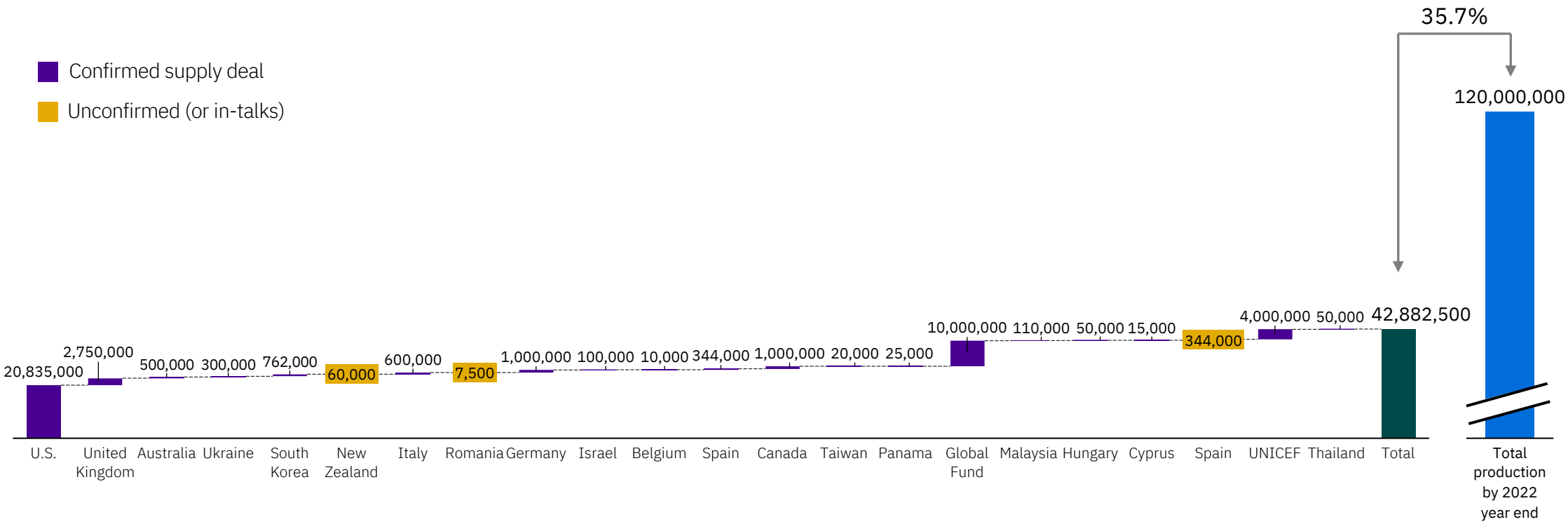
Paxlovid Pfizer Supply Deals: No updates

Total number of courses in confirmed, or in-talks, supply deals – from Airfinity data

Pfizer has announced it has production capacity for 120 million courses of Paxlovid in 2022. Currently 35.7% of this total production capacity has been procured by governments around the world with the majority, similarly to Molnupiravir, being procured by the U.S.

Limitations:

→ Only publicly available supply deals with a confirmed number of courses.



Data: Airfinity
Visualisation: Airfinity

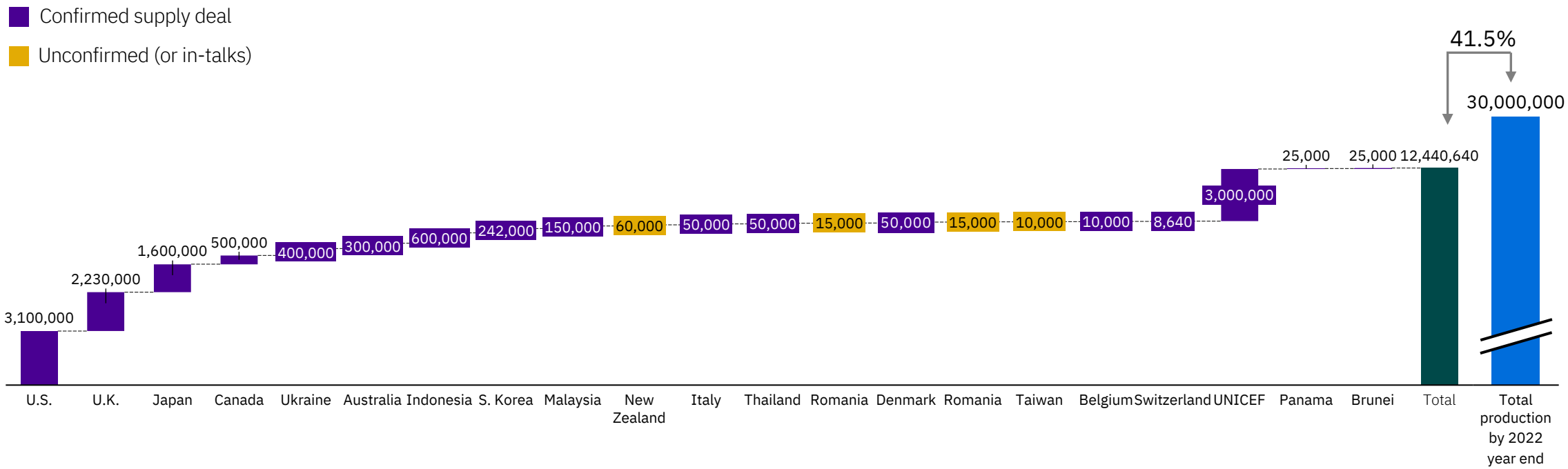
Molnupiravir Merck Supply Deals: No updates

Total number of courses in confirmed, or in-talks, supply deals – from Airfinity data

Merck has announced it has production capacity for 30 million courses of Molnupiravir until 2022 year end. Currently 41.5% of this total production capacity has been procured by governments around the world with the majority being procured by the U.S., U.K., and UNICEF.

Limitations:

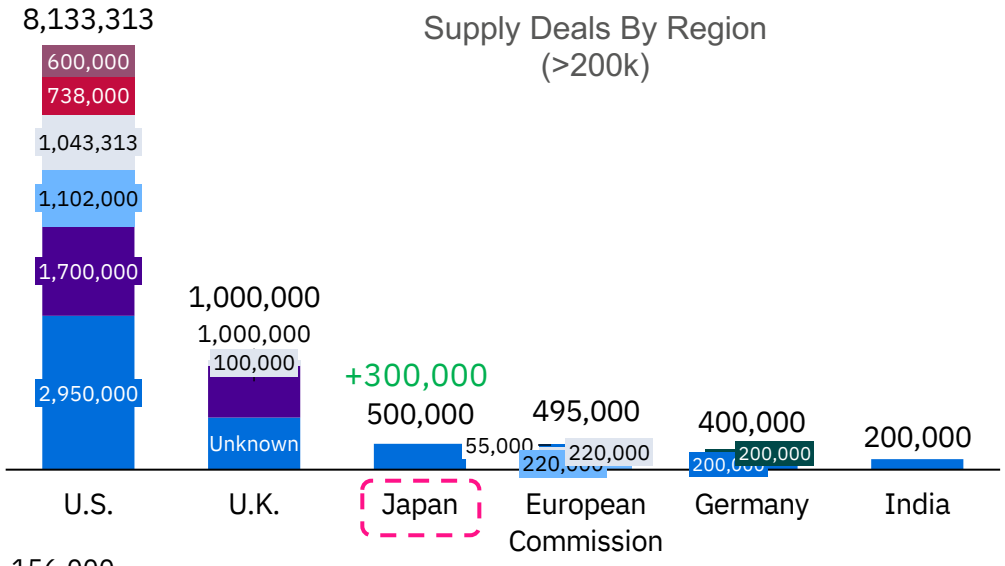
→ Only publicly available supply deals with a confirmed number of courses.

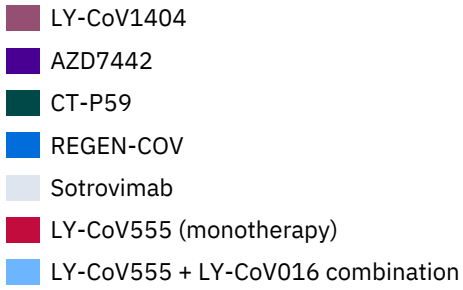


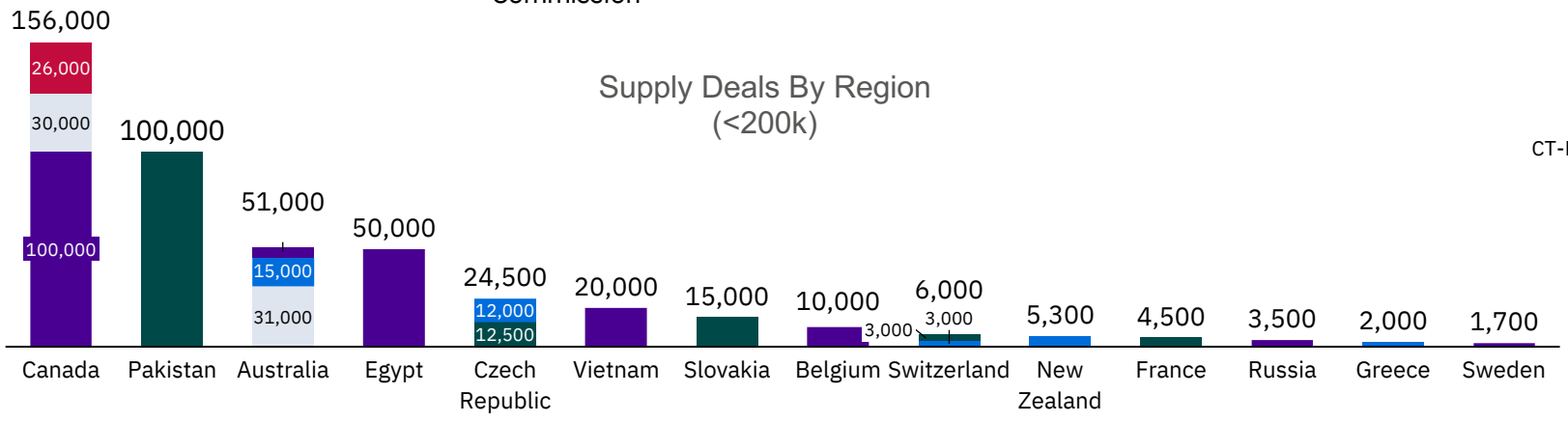
Data: Airfinity
Visualisation: Airfinity

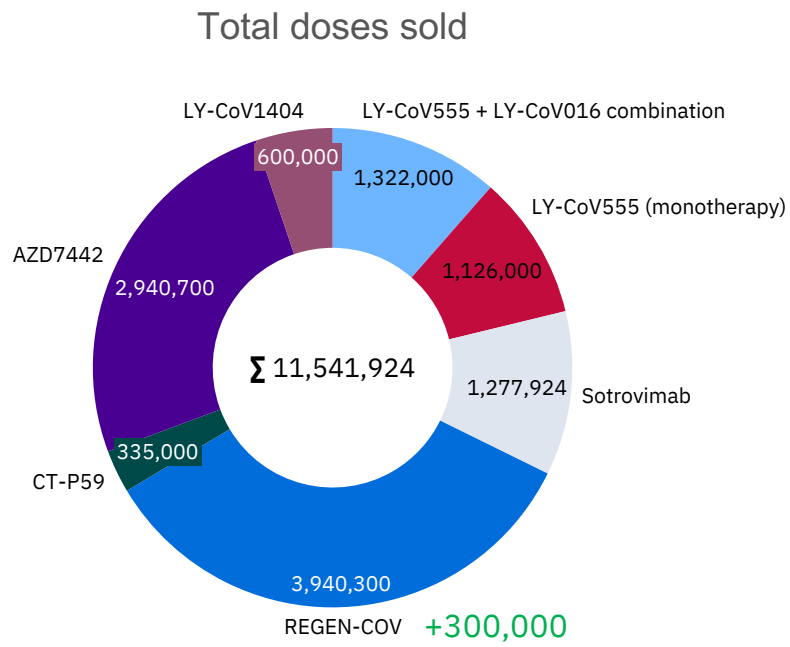
Japan procured 300,000 more REGEN-COV doses than previously reported in October 2021

Overview of monoclonal antibody supply deals









Data: Airfinity
Visualisation: Airfinity

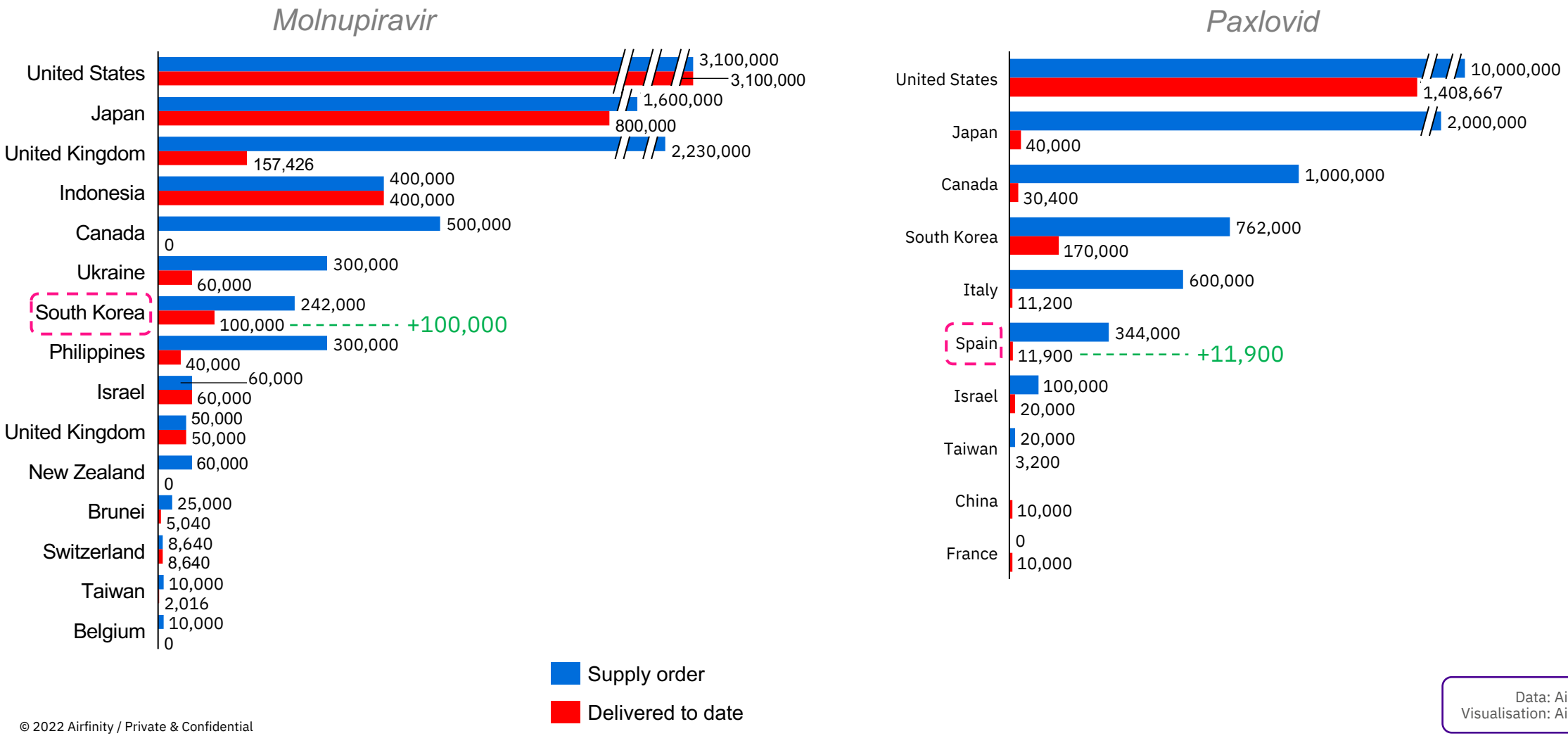
→ Deliveries and Distribution:

South Korea receives 100,000 Molnupiravir courses

Spain receives first delivery of Paxlovid

Global Deliveries: S. Korea receives 100,000 courses of Molnupiravir; Spain receives first courses of Paxlovid

Known global deliveries of Molnupiravir and Paxlovid



Data: Airfinity
Visualisation: Airfinity

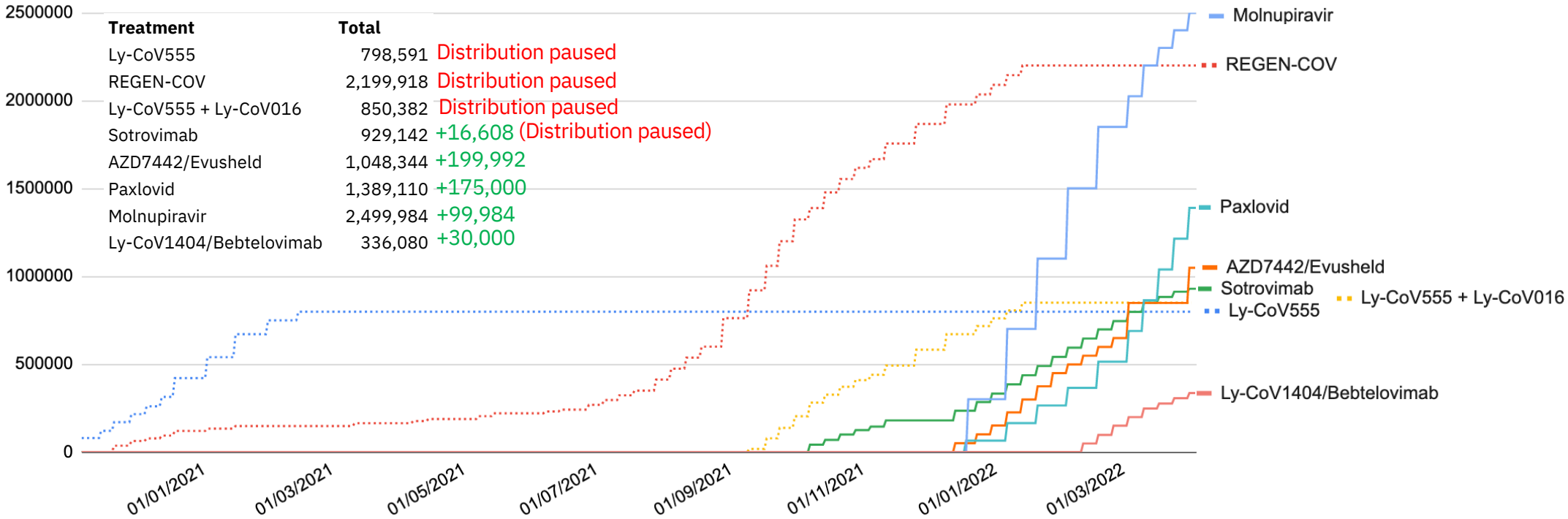
U.S. Distribution: U.S. pauses distribution of Sotrovimab

Cumulative outpatient treatment distribution in the U.S.

The roll out of Molnupiravir since distribution began in the U.S. in December 2021 has been quicker and on a larger scale than any other treatment. This is despite being jointly 4th on the NIH clinical guidelines for mild/moderate outpatient care, behind Paxlovid (first choice), Sotrovimab, and Remdesivir.

Limitations:

→ Does not include Remdesivir, which is used in the outpatient setting in the U.S.



Treatment	Total	
Ly-CoV555	798,591	Distribution paused
REGEN-COV	2,199,918	Distribution paused
Ly-CoV555 + Ly-CoV016	850,382	Distribution paused
Sotrovimab	929,142	+16,608 (Distribution paused)
AZD7442/Evusheld	1,048,344	+199,992
Paxlovid	1,389,110	+175,000
Molnupiravir	2,499,984	+99,984
Ly-CoV1404/Bebtelovimab	336,080	+30,000

Data: HHS
Visualisation: Airfinity

→ Global Production:

AZD7442 production and sales adjusted to reflect expected doubling of approved dosage worldwide

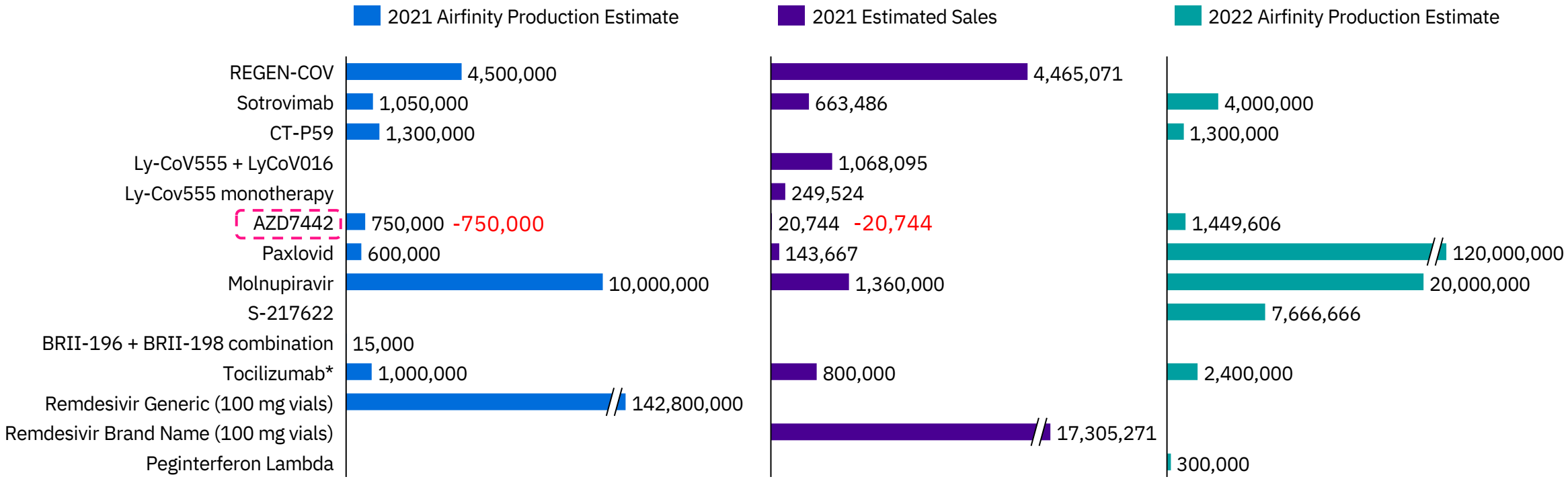
Production: AZD7442 Production and sales estimates adjusted for doubling of dosage

Treatment production and sales estimates

Following the U.S. FDA updating the EUA for AZD7442, doubling the required dosage, we expect other regulatory bodies to do the same. Doubling the dosage of AZD7442 effectively halves the production capacity, and previous sales of the prophylactic (assuming individuals who received AZD7442 at the previous dosage receive another dose, as is the case in the U.S.).

Limitations:

- → Sales are estimated from revenues.
- → Some estimates are extrapolated from company stated quarterly/half-year production capacities.

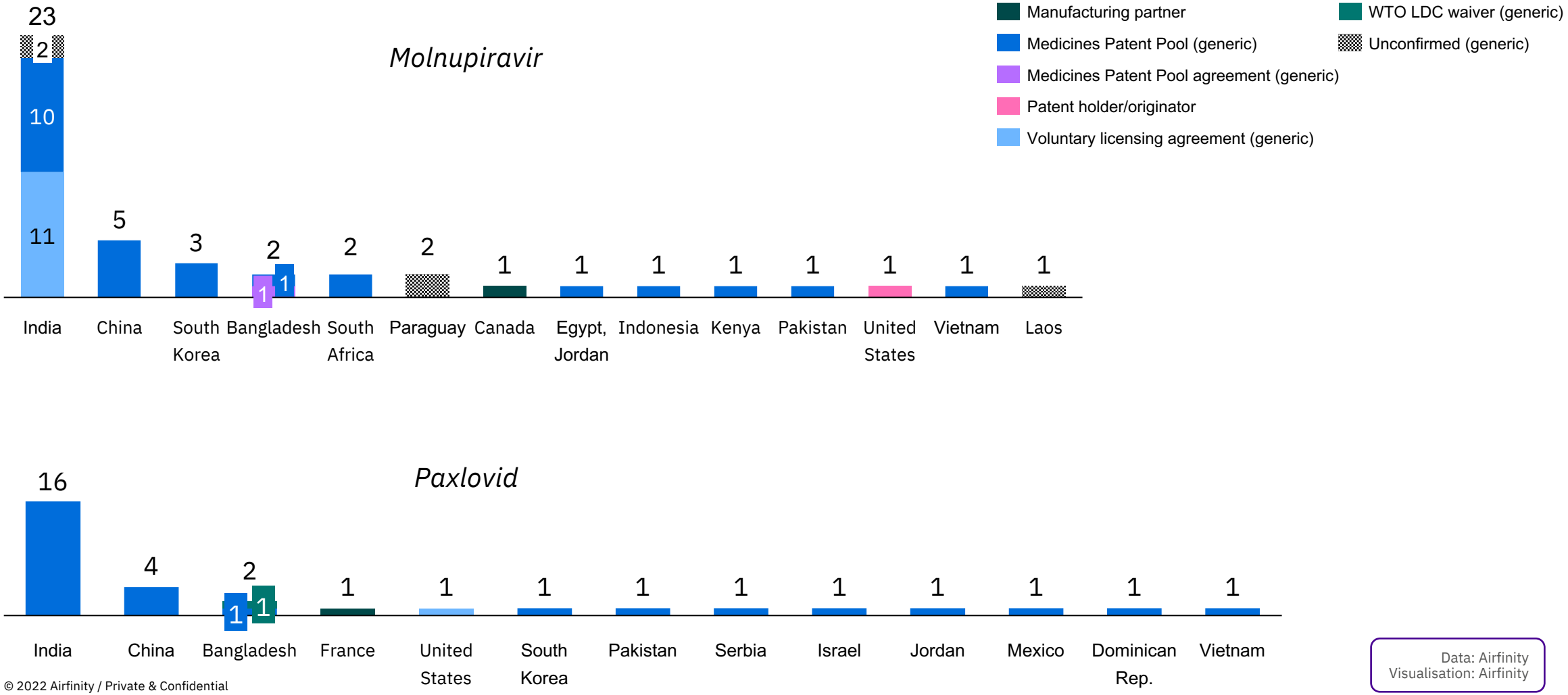


*Tocilizumab figures are estimated as COVID-specific production capacity and excludes production for other indications.
Note: where no value is given, production/sales may not be zero, instead there is not enough data to make an estimate.

Data: Airfinity
Visualisation: Airfinity

Molnupiravir & Paxlovid Manufacturing of Finished Product: No updates

Manufacturing locations for oral antivirals by country and licensing agreement



Data: Airfinity
Visualisation: Airfinity

→ Pricing:

Japan has paid the highest price points for two outpatient treatments

Japan has paid the highest known price point for Molnupiravir and REGEN-COV

Overview of price points for COVID-19 outpatient treatments

Only two price points paid for COVID-19 treatments by Japan are known, however for both REGEN-COV and Molnupiravir, Japan have paid the highest (known) price per dose.

Limitations:

→ Price points are not known for all supply deals.

Data: Airfinity
Visualisations: Airfinity

→ Appendix

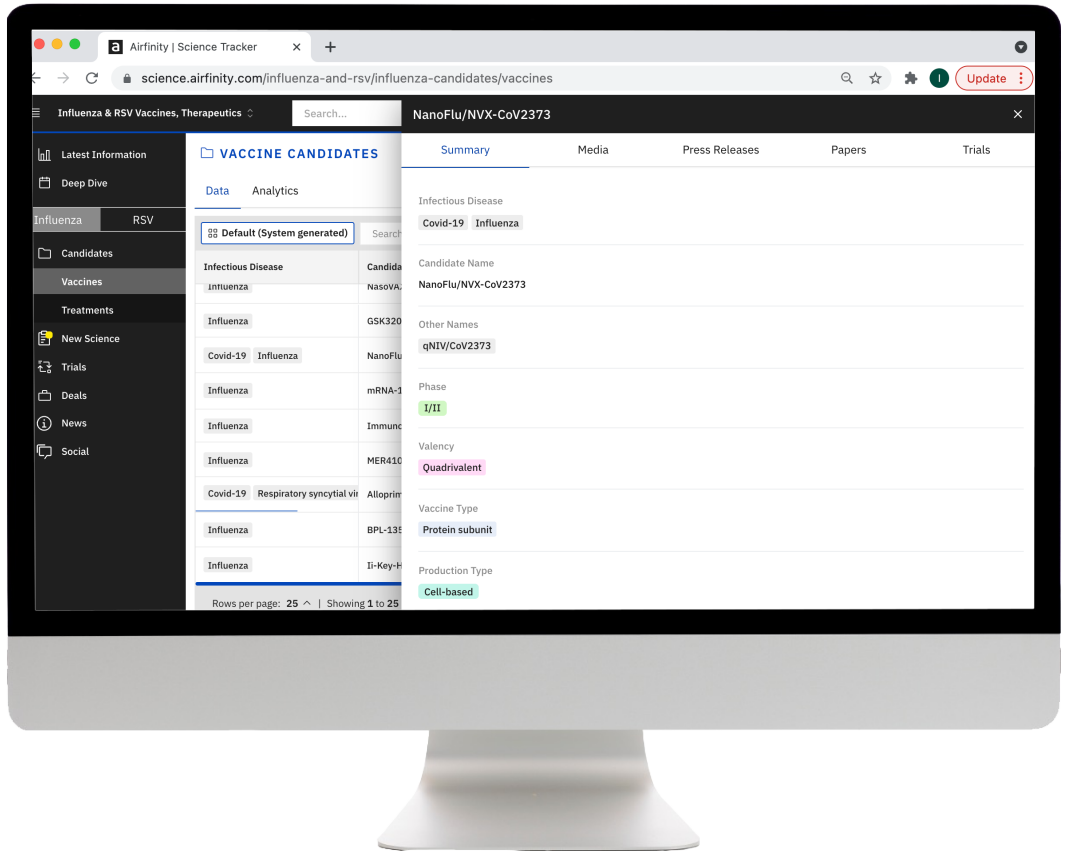
Full Remdesivir results added from DISCOVERY trial

Hydroxychloroquine results added

Other infectious diseases

Influenza and RSV platforms

If you are looking for information on combined COVID and Influenza and RSV candidates please get in contact for more information on our Influenza and RSV platforms.



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More info.

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