Daily Change in COVID-19 Cases, US
January 22, 2020 – November 08, 2021

TOTAL Cases Reported Since 1/22/20
46,541,113

NEW Cases Reported to CDC on 11/8/21
134,072

Change in 7-Day Case Average
-2.5%

Current 7-Day Case Average (11/2/21 - 11/8/21)
73,313

Prior 7-Day Case Average (10/26/21 - 11/1/21)
75,210
New Admissions of Patients with Confirmed COVID-19, US
August 1, 2020 – November 07, 2021

Patients Currently Hospitalized with COVID on 11/7/21
38,147

New Admissions on 11/7/21
5,086

Peak in New Admissions (1/5/21)
17,949

Change in 7-Day Average of New Admissions
-2.1%

Current 7-Day Average of New Admissions (11/1/21 - 11/7/21)
5,088

Prior 7-Day Average of New Admissions (10/25/21 - 10/31/21)
5,194
Daily Change in COVID-19 Deaths, US
January 22, 2020 – November 08, 2021

TOTAL Deaths Reported Since 1/22/2020
753,564

NEW Deaths Reported to CDC on 11/8/21
1,307

Change in 7-Day Death Average
-11.0%

Current 7-Day Death Average (11/2/21 - 11/8/21)
1,078

Prior 7-Day Death Average (10/26/21 - 11/1/21)
1,211

Forecasted Total Deaths by 11/27/21
765,000 to 789,000

*7-day averages exclude historical cases reported retroactively by states
ACIP Recommended Pediatric Vaccines

Average annual deaths, by age group, before implementation of an ACIP recommendation

- **Hepatitis A**: 3 deaths per year from 1990-1995 among <20 year olds
- **Meningococcus**: 8 deaths per year from 2002-2004 among 11-18 year olds
- **Varicella (Chickenpox)**: 16 deaths per year from 1990-1994 among 5-9 year olds
- **COVID-19**: 66 deaths from 2020-2021 among 5-11 year olds
Recent Advances in Antiviral Therapy for COVID-19
Identification of Vulnerable Targets in the SARS-CoV-2 Replication Cycle

Design Drugs to Inhibit Vulnerable Targets
SARS-CoV-2 Replication Cycle: Targets for Antiviral Therapeutics

Preclinical, Phase 1, Phase 2/3

Protease Inhibitors

Polymerase Inhibitors

Preclinical, Phase 2, Phase 3

Entry Inhibitors

Virion release

Packaging & lysosomal trafficking

Endoplasmic reticulum

Replication-transcription complex

Translation & RNA replication

Uncoating/virion RNA translation

Viral RNA

Viral protease cleavage

Polypeptide chains

ACE2

TMPRSS2

SARS-CoV-2

RNA

Spike protein
SARS-CoV-2 Replication Cycle: Targets for Antiviral Therapeutics

Preclinical, Phase 1, Phase 2/3

Protease Inhibitors

Polymerase Inhibitors

Preclinical, Phase 2, Phase 3

Entry Inhibitors
Molnupiravir: Clinical Data Announced Oct. 1, 2021 by Merck and Ridgeback

- Placebo-controlled trial of ~1500 people; DSMB stopped study early at first analysis of 775 people
- End point: prevention of hospitalization or death
- 7% hospitalization in treatment arm and 14% hospitalization or death in placebo arm → 50% decrease
- Placebo – 8 deaths; treatment – 0 deaths
SARS-CoV-2 Replication Cycle: Targets for Antiviral Therapeutics
**Paxlovid (Protease Inhibitor + Ritonavir): Clinical Data Announced Nov. 5, 2021 by Pfizer**

- Placebo-controlled phase 2/3 trial of ~3,000 people; DSMB stopped study early at scheduled interim analysis of 1,219 people

- Subjects with a laboratory-confirmed diagnosis of SARS-CoV-2 infection with mild-to-moderate symptoms and at least one characteristic/medical condition associated with an increased risk of developing severe illness from COVID-19

- Patients randomized (1:1) to receive Paxlovid or placebo orally every 12 hours for five days.

- **89% reduction in hospitalization or death compared to placebo; 10 deaths in placebo arm, no deaths in treatment arm.**

- Adverse events similar in placebo and treatment arms
U.S. Government Role in Development of Paxlovid

- NIH consultations with Pfizer and referrals to researchers with specific capacities that proved essential
  - Provided novel screening methods for anti-protease activity, helped select the clinical lead
  - *In vitro* testing systems demonstrated the antiviral activity of Paxlovid
  - Animal model testing showed the need for ritonavir boosting

- NIH-led Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) team generated the clinical trial protocol, which Pfizer implemented
Antivirals Are Promising, but Be Sure To Get Vaccinated

- Antivirals are not our first line of defense against COVID-19.

- Get vaccinated to prevent SARS-CoV-2 infection and COVID-19 complications.

- Get a booster shot when it is your turn.