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Genentech Influenza Clinical Development Program:
Clinical Studies

M-US-00002229

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Baloxavir's Clinical Development Program

Completed Trials

- **Acute uncomplicated influenza in patients 12 and older**

  CAPSTONE-1

- **Patients 12 and older at high-risk of developing flu-related complications**

  CAPSTONE-2

- **Post-exposure prophylaxis**

  BLOCKSTONE

- **Pediatric patients 1 to <12 years old (oral suspension)**

  miniSTONE-2

Enrollment Completed

- **Hospitalized patients with severe influenza**

  FLAGSTONE

Ongoing Trials

- **Influenza household transmission study**

  (CENTERSTONE)

  Estimated Completion Q2 2021

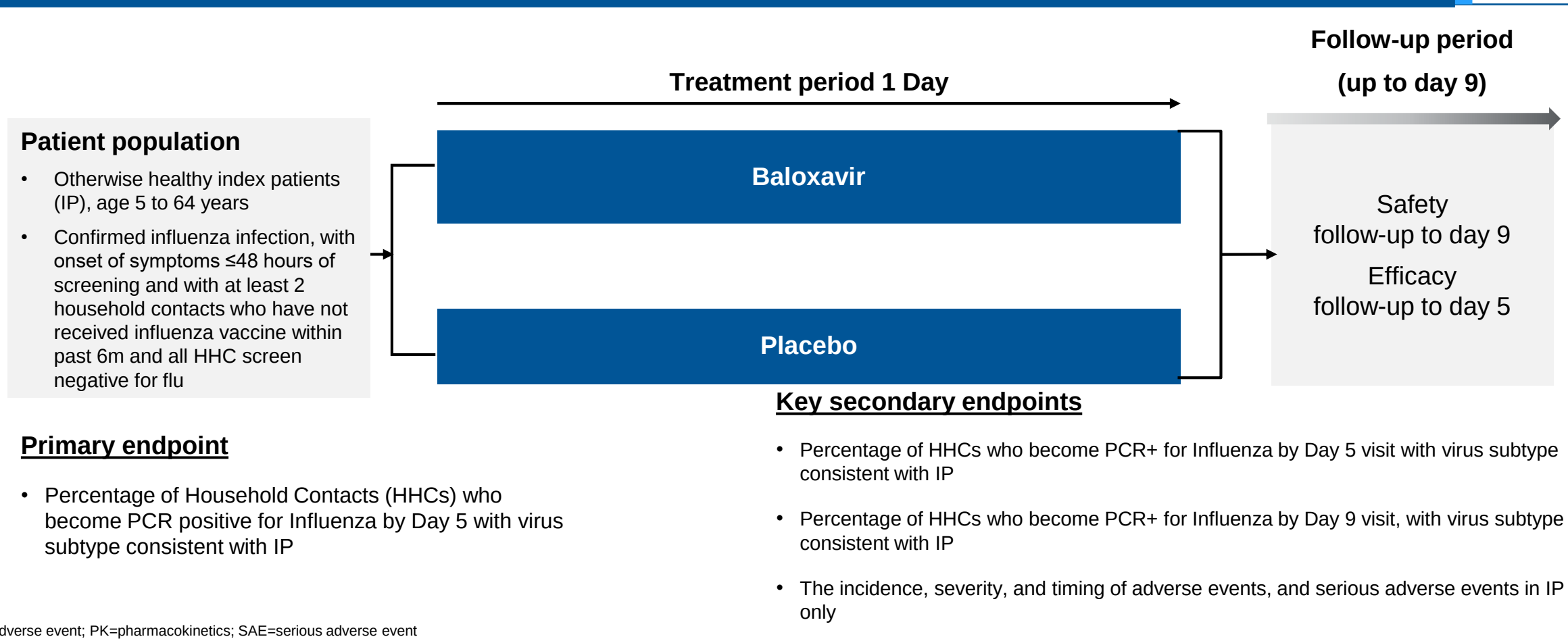
- **Pediatric patients <1 years old (oral suspension)**

  (*miniSTONE-1*)

  Estimated Completion Q2 2021

CENTERSTONE: Study to Assess the Efficacy of Baloxavir Versus Placebo to Reduce Onward Transmission of Influenza A or B in Households

Objective: Assess the **safety** and **efficacy** of baloxavir to reduce the onward transmission of Flu in Households



Primary endpoint

- Percentage of Household Contacts (HHCs) who become PCR positive for Influenza by Day 5 with virus subtype consistent with IP

Key secondary endpoints

- Percentage of HHCs who become PCR+ for Influenza by Day 5 visit with virus subtype consistent with IP
- Percentage of HHCs who become PCR+ for Influenza by Day 9 visit, with virus subtype consistent with IP
- The incidence, severity, and timing of adverse events, and serious adverse events in IP only

AE=adverse event; PK=pharmacokinetics; SAE=serious adverse event

References: 1. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03969212 Accessed August 11, 2020

CENTERSTONE: Assess the Efficacy of Baloxavir Versus Placebo to Reduce Onward Transmission of Influenza A or B in Households

Key Inclusion Criteria

- Otherwise healthy index (HI) patient Age ≥5 and ≤64 years at time of signing ICF.
- Diagnosis with acute influenza infection by investigator
- PCT(+) or RIDT (+) for influenza A/B
- PCR (-) or antigen test (-) for SARS-CoV-2
- Presence of a fever ≥38ºC (tympanic temperature) or any influenza symptoms
- ≤48 hours between onset of influenza symptoms* and pre-dose examination
- IP lives in a household where no household contact (HHC) known to have been diagnosed with influenza or SARS-CoV-2 infection, all HHCs are expected to meet the key HHC inclusion criteria and none of the HHC exclusion criteria, ≥ 2 HHCs are expected to participate in the full study who have not received the influenza vaccine within 6 months prior to screening.

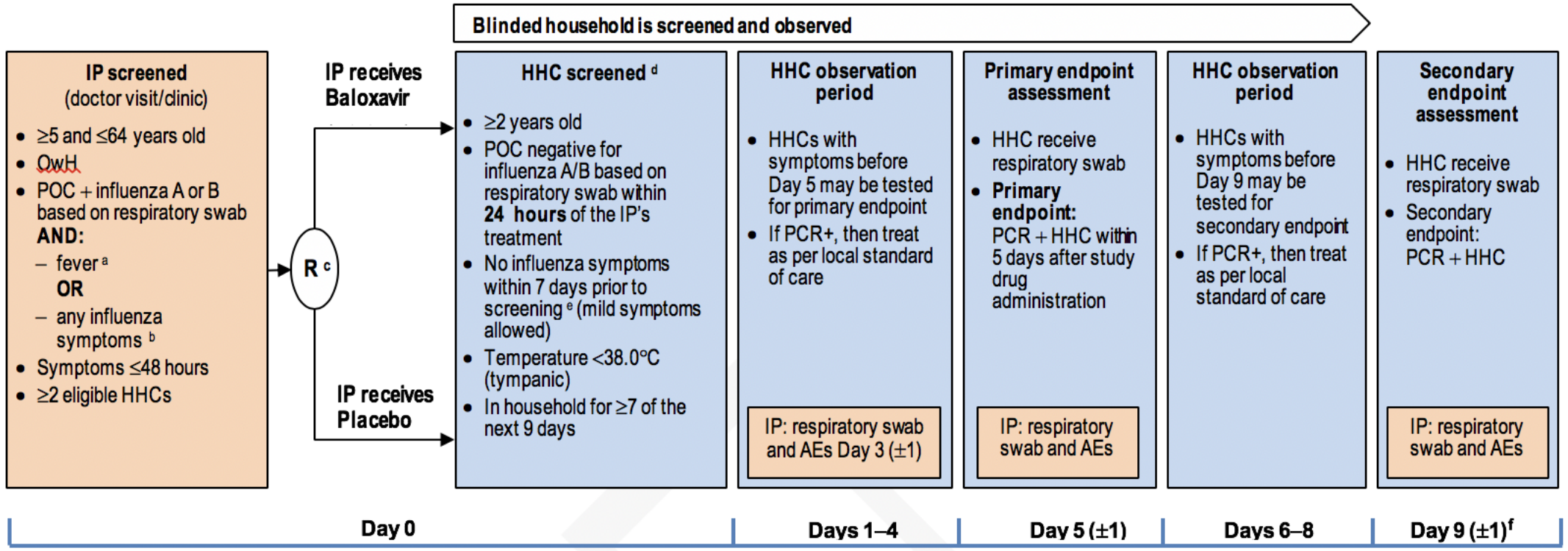
Key Exclusion Criteria

- IPs with severe influenza virus infection requiring inpatient treatment.
- IPs known by the investigator to have any of the risk factors which may increase the risk for complications of influenza
- IPs who have received baloxavir marboxil, peramivir, laninamivir, oseltamivir, zanamivir, rimantadine, umifenovir or amantadine, or an investigational drug, within 30 days prior to screening
- IPs with concurrent (non-influenza) infections requiring systemic antimicrobial and/or antiviral therapy at the pre-dose examinations
- HHC who are immunocompromised, less than 2 years old or who have received an investigational therapy within the 30 days prior to screening
- HHCs who are diagnosed with influenza or SARS-CoV-2 infection by a healthcare professional in the past 4 weeks.

*ICF: Informed Consent Form. Influenza symptoms include cough, sore throat, nasal congestion, headache, feverishness or chills, muscle or joint pain, fatigue. Onset of symptoms defined as the time when body temperature first exceeded 37.5ºC if known, or the time when the first symptom was noticed by the parent or caregiver

References: 1. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/ NCT03969212. Accessed August 11, 2020

CENTERSTONE: Phase 3 Onward Transmission Study Schema



AEs = adverse events; HHC = household contact; IP = index patient; OwH = otherwise healthy; PCR = polymerase chain reaction; POC = point of care.

[a]≥38.0 °C per tympanic or rectal thermometer; ≥37.5 °C per axillary, oral or forehead/temporal thermometer.; [b]cough, sore throat, nasal congestion, headache, feverishness or chills, muscle or joint pain, fatigue. [c]Stratification factors: age; household size; region; time since symptom onset. [d]HHC screening must start within 24 hours of IP randomization, and may occur on IP study Day 0 or 1. for HHC ≥12 years old: cough, sore throat, nasal congestion, headache, feverishness or chills, muscle or joint pain, fatigue; Symptoms for HHC ≥2 to <12 years old: [e]Symptoms cough, nasal congestion or rhinorrhea. [f]IPs <12 years old will have a safety follow up visit on Day 21 (+2 day).

References: 1. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/ NCT03969212. Accessed August 11, 2020

MINISTONE-1: an open-label study to assess the safety, pharmacokinetics, and efficacy of baloxavir in participants aged <1 year with influenza-like symptoms

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Ongoing Studies:
<1 Year Old Pediatric Study

Objective: Assess the **safety**, **PK**, and **efficacy** of baloxavir 2% granules in healthy pediatric patients <1 year of age with influenza-like symptoms

Patient population

- Aged <1 year
- Confirmed influenza infection, with onset of symptoms ≤96 hours before screening

Treatment period 1 Day

- **Cohort 1: ≥3 months to <12 months old: baloxavir 2 mg/kg**
- **Cohort 2: ≥4 weeks to <3 months old: baloxavir 1 mg/kg**
- **Cohort 3: birth to <4 weeks old: baloxavir 1 mg/kg**

Follow-up period (up to day 29)

Safety
follow-up to day 29

PK
follow-up to day 10

Efficacy
follow-up to day 15

Primary endpoint

- Percentage of participants with AEs and SAEs

Key secondary endpoints

- **Clinical:** time to alleviation of influenza signs and symptoms, duration of fever and symptoms, time to return to normal health/activity
- **Virologic:** changes in baseline viral titer, time to cessation of viral shedding
- **PK:** plasma concentrations of baloxavir, half-life of baloxavir

AE=adverse event; PK=pharmacokinetics; SAE=serious adverse event

References: 1. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03653364. Accessed August 11, 2020

MINISTONE-1: Phase 3 pediatric (<1 year old) open-label study
Inclusion/exclusion criteria

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Ongoing Studies:
<1 Year Old Pediatric Study

Key Inclusion Criteria

- Birth to <1 year of age at screening
- Diagnosis of influenza confirmed by the presence of all of the following:
  - Fever ≥38ºC (tympanic temperature) at screening or within the 4 hours prior if antipyretics were taken
  - ≥1 respiratory symptom (either cough or coryza)
- ≤96 hours between onset of influenza symptoms* and screening

Key Exclusion Criteria

- Hospitalization for complication of influenza or significant comorbidities
- Concurrent infections requiring systemic antiviral therapy at screening
- Preterm neonates (born at <37 weeks gestation) or weighing <2.5 kg
- Previous treatment with peramivir, laninamivir, oseltamivir, zanamivir, or amantadine within 2 weeks before screening
- Immunization with live/attenuated influenza vaccine during the 2 weeks before screening
- Concomitant treatment with steroids or other immunosuppressant therapy

*Onset of symptoms defined as the time when body temperature first exceeded 37.5ºC if known, or the time when the first symptom was noticed by the parent or caregiver

References: 1. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT03653364. Accessed August 11, 2020