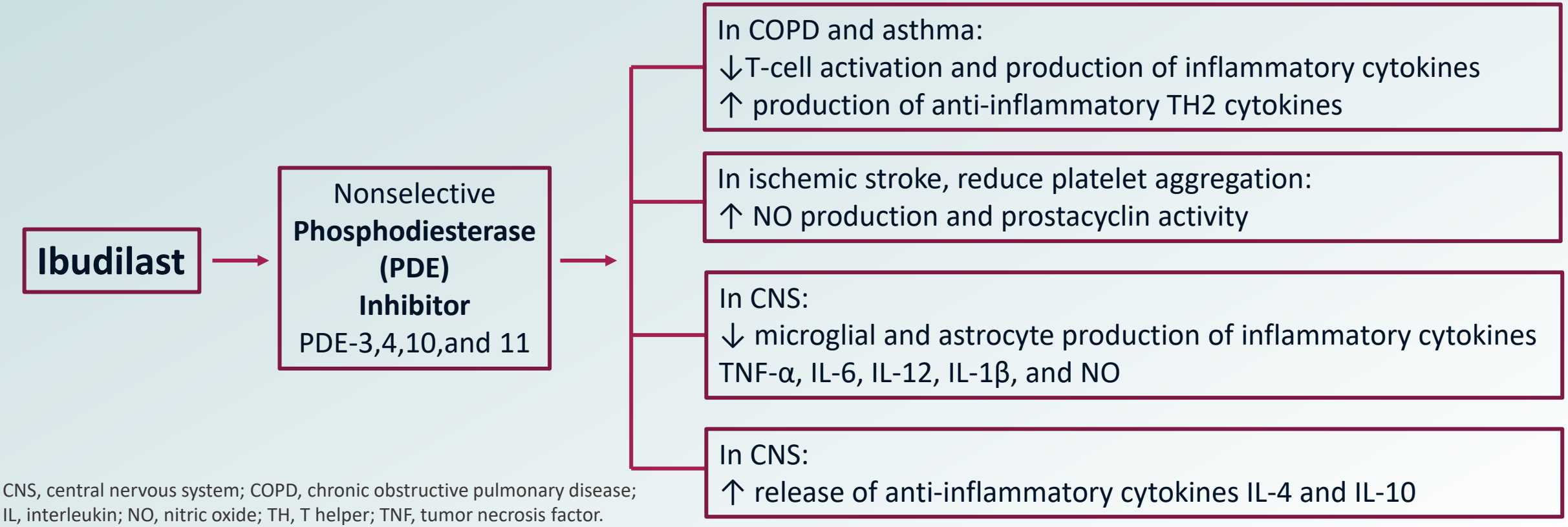
# Ibudilast Mechanisms of Action

- Ibudilast is currently being studied in a variety of neurologic conditions
- Anti-inflammatory, immunomodulatory, and neuroprotective effects

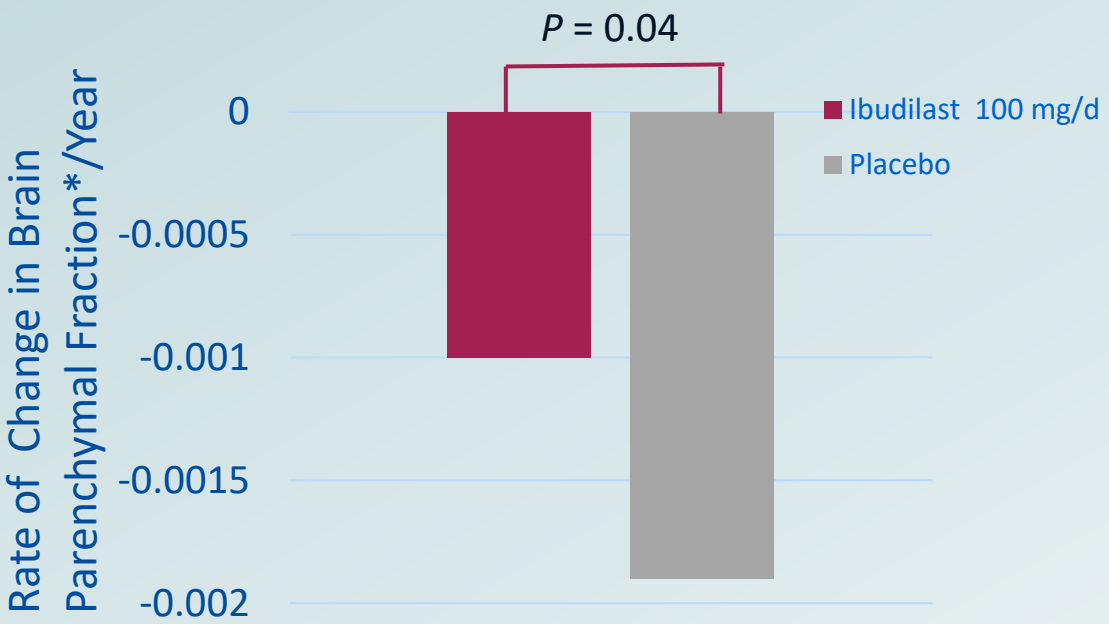



CNS, central nervous system; COPD, chronic obstructive pulmonary disease; IL, interleukin; NO, nitric oxide; TH, T helper; TNF, tumor necrosis factor.

Goodman AD et al. *Expert Opin Investig Drugs*. 2016;25:1231-1237.

# Ibudilast in 96-week Phase 2 Trial of PPMS and SPMS

## Primary Endpoint: Brain Atrophy[1]




Patients had option to take glatiramer acetate or β-interferon.
31% of ibudilast group and 32% of placebo group taking DMT at baseline.

## Other MRI Endpoints[2]

| Endpoints | Ibudilast | Placebo | *P* value |
|---|---|---|---|
| Individuals with new/enlarging T1 lesions | 33.3% | 23.5% | 0.11 |
| Individuals with new/enlarging T2 lesions | 37.2% | 29.0% | 0.82 |
| Gray matter reduction (mean change from baseline) | -0.09% | -0.14% | 0.04 |

*Brain parenchymal fraction is brain size relative to volume of outer surface contour of brain
DMT, disease-modifying therapy; PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.
1. Fox RJ et al. *N Engl J Med.* 2018;379:846-855; 2. Naismith RT. *Neurology*. 2021;96:e491-e500.

# Ibudilast Efficacy Primarily in PPMS Subpopulation

- Population of phase 2 trial of ibudilast: 134 PPMS and 121 SPMS[1]
  - SPMS included active and nonactive (no relapse in prior 3 months)[2]

| Endpoints[1] | PPMS | | | SPMS | | |
|---|---|---|---|---|---|---|
| | Ibudilast | Placebo | *P* value | Ibudilast | Placebo | *P* value |
| Annualized rate of change in BPF | -0.0009% | -0.0025% | <0.01 | -0.00106% | -0.00108% | 0.97 |
| Annualized rate of change in BPF, adjusted for differences in baseline characteristics | -0.0008% | -0.0024% | <0.01 | -0.00112% | -0.00115% | 0.95 |

Low level of brain atrophy in SPMS placebo group contributed to lack of perceived efficacy in SPMS population[1]

BPF, brain parenchymal fraction (measure of brain size); PPMS, primary progressive multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

1. Goodwin AD et al. *Ann Clin Transl Neurol*. 2021;8:111-118; 2. Fox RJ et al. *N Engl J Med*. 2018;379:846-855.

# Safety Analysis for Ibudilast in Phase 2 Trial of Progressive MS

- Serious adverse events, infections, and discontinuations – no significant between-group differences
- Adverse events that occurred more frequently in ibudilast group ($P \leq 0.1$)
  - Depression
  - Gastrointestinal symptoms (nausea, diarrhea, abdominal pain, vomiting)
  - Headache frequency

Fox RJ et al. *N Engl J Med*. 2018;379:846-855.