Evolution of Nonclinical Safety Post COVID-19: A Pharma Product Development Perspective

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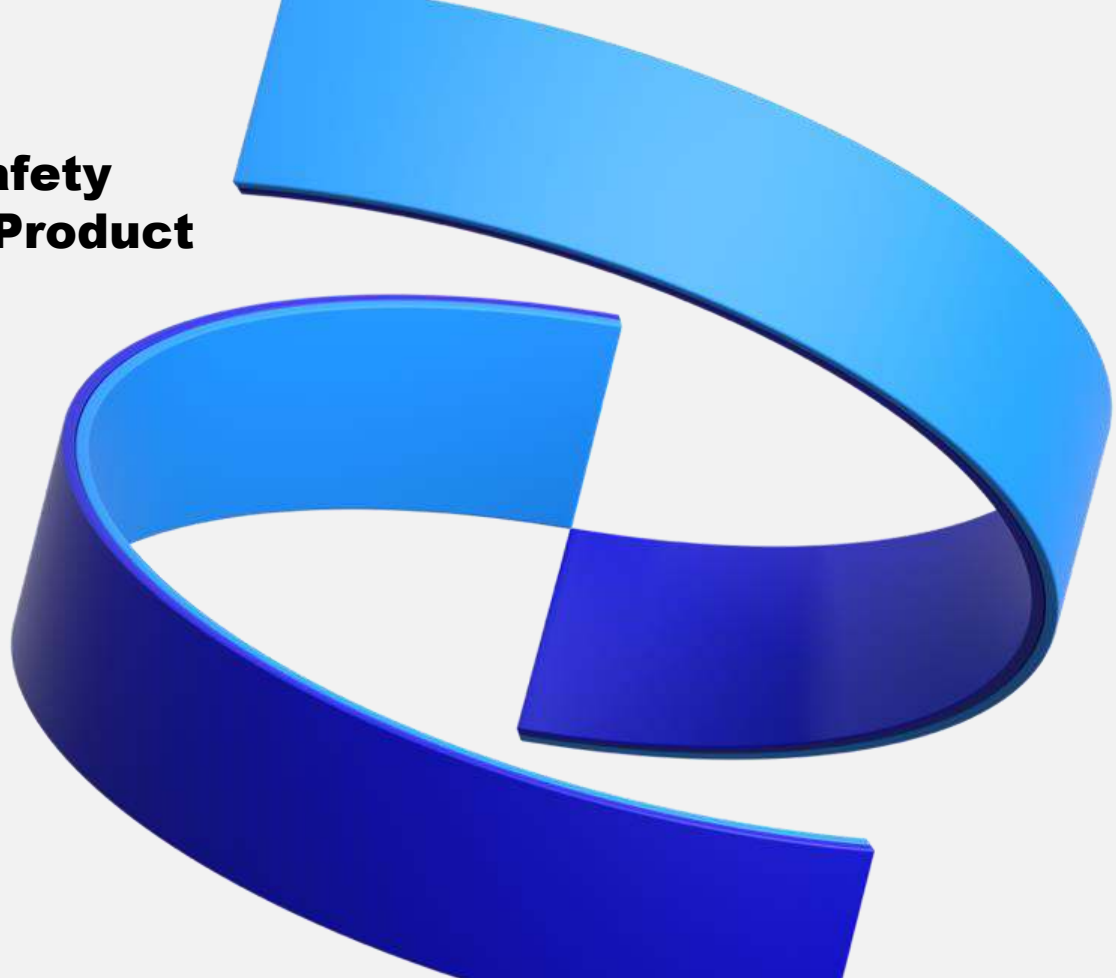

Outline

- **COVID-19 as a Severely-Debilitating or Life-Threatening (SDLT) disease**
- **The Pfizer COVID-19 IV therapeutic experience**
  - What was different?
  - What remained the same?
- **Potential positive post-COVID evolutionary steps**

SDLT

Conditions in which life expectancy is short or quality of life is greatly diminished despite available therapies

FDA's SDLT definition:

Life threatening diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the endpoint of clinical trial analysis is survival

Severely debilitating diseases or conditions that cause major irreversible morbidity

Major unmet medical need with high global socioeconomic healthcare costs

COVID-19 as a case example of SDLT

COVID-19, especially in its severe form, can be characterized as an SDLT indication based on the life-threating nature of the disease and while long-term consequences require further study, possibility of irreversible morbidity particularly affecting pulmonary, cardiovascular, and central nervous systems

The Pfizer COVID-19 IV therapeutic experience

Existing continuous IV infusion compound from the 2003 SARS COV1 epidemic

Limited nonclinical safety data
Limited solubility

Rapidly developed an analog that improved solubility/exposure

Moved forward to Phase 1 clinical studies in hospitalized COVID patients with single dose 24 hr infusion single species data + limited Safety Pharmacology + in vitro studies

Differences from standard:

Close coordination with the FDA and rapid information interchanges
Single species, single dose data to move directly into hospitalized patients

What remained the same:

Patient/subject safety was paramount
Clinical study in normal volunteers required standard nonclinical support package

Potential positive post-COVID evolutionary steps

Rapid exchange of information with Health Authorities

Agreement on sufficient nonclinical packages needed to safely get potential SDLT therapies to patients

Upfront agreement on what nonclinical support is needed for EUA/Conditional Marketing Approval vs NDA/full MAA

Global Guidance for Non-Oncology SDLT Therapeutics

Rationale: medical context of SDLTs is comparable to advanced cancer and COVID 19, therefore a similar streamlined development approach should apply

Although there are regional regulatory guidances for rare diseases, SDLT hematologic disorders, COVID-19, etc., and regulatory programs to expedite late-stage clinical development/regulatory approval, there is minimal (and no global) guidance for non-oncology SDLT disease therapeutics across therapeutic areas

A global SDLT guidance will facilitate patient access to SDLT pharmaceuticals and enable global alignment across regulatory agencies