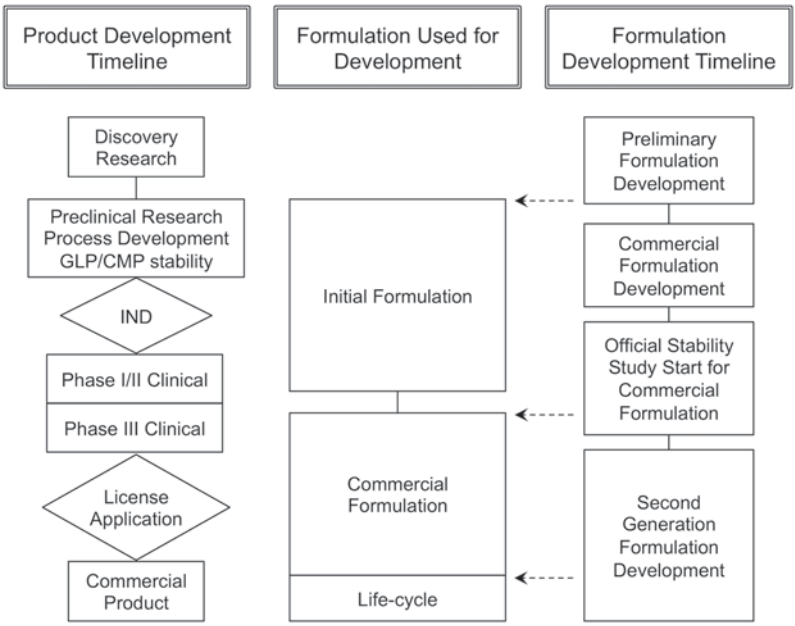

Fig. 1 Formulation strategy for phases of biopharmaceutical development and introduction

Frozen Liquid Formulation

For products with a reasonably well-defined stability in solution and good solubility at the anticipated dose, a frozen formulation can be a cost-effective way to accelerate the timeline and provide a good candidate for an initial preclinical and/or clinical formulation. As the rates of most degradation reactions decrease with decreasing storage temperature, frozen storage is often effective in maintaining product integrity over a short storage duration. Fortunately, freezers with suitable temperature control are available at most research facilities, doctors' offices, and hospitals. Additionally, there are warehouses and transportation options that can accommodate frozen products and reliable temperature control.

Overall, a frozen formulation is considered a relatively safe and effective way to introduce the initial formulation. Once its long-term real-time stability in a liquid state is demonstrated, the same formulation can be commercialized without further changes. However, simply freezing a liquid formulation does not necessarily improve the stability of a formulation. Freezing can accompany various undesirable environmental changes, such as shifts in localized concentration, crystallization of excipients, shifts in pH, phase separation of potential stabilizers, etc. It is important to note that certain excipients are prone to these undesirable changes during