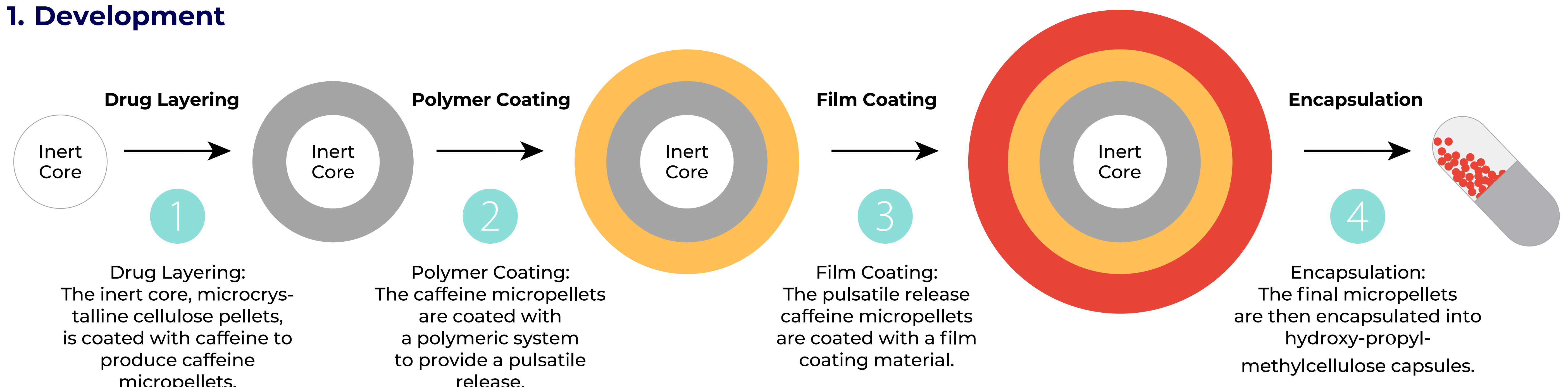


# InventaSpheres®

We developed a pulsatile-release (caffeine) formulation, which is administered before sleep, but releases only insignificant amounts of caffeine during sleep and provides adequate caffeine blood plasma levels before the planned awakening time. Our Multi-Unit Pellet System Formulations (MUPS) offers several advantages over traditional systems, including predictable *in vivo* release, reduced dose dumping, and minimized fluctuations in plasma concentration. Our technology thus provides opportunities to develop a more reliable formulation than with single unit formulations while minimizing the alteration in drug release profiles and formulation behaviour due to unit-to-unit variation, change in gastrointestinal pH and enzyme compositions.

Our formulation does not significantly release caffeine in the initial parts of the gastrointestinal tract while passing through it and being exposed to different pH values varying from strongly acidic in the stomach to slightly basic in the colon. Once the formulation passes to the further parts of the gastrointestinal tract (neutral-to-basic) the release-controlling polymeric system immediately dissolves to provide a rapid release of the caffeine.

## 1. Development



## 3. In Vivo Characterization

### A: Pharmacokinetic Study

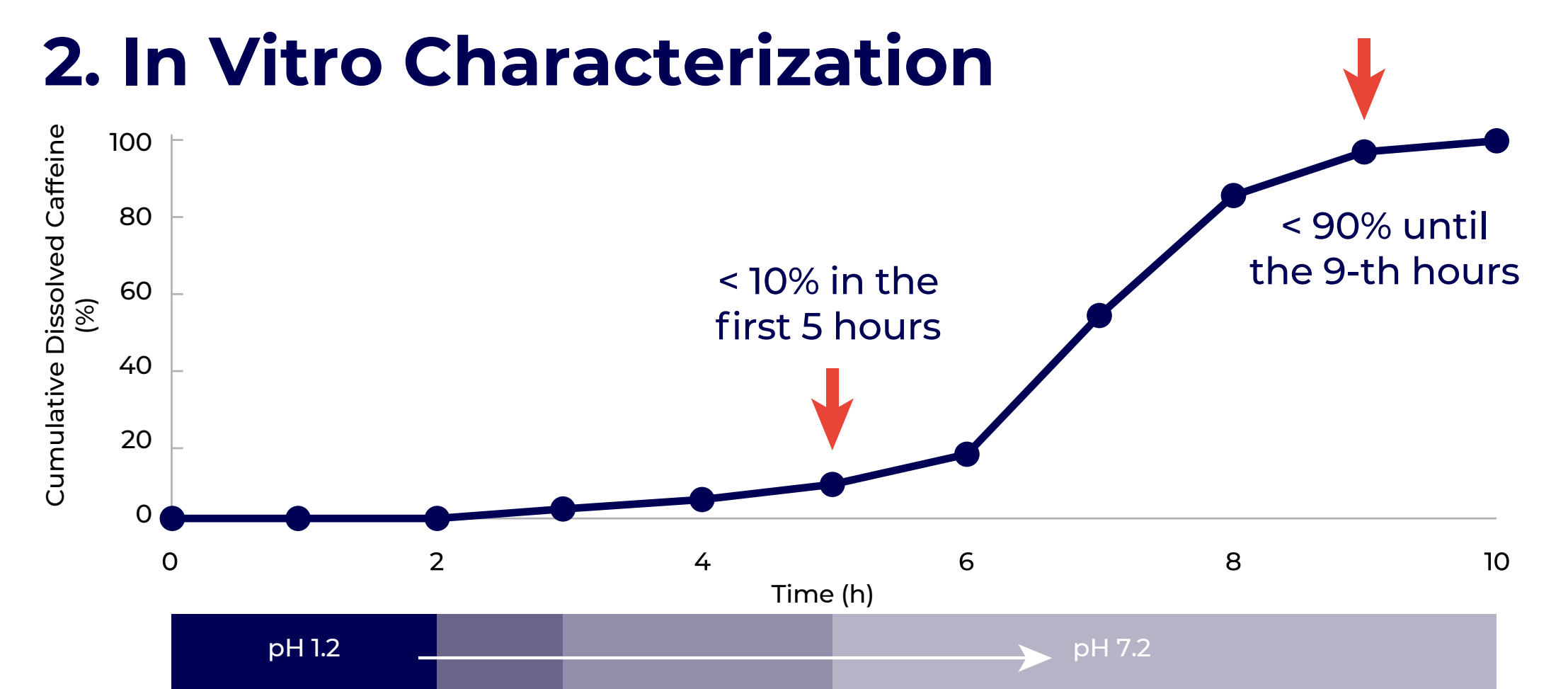
The *in vivo* caffeine release profile was determined in 10 volunteers

A total of 32 healthy young men (mean age:  $25.6 \pm 3.7$  years)

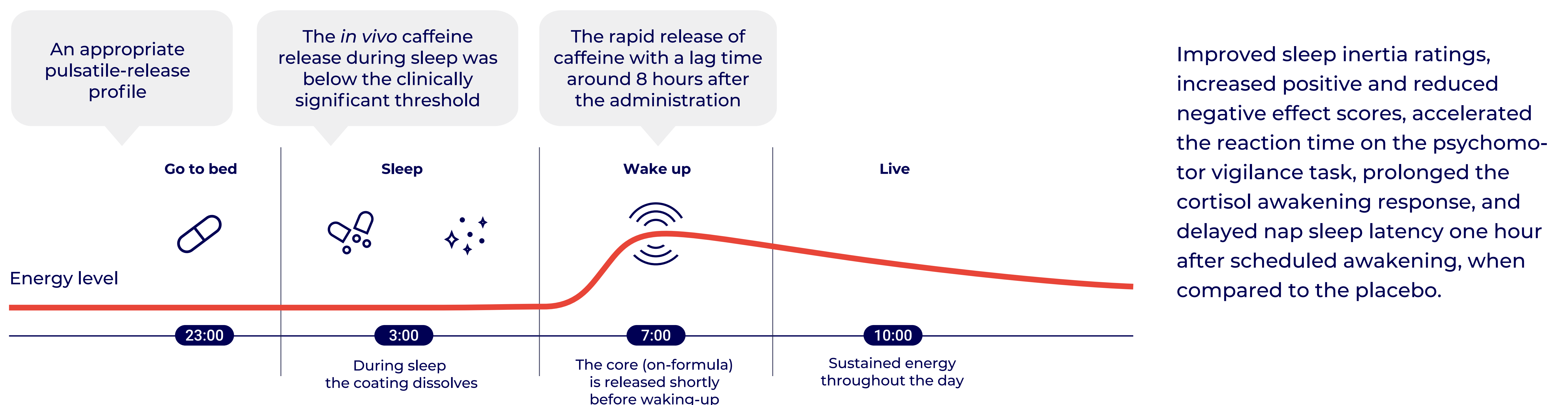
### B: Pharmacodynamic Study

**placebo-controlled, double blind,** cross-over fashion the formulation's ability to improve sleep inertia in 22 sleep-restricted volunteers

## 2. In Vitro Characterization



## 4. Product (B-Sync ON)



## Future Indications

### Technology benefits are best when targeting

- Specific time points
- Colon release
- During sleep treatment

### For indications such as

- Early morning joint stiffness
- Early morning pain
- Morning depression
- Circadian rhythm disorders

### To increase patient convenience and timing options of drug intake