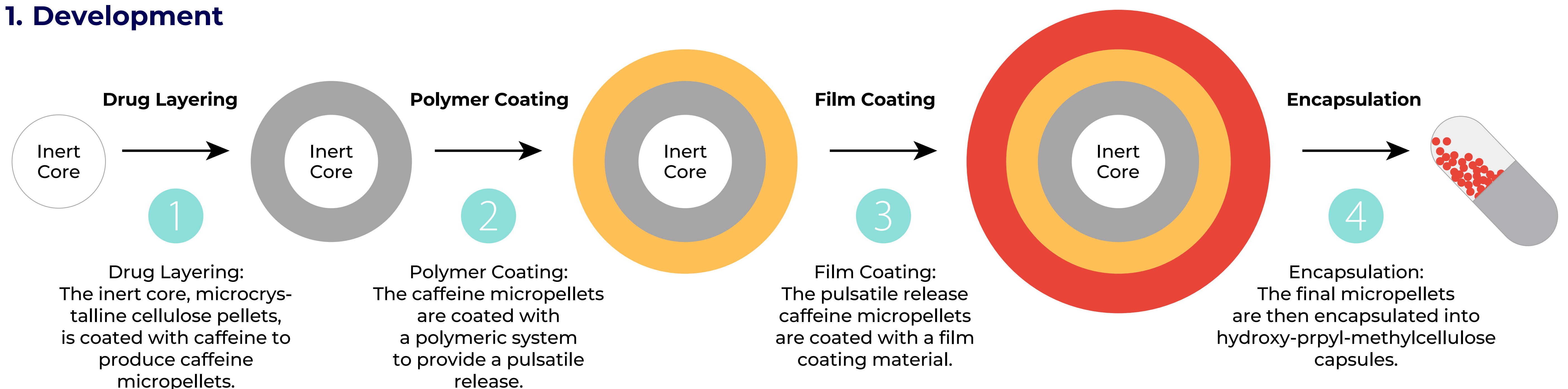


Micropellets Delayed Release

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) offer 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 its active ingredient 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 active ingredient (in our case caffeine).

1. Development



3. In Vivo Characterization

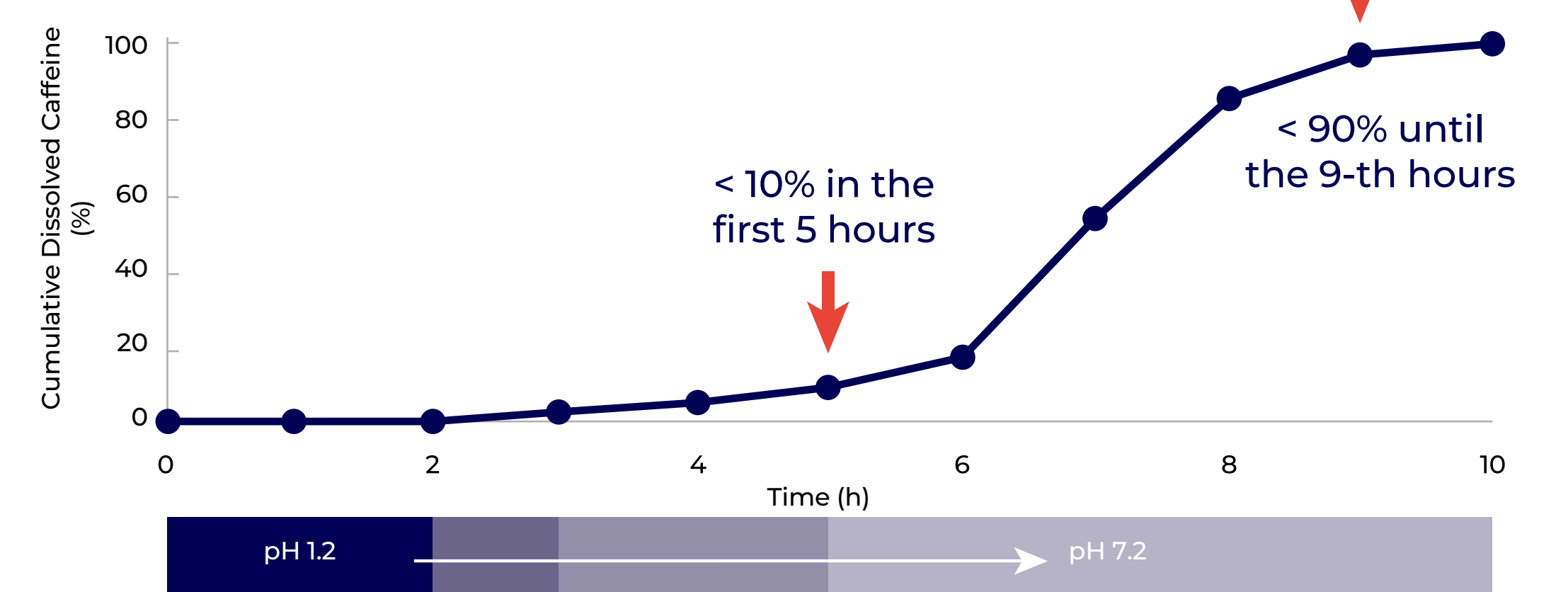
- Improved sleep inertia ratings,
- increased positive and reduced negative effect scores
- accelerated reaction times on the psychomotor vigilance task
- prolonged cortisol awakening response

A total of 32 healthy young men (mean age: 25.6 ± 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

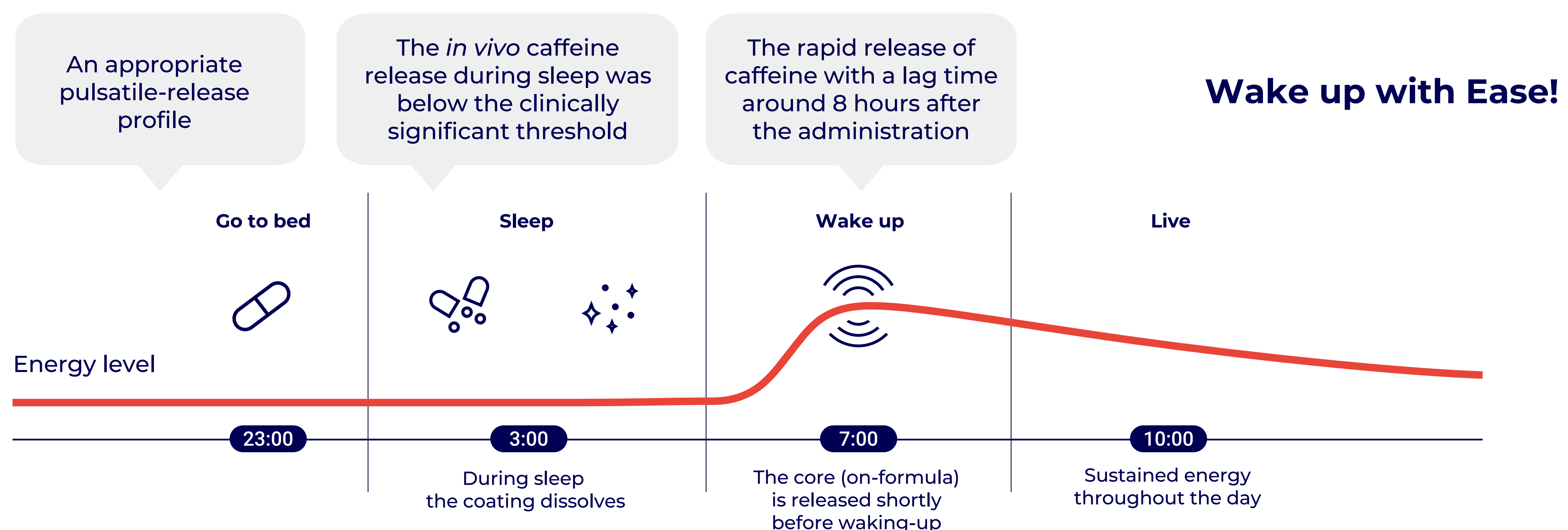
when compared to the placebo.

2. In Vitro Characterization



For simulating gastrointestinal tract conditions, the *in vitro* release studies were carried out in the media with a pH transition from 1.2 to 7.2 in a 10-hour period.

4. Product (B-Sync ON)



Future Indications for the Technology

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