Figure 1: Malaria liver-stage biology and assays to identify compounds to kill it

**HUMAN LIVER STAGE**

- **1 HOUR**
  - Sporozoite
  - Hepatocyte

- **5-7 DAYS**
  - Schizont
  - Nucleus

- **≥ 8 DAYS**
  - Merozoite
  - Erythrocyte (reticulocytes in the case of P. vivax)

**HUMAN BLOOD STAGE**

**TRANSMISSION TO MAN**

**INFECTED BLOOD**

**Number of parasites by lifecycle stage:**

- ≈ 10-100 sporozoites injected in blood stream following a mosquito bite
- ≈ 10-100 liver schizonts
- Number of liver hypnozoites unknown
- ≈ 10,000 to 50,000 merozoites per schizont

**In vitro liver stage assay:**

Hepatocytes infected with sporozoites are incubated with a compound for 1-5 days. The viability of the parasite developing into schizonts and/or hypnozoites is then assessed.

**In vivo relapse assay:**

Patients/subjects infected with P. vivax, P. ovale or P. cynomolgi malaria are treated with a blood-stage agent together with an experimental anti-relapse agent. Parasitemia in the patients’/subjects’ blood is then monitored over time to determine whether hypnozoites (I) remain and reanimate.

Hypnozoite

The hypnozoite is a dormant liver-stage form of P. vivax, P. ovale or P. cynomolgi that can reanimate leading to schizont formation and the symptoms of malaria in the absence of an infectious mosquito bite. This can occur at any time between 3 weeks and several years following the initial infection.