

## Hard-Shelled Liposomes - HSL: A unique way to target and control the delivery of drugs

### Company Highlights

Acthera Therapeutics is a preclinical-stage biopharmaceutical company. It develops hard-shelled liposomes, a nanoparticle-based technology for the targeted and controlled delivery of drugs by introducing a disruptive biophysical trigger mechanism as a powerful principle to significantly improve both efficacy and safety of many therapeutic molecules in all major disease areas.

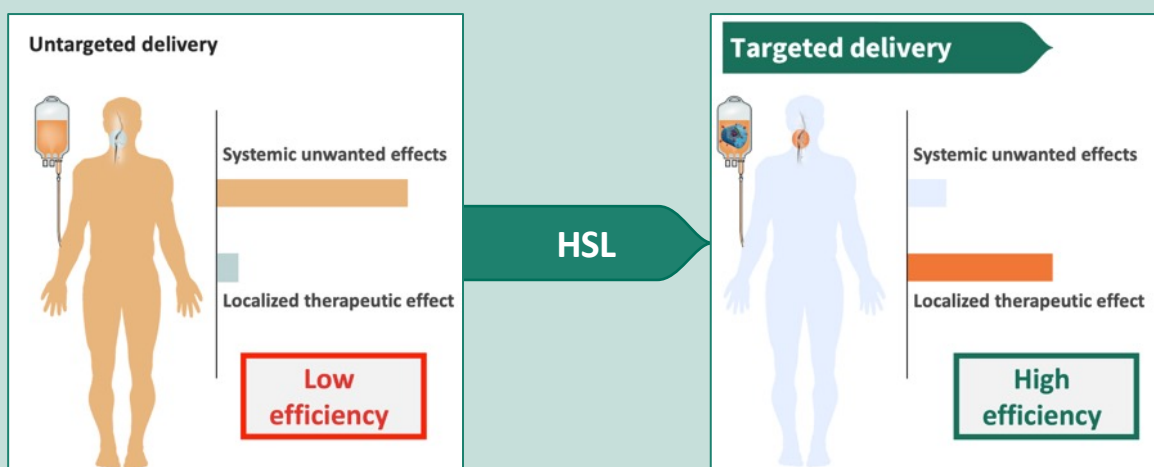
**Leadership is a team** of senior biotech professionals and three former professors.

**Top results:** In animals, Acthera proved that the pharmacological effect could be maintained with a targeted delivery through hard-shelled liposomes (HSL) with only 1/3 of the usual dose of an approved drug.

### Drug Adverse Reactions vs. Efficacy

All things are poison, and nothing is without poison; only the dose makes a thing not a poison (Paracelsus).” The cost of efficacy of most therapeutic drugs are various ranges of unwanted Adverse Drug Reactions (ADR) – ADRs are even presumed to be a major global cause of death and chronic health burden. Very often, only a small portion of the therapeutic molecules reach their pharmacological target, while the bigger portion will end up in off-target organs and cells. This is a reason why many drugs can only be administered either to a limited patient population or at less effective doses which severely limits their benefit potential. An unfavourable balance between intended therapeutic and unwanted side effects is eventually the main reason why most therapeutic molecules fail in research and development. Any major improvement of this would be a paradigm shift for the multiple drugs with a narrow therapeutic index.

**45 % of oncology patients suffer from severe drug toxicities**  
**5 % of hospital admissions are related to adverse drugs reactions**



### Controlled, Targeted Release and Delivery

The holy grail of pharmacology is to take control of the biodistribution of therapeutic molecules and deliver them exactly and only to their target organs and/or cells and thus to massively improve their therapeutic index. Acthera's Hard-Shelled Liposomes (HSLs) are unique in responding to physical pressure and release their payload when submitted to mechanical stress, generated internally by the pathological shear stress associated with an acute thrombosis, or externally by ordinary ultrasound or sub-toxic pulsed laser. HSLs are well and positively differentiated against other nanocarriers.

## Release Triggers and Payload Categories

### Trigger

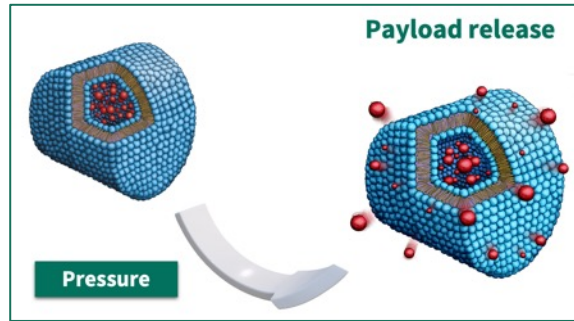
Shear stress



Laser

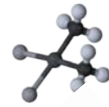


Ultrasound



### Payloads

Small Molecules



Biologics/  
Peptides



RNA



#### Preclinical evidence:

Shear Stress: Animal Proof-of-Concept for acute carotid thrombosis  
 Laser: Animal Proof-of-Method (rapid targeted release)  
 Ultrasound: in-vitro Proof-of-Concept of encapsulation and release.

## HSL Disease Areas and Indications

HSL technology is a versatile and adaptive platform, to be used in all disease areas and indications where higher local concentrations and significantly reduced systemic overall exposure of drugs will massively improve their therapeutic index. Strong rationale for early partnering/co-development for the improvement of both investigational and approved drugs.

### Cardiovascular diseases\*

Acute ischemic stroke

Acute myocardial infarction

Acute thromboembolic disease

### Oncology\*

Solid tumors

(Lymphoma)

\* focus areas

### Other

Rare diseases (non-discl.)  
 Vaccines

## Major Achievements & Milestones

- in-vivo **proof-of-concept** with a prototypical payload, Eptifibatide® (a marketed antiplatelet drug with potentially severe side effects), in rat carotid thrombosis, with a reduction of 2/3 of the efficacious dose
- in vitro validation of **encapsulation and release** of >12 molecules, incl. all important payload modalities
- bench and in-vivo development and validation of **external triggers**
- **low immunogenicity** in vitro in human whole blood and in vivo in pigs
- good **tolerability** (Maximum Tolerated Dose, Dose Range Finding) in rats
- **manufacturing process** established, large-scale manufacturing assessed, long shelf life
- **strong advisory board** and references from senior industry opinion leaders

## Investment Opportunity

ACTHERA is owned by its founders, a professional biotech investor and some business angels. It is currently raising a Seed-B funding round of CHF 3 M. Estimated total capital need until end of **phase 1** of lead asset and completed **pre-clinical development** for the follow-up asset by 2025: CHF 20M (via equity and/or non-dilutive sources from grants and partnering).

**2019**  
year of  
incorporation



**7**  
PhDs, MDs and  
biotech experts  
Recognized advisors



**2 Patents**  
For composition  
of matter filed in 2018 (in  
nationalization phase)



**CHF 6.4 M**  
Capital raised  
to date  
(incl. 1 M non-dilutive)



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