

Additional studies performed for establishing similarity

- Peptide mapping
- Biological activity
- N-terminal sequencing
- Isoelectric focusing
- Mass spectrometry
- SEC HPLC

Proposal: AVVA Pharmaceuticals is seeking partners to license its developed API manufacturing technology recombinant Liraglutide. This technology encompasses many improvements vs the originator for the production of a cost competitive medicine. Technical support could be provided for the FDF stage.

License Conditions

License Conditions

Exclusive rights within the Territory

Patent validity within the Territory

License Fee:

- Territory based

Milestone Payments:

- Upon signature
- On Dossier disclosure
- Upon successful tech transfer completion
- Upon M.A.

Tech Transfer expenses:

- Covered by the licensee

Time to market:

- Within 5 years post successful tech transfer

Royalties:

- For 15 years post commercialization

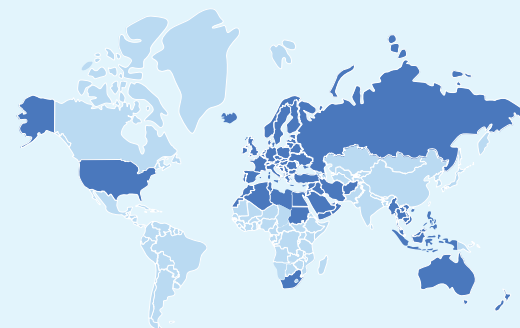


About the Company

AVVA Pharmaceuticals Ltd is a European based pharmaceutical company, aiming on becoming a reference innovation hub for the development of biological medicines and new small molecules, with ultimate goal on providing a meaningful and affordable healthcare.

Presence:

- AVVA's reach through owned companies, subsidiaries and partners extends around the globe, over 40 countries.
- Dossier available for all major regulated markets.



AVVA Pharmaceuticals Ltd
23A Spyrou Kyprianou, 4001 Mesa Geitonia, Limassol, Cyprus

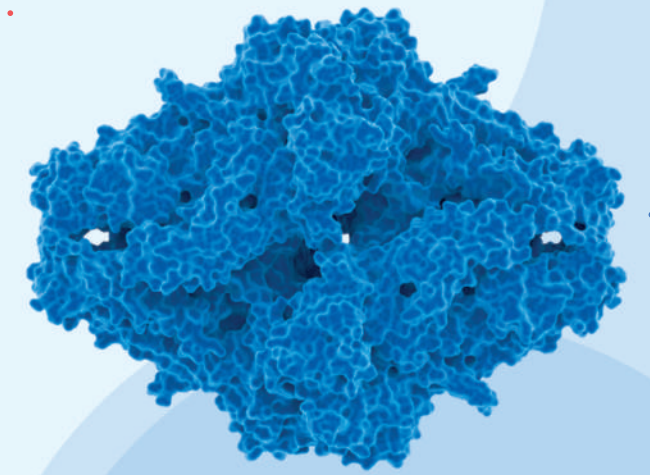
T: +357 25 572 200
F: +357 25 572 201

E: info@avvapharma.com
E: a.n@avvapharma.com



Liraglutide API Technology

Partnering / Licensing Opportunity



DMF (ASMF) is ready including modules:

- 3.2.S.1 - GENERAL INFORMATION
- 3.2.S.2 - MANUFACTURE
- 3.2.S.3 - CHARACTERISATION
- 3.2.S.4 - CONTROL OF DRUG SUBSTANCE
- 3.2.S.5 - REFERENCE STANDARDS OR MATERIALS
- 3.2.S.6 - CONTAINER CLOSURE SYSTEM

Liraglutide

Indications:

- As monotherapy or in combinations with other medicinal products for the treatment of type 2 diabetes weight management
- Weight management

Liraglutide:

- Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist also known as incretin mimetic
- 97% similarity with human glucagon-like peptide-1
- By binding to GLP-1 receptors, Liraglutide stimulates insulin secretion
- Liraglutide inhibits glucagon production, inhibits gastric motility and stimulates the hypothalamic satiety center
- Solution for injection in multi-dose disposable pre-filled pen (subcutaneous administration)
- Originator - Victoza by Novo Nordisk
- Off-patent



Key Facts

21,7 mln

Liraglutide packs were sold in 2021 worldwide*

*MIDAS Data by IQVIA

6,1 bln

Total market in 2021 6,1 Bln USD*

*MIDAS Data by IQVIA

2009

MA in Europe

2010

MA in USA



AVVA's Technology

AVVA's Liraglutide API Technology was developed in cooperation between AVVA Pharmaceuticals Ltd (Cyprus), and the Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry (Russia).

Know-how and patent protected IP rights:

- Recombinant plasmid DNA for fusion protein expression
- E. coli strain
- Recombinant fusion protein production method
- Liraglutide production method

Main Technology Features:

- **Specific Kanamycin – resistant E.coli:**
 - Reduced contamination risk
 - Does not require dedicated production
- Increased protein yield: result of producing strain genetic construct
- Reduced fermentation cycle
- Scalable technology
- Specific impurities lower detection limits
- Optimized purification process

AVVA's Technology Advantages and Completed Milestones

Nº	Characterization	AVVA	NOVO Nordisk	AVVA's Advantage
1	Strain-based technology	E. coli	S.cerevisiae	More robust technology, less lower possibility of target protein degradation
2	Reduced fermentation cycle	~8 hours	~5 days	Faster production cycle
3	Process nutrient demand	less	more	Cost effective
4	Target protein yield	up to 5.3 g/l	-	Generally higher than S.cerevisie-based technology
5	Impurity profile	1 identified impurities*	4 identified impurities*	Higher purity product

*based on HPLC analysis

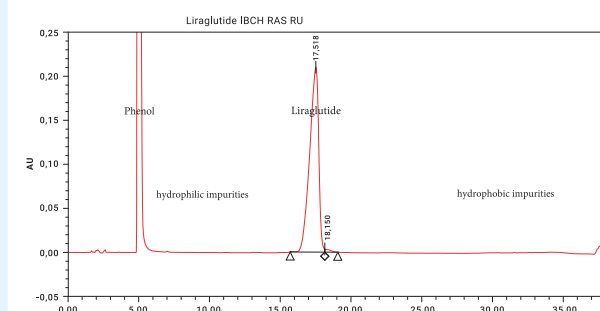
Completed Milestones:

- Specific E. coli strain creation
- Master bank and Working bank are ready
- Similarity to originator
- Analytical method development
- Manufacturing:
 - 25 Pilot batches: 20 L reactor with fusion protein yield up to 3.7 g / l
 - 5 Scale up batches: 100 L reactor with fusion protein yield up to 5.3 g / l

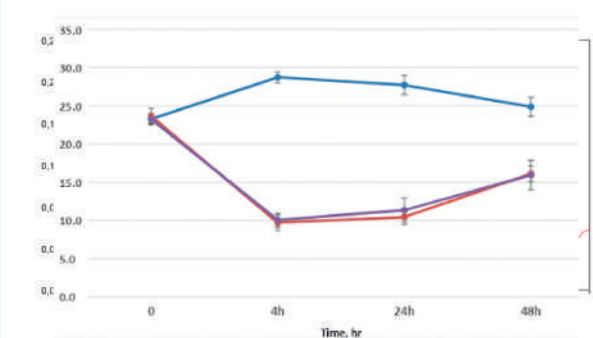
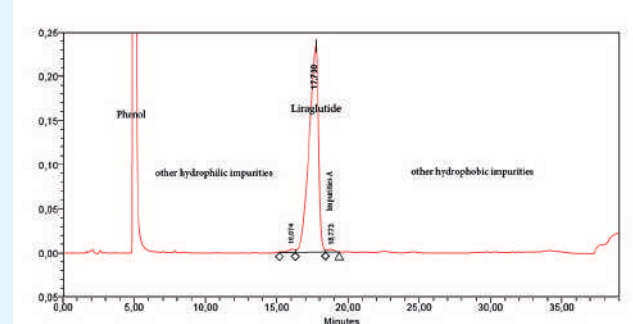
Established Similarity

AVVA's Liraglutide VS Victoza

AVVA's Liraglutide



Victoza



Pre-Clinical Study in db/db mice

Victoza (300 µg/kg) and AVVA's Liraglutide (300 µg/kg) show similar decrease on blood glucose levels at 4, 24 and 48 hours after administration, p> 0.9*

*data analysis by LSD test

- Victoza 300 µg/kg
- Liraglutide AVVA 300 µg/kg
- Control group