

### 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

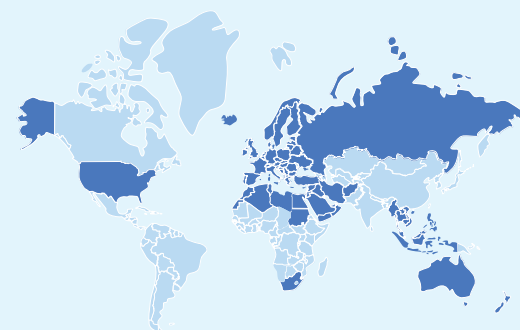


## About the Company

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  
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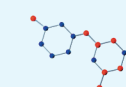
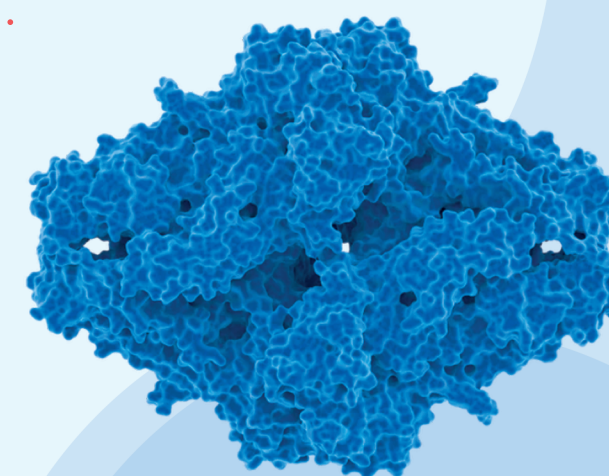
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# Liraglutide API Technology

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.cerevisiae-based technology
5	Impurity profile	1 identified impurities*	4 identified impurities*	Higher purity product

\*based on HPLC analysis

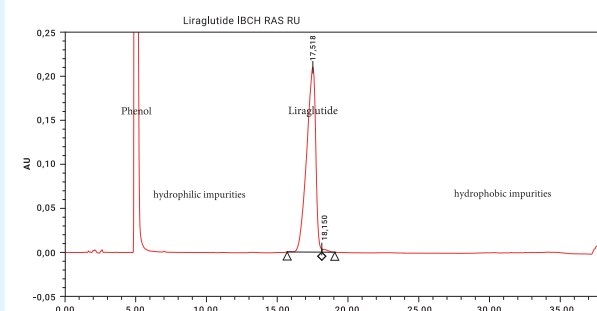
### Completed Milestones:

- 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

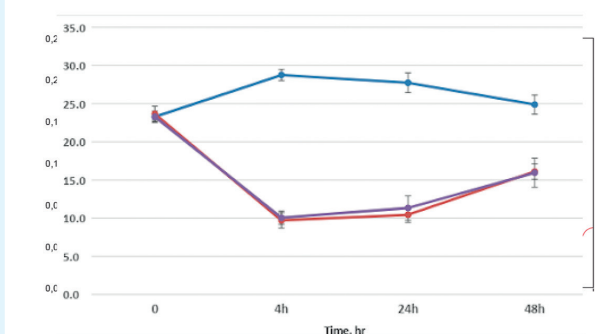
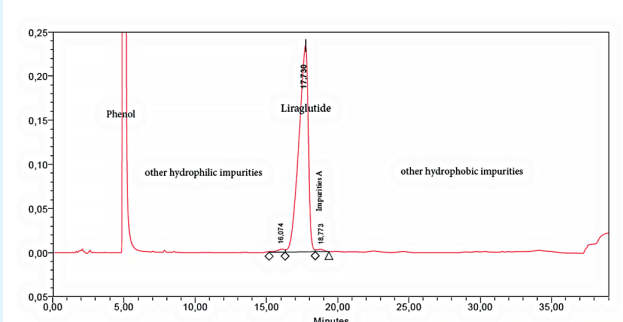
## Established Similarity

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