VIVEbiotech S.L.

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Location: The facility is located in San Sebastian, Spain
Address: EDIFICIO TANDEM Miramon Pasealekua 170, 1st floor – Donostia/San Sebastián 20014 SPAIN
In the same facility development, manufacture and analytical characterization take place.

Manufacturing facilities footprint & capacity:
The facility has a surface of 32292 square-feet (+3000 sqm), fully LVV dedicated, in which development and manufacture is carried out from R&D to GMP being able to cover up to commercial stages.
The facility is GMP certified, counts on 7 cleanrooms, being one of the biggest globally in terms of LVV manufacturing capacity, in house automatic Fill&Finish, intermediate bioreactors sizes from 4.8 sqm to 200sqm. Please note that "sqm" refers to the surface in which the cells are grown and the technology is defined as "high capacity" technology.
Importantly, all the batches in reactors, R&D, engineering and GMP, are produced in class C cleanrooms employing VIVEbiotech's Plug&Play platform.
The current facility has a capacity of +40 batches in reactors per year (R&D, engineering or GMP) guaranteeing high flexibility and good slots availability in a timely manner.

Modalities/tech platforms supported:
Since 2015, VIVEbiotech has been developing and has implemented a Plug&Play platform for LVV manufacture, which has been used for the manufacture of +150 batches in reactors. The platform is fully integrated and includes manufacturing (Upstream, Downstream and Fill&Finish), analytical characterization and regulatory support until release. The platform has been optimized to provide a LVV product with good titers and purity. The same platform is used for manufacture of R&D batches in reactors, engineering and GMP runs.
VIVEbiotech's Plug&Play platform has shown the following characteristics:

- Increased productivity obtaining highly functional vectors
- Higher recovery and purer vectors: Reaching purity levels adequate for ex vivo and in vivo
- Low complexity/footprint/integration of processes into one including F&F: Industrial system to commercial scales

- Scalable and reproducible process offering a wide range of scales: Adequate for the different therapies and developmental phases guaranteeing scalability between Hydro (2.4, 4.8 and 9.6 sqm), Carbo (10 and 30 sqm) and Nitro (200 sqm) reactors
- In a timely manner / Rapid transfer to reactor
- Versatility for all the vectors: Ex vivo & In vivo, different generations, integrating and non-integrating, different pseudotypes
- Regulatory compliant: along EMA and FDA for Ex vivo and In vivo LVVs

Process & analytical development capabilities:
VIVEbiotech's team has a strong knowledge and expertise in virology and bioprocessing being worldwide a leader in terms of capability. In the development field it is possible to identify three dedicated departments:

- The technological innovation department is working on several LVV related projects focused on the optimization of LVV constructs, pseudotyping, stable cell lines and production conditions.
- The process development department focuses on the optimization and finetuning of VIVEbiotech's Plug&Play platform, both in Upstream and Downstream, ensuring its high versatility.
- The analytical Development Department is involved in the implementation, Tech Transfer and validation of ad hoc methods, specific for each project. The team has strong experience in developing i.e. biological assays and potency assays among others. Additionally, validation of analytical methods per product required for commercial stages is also available for execution.

GMP manufacturing capabilities:
VIVEbiotech has produced GMP batches since 2017, once the first GMP authorization was granted. Since then, +40 GMP batches have been released according to EMA and FDA regulations for both ex vivo and in vivo programmes. Importantly, clinical trials using LVV produced by VIVEbiotech for both ex vivo and in vivo indications have been approved in several countries in US, Australia, Europe and Asia.
It is worth noting that the same manufacturing process in clean rooms is followed for the production of all quality of batches (R&D, engineering and GMP), thus the same platform has been used for the manufacture of +150 batches.

Analytical capabilities:
VIVEbiotech performs most of the analytical release assays in house and is continuously internalizing additional methods. Methods are fully validated for Phase I/II and can be further validated for most advanced stages until commercial. For that, the analytical development department is directly involved. Additionally, VIVEbiotech has capabilities of developing ad hoc analytical methods, such as potency assays, specifically for each project.
To complete the release analytical panel required by FDA and EMA, VIVEbiotech also

relies on a trusted GMP partner, Clean Cells, analytical leader in Europe. Clean Cells has been successfully audited and a Quality Agreement is in place between the parties. Importantly, VIVEbiotech takes full responsibility of the outsourcing activities.

Track record:
Since 2015, VIVEbiotech has been working with 46 internation customers (from US, Europe, Australia and Asia) developing more that 60 projects for different indications: 65% in cancer immune-cell therapy, 20% in rare/ultrarare diseases and 15% in in vivo programmes (8 in vivo programmes so far). Customers are mainly biotech companies (such as Zelluna Immunotherapy, Theravectys among others), together with academic institutions and big pharma (Astellas, Evotec and Galapagos among others).
The projects are at different stages, from early development phase, preclinical, clinical and soon commercial (currently working on PPQ runs as one candidate is expected to reach commercial in 2026). LVV produced so far are very diversified and VIVEbiotech counts on experience with different pseudotypes, producer cell lines, Ex vivo & In vivo, different generations, integrating and non-integrating.
Importantly VIVEbiotech's Plug&Play platform has been used for the manufacture of +150 batches in reactors, of which +40 GMP along FDA and EMA regulations. Clinical trials using LVV produced by VIVEbiotech for both ex vivo and in vivo indications have been approved in several countries in US (at least 13), Australia, Europe (at least 7) and Asia.

Facility certifications:
VIVEbiotech is GMP authorized to release LVV for ex vivo application ("production and quality control of lentiviral vectors as sterile active pharmaceutical ingredient") and in vivo application ("manufacture of investigational drug as gene therapy medical product for human use") along FDA and EMA standards.

Regulatory inspections & corrective actions:
VIVEbiotech has been inspected by EMA through the Spanish National Agency (AEMS) and was granted GMP certification for both ex vivo and in vivo LVV release.
In Summary:
θ Former facility (2015-2021): initial authorization and GMP certification – February 2017. This certificate was renewed in 2020
θ Current facility (2021 – present): initial authorization and GMP certification – December 2021. Certificate to be renewed in 2024
θ Inspection received in November 2023 to authorize major change in facility (C4 room) and new process (automatic filling in bags)
Additionally, so far VIVEbiotech has received 25 audits along FDA and EMA standards by customers.
FDA inspection will come once one product reaches commercial (expected in 2025). VIVEbiotech has already received a mock-inspection by a well-known consulting partner in view of the coming FDA inspection and a CAPA plan is being implemented.

Value proposition:
VIVEbiotech is a GMP CDMO fully specialized in LVV along FDA and EMA regulations. VIVEbiotech develops and manufactures LVV from very early stages to clinical, with capabilities up to commercial in the current facility, 32292 square-feet (+3000 sqm) fully dedicated to LVV, being one of the biggest CDMO in terms of capacity for LVV. Current capability is up to 40 GMP batches per year, with good slot allocation in a timely manner.

An integrated Plug&Play platform (including manufacturing process, characterization and Fill&Finish) is used for manufacturing in reactors independently from the quality of the product (R&D, engineering or GMP). The platform has the advantage of providing good titers and purity of LVV product and has been shown to be versatile to different LVV characteristics (different pseudotypes, cell lines, generations) and viral-like-particles.

Importantly, VIVEbiotech offers regulatory support for IND/IMPD submission and process validation for commercial stages.
VIVEbiotech collaborates with different partners, among which Xpress Biologics for plasmids manufacture (R&D, High Quality and GMP) and CleanCells for analytical characterization.

The projects and also the pricing model are milestone-based guarantying high flexibility to our customers, mainly addressing the needs of early stage projects. The high capabilities ensure to run projects smoothly in short and competitive timelines avoiding any bottleneck linked to slot availability or for example plasmids availability. Indeed, a very good relationship is maintained with the outsourcing partners in order to finetune the timelines of the activities at each site and ensure a straightforward project progression.