Miltenyi Biotec

Friedrich-Ebert-Str 68, 51429 Bergisch Gladbach, Germany
Contact: Dr. Michael Apel
Phone +49 2204 8306-4236
Fax +49 02204 8306-85197
Michael.Apel@miltenyibiotec.de

Comment to:
IMI Advanced Therapies Concept Paper Consultation, Deadline: 25 July 2016

Relevance of Miltenyi Biotec GmbH as an ATMP stakeholder

Miltenyi Biotec is one of Germany's most successful biotechnology companies with currently more than 1,500 employees worldwide and €200 million annual sales. As a major **global stakeholder** for **manufacture of ATMP** Miltenyi has developed its unique Magnetic Cell Sorting Technology (**MACS®**) that has become an established standard method in biomedical research areas like cancer research, hematology, stem cell biology or neurosciences, and furthermore in novel clinical approaches such as cellular immunotherapy, transplantation or regenerative medicine (www.miltenyibiotec.com).

The company´s **mission** is **to translate cellular therapies into clinical routine**. Accordingly, the first device in **CliniMACS® System portfolio** has been released to the market already in 1998 and since then more than 80.000 patients have been treated with cells sorted by CliniMACS systems. Notably, in 2014 the CliniMACS System obtained **approval by the U.S. Food and Drug Administration (FDA)** for a specific treatment of Acute Myeloid Leukaemia (AML). CliniMACS devices provide stable cell separation technology and the most advanced member of this product line, the **CliniMACS Prodigy®**, enables automated cell processing in a GMP-compliant, functionally closed disposable (more details below).

Comment to concept paper questions:

1. Have the **key challenges** that can be addressed through collaborative, public-private initiatives been properly identified?

Yes

2. Which of the proposed potential initiatives should be **prioritised**?

Clinical development. Most ATMP trials are presently initiated in the US due to easier access to funding and less regulatory hurdles. Remarkably, China is presently catching up. In Europe, translation of cellular therapies into clinical trials is still very complicated and time-consuming. Consequently, only few clinical investigations predominantly in niche applications have been performed in Europe so far and there is still a long way to go for broad application and spreading of standardized ATMP based therapies: Many researchers have difficulties to overcome the regulatory obstacles and to get funding for their ATMP trials. Accordingly, a significant funding for ATMP trials and a fast track for regulatory approval are urgently missing.

Pricing, reimbursement and access. As stated in the concept paper, the first cellular therapy trials are now on their way in Europe. Hence, there needs to be clarity what will happen afterwards and what the financial situation will be in order to encourage private investors.

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3. Are any areas **missing**?

The **CliniMACS Prodigy® technology**[1,2] isn't considered properly in the concept paper discussed here (under 3.3 Manufacturing). This instrument has been developed to **fully automate** and standardize the manufacturing process of cellular products. It maintains a closed system by using disposable tubing sets equipped with multiple input lines with tubing connections for use of sterile docking devices. This closed system meets the requirements of GMP-grade processing of almost any kind of cellular products and may allow reducing clean room requirements. In summary, automation by the CliniMACS Prodigy enables **upscaling of cell manufacture to large patient cohorts** and simplification of the handling processes will allow **spreading of cellular therapies** from specialized university clinics to less experienced local hospitals.

Moreover, the new **MACSQuant® Tyto™** represents another innovation for clinical cell manufacture: **microchip-based cell sorting** yields ultra-pure cell preparations within a closed microfluidic cartridge[3].

4. What are the key **European or national initiatives** that IMI shall synergise with?

Examples for H2020 key collaborative projects:
CARAT: http://carat-horizon2020.eu/
PROCROP: http://www.procrop.eu/
SCIDNET: https://scidnet.eu/

Conclusion

Miltenyi Biotec clearly is a major stakeholder in Europe providing innovative solutions for manufacture and clinical translation of ATMP.

Hence, we believe a collaboration of Miltenyi Biotec and IMI / EFPIA would create significant synergies to jointly advance translation of cellular therapies into clinical routine in Europe. In this respect and as an initial step, we would like to offer to contribute to the IMI Stakeholder Forum on 28/29.09.2016 in Brussels.

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[1] **Apel M, et al.** Integrated Clinical Scale Manufacturing System for Cellular Products Derived by Magnetic Cell Separation, Centrifugation and Cell Culture. Chemie Ingenieur Technik 2013; **85**(I-2): 103-110.

[2] **Kaiser AD,** et al. Towards a commercial process for the manufacture of genetically modified T cells for therapy. Cancer Gene Ther. 2015; **22:** 72–78.

[3] **Linton J, Oram SW**. Next-Generation Flow Sorting : Silicon Microchip Capable of High-Frequency Fluidic Valving at Heart of Technology. Genetic Engineering & Biotechnology News 2013, **33**(12): 30-31.