Health by Advanced Therapies

D 1.4
Map of European´s ecosystem and non-European network activities for advanced therapies

Public

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Table of contents

1. Deliverable's description

This deliverable aims to give a timely and realistic perspective of the current landscape in terms of facilities and installed capacity to develop, produce and use ATMPs in the clinic both in Europe and also abroad. There are currently no reliable sources of information nor official registries or even publicly accessible publications that would help in identifying this kind of facilities to compile this type of data.

The information herein collected was generated among the partners and supporters of the RESTORE project. This information may be complemented with the information regarding the ATMPs currently approved by the EMA to be used in Europe. As a consequence of this implemented method to generate the information reported in the Deliverable 1.4, the list is not exhaustive and some important facilities and capacities both in Europe and abroad may still be missing from this list.

The deliverable was accomplished successfully.

2. State of the art

The analysis of the map in Figure 1 shows 52 installations and facilities and indicates that they are distributed throughout Europe, having different stages of clustering and maturity into clinical translation. The landscape of ATMPs is very much dominated by clinical and hospital research groups and facilities, frequently located in Universities or Research Institutes. The national and regional health authorities and policy can facilitate and promote more adequate contexts for the advancement of ATMPS into the clinic in Europe. A good example is the government of Andalusia in Spain that has a strong drive to favour clinical translation of ATMPs.

The EU country listing the most facilities is Italy, with 14 entries, followed by Spain and Germany, with 7 and 5, respectively. It is notable that Ukraine lists 4 entries with a large number of patients treated with ATMPs.

Most of the facilities identify Cell Therapy or Cell and Gene Therapy (Table 1) as the main area of activity. Tissue engineering or Combination Therapy is referred to by 16 of the facilities listed.

Spain is the EU Country identifying the largest number of patients treated with ATMPs in the order of 900 patients. Ukraine refers the treatment of over 15.000

Regarding the conditions treated, there is a very large range of diseases listed. The most frequent group of diseases treated with ATMPs are oncologic (13), musculoskeletal disorders (8) and those associated with transplantation (7).

There is a large number of organizations (22) that refer being possible to develop contract research for the industry what indicates that half the facilities are prepared to team up with the industry to develop ATMPs.

Only 6 of the facilities refer to routinely using ATMPs to treat patients. This number is important since it shows that most facilities and organizations still do not have the capacity to perform treatments on a regular basis for patients.

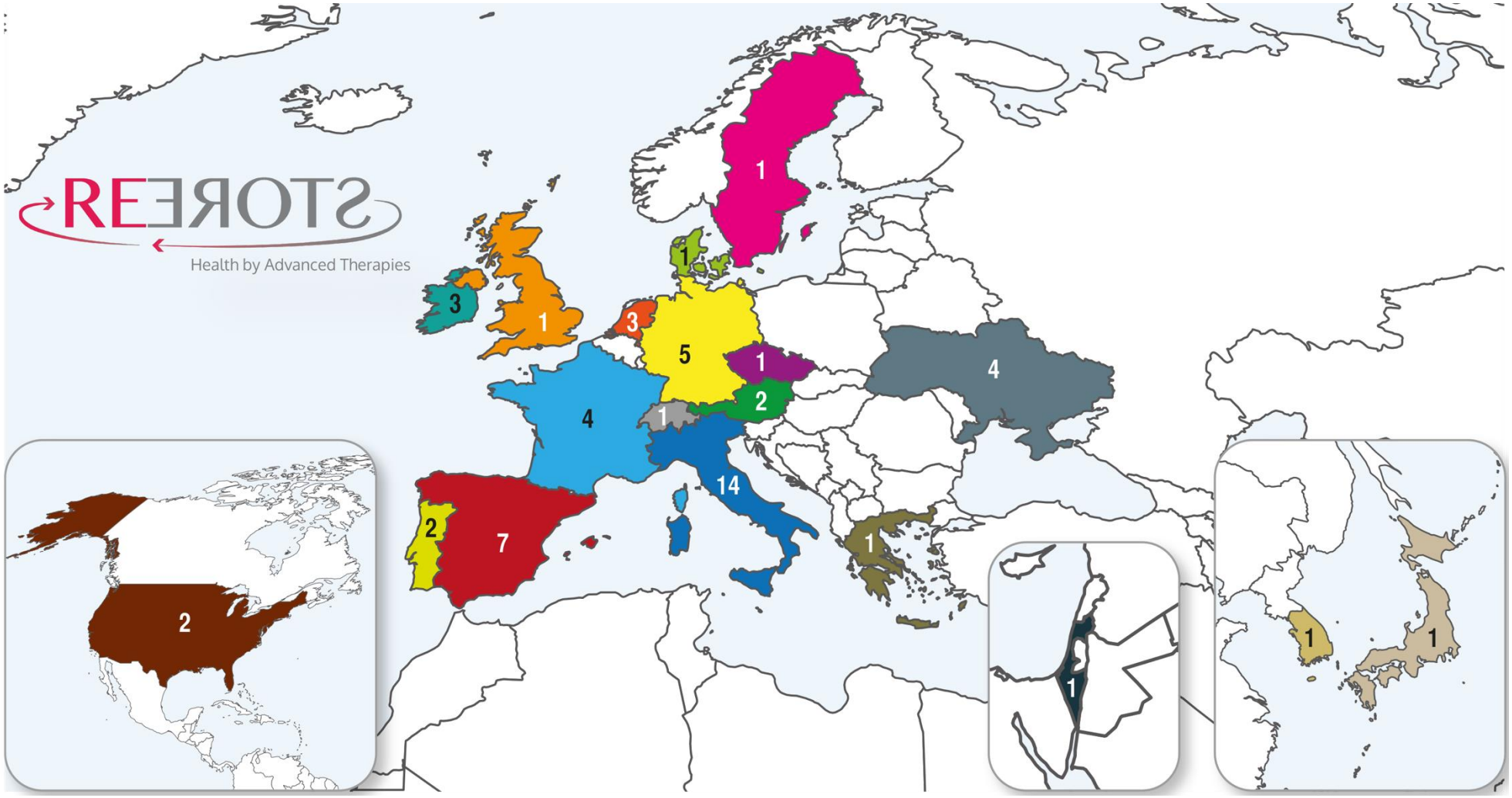
Health by Advanced Therapies
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Figure 1 – Number of facilities for the development, production and clinical application of ATMPs by country

Table 1 – List of the ATMP facilities available including, responsible person, website, clinical conditions and number of treated patients

Country Legenda	Institution	Contact person	Country	Website	Type of ATMP (Gene therapy, somatic cell therapy, tissue engineering or combined ATMP)	Number of patients treated	Diseases targeted	Other diseases in pipeline	Contract research for industry	Routine application of approved ATMP
	Austrian Cluster for Tissue Regeneration	Prof. Dr. Johannes Grillari	Austria	www.trauma.lbg.ac.at	Cell (EV) therapy, gene (miRNA) therapy/diagnostics, tissue enginering					
	Austrian Cluster for Tissue Regeneration	Prof. Dr. Heinz Redl	Austria	www.tissue-regeneration.at	TERM from molecule to clinic					
	Scimed Biotechnologies, Czechia	Dr. Nicole Matejckova	Czech Republic	www.scimed.cz	Somatic cell therapy	0	Chronic wounds, Atopic dermatitis, Psoriasis, Burn wounds		Yes	No
	National Center for Cancer Immune Therapy (CCIT-DK), Copenhagen University Hospital Herlev	Dr. Inge Marie Svane	Denmark	https://www.herlevhospital.dk/ccit-denmark/Sider/default.aspx	Somatic cell therapy	114	sarcoma, uveal melanoma, rectal cancer, oropharyngeal cancer, colon cancer, myoepithelial carcinoma, cervical	No	Yes	No
	Institut national de la santé et de la recherche médicale, Institut Cochin, Paris	Dr. Emmanuel Donnadieu	France	https://www.institutcochin.fr/	preclinical tumor models to test ATMPs	0	lung, renal carcinomas		Yes	No
	YPOSKESI	Alain Lamproye, CEO	France	https://www.yposkesi.com/	Gene Therapy				Yes	
	CTSA Jean Julliard		France	https://www.defense.gouv.fr/english/sante/notre-	Cell Therapy					
	Hospices Civils de Lyon (HCL) - Banque de Tissus et de Cellules	Pascale Pascal	France	http://www.biobanques.eu/fr/nous-	Cell Therapy					
	Translational Center Regenerative Medicine TLC-RT Würzburg	PD Dr. Oliver Pullig	Germany	https://www.regenerative-therapien.fraunhofer.de/en/fields-	Tissue Engineering	80	Degenerative cartilage defects	Osteoarthritis	Yes	No
	Translational Center Regenerative Medicine TLC-RT Würzburg	PD Dr. Oliver Pullig	Germany	https://www.regenerative-	Somatic cell therapy	0	Osteoarthritis	Degenerative cartilage defects	Yes	No
	Translational Center Regenerative Medicine TLC-RT Würzburg	PD Dr. Oliver Pullig	Germany	https://www.regenerative-	Gene therapy	0	Hemophilia A	Yes	Yes	No
	Center for Regenerative Therapies CRTD, TU Dresden, Germany	Prof. Dr. Michael Brand	Germany	www.crt-dresden.de	Cell therapy, gene editing, Models of Regeneration		GvHD	Neurodegenerative, Retina,	No	Yes
	Berlin-Brandenburger Centrum für regenerative Medizin	Dr. Michael Schmueck-Henneresse	Germany	www.b-crt.de	cell therapy, gene editing	0	GvHD	Diabetes, Neurodeg., Retina, Liver	Yes	No
	Biomedical Research Foundation, Academy of Athens	Dr. Eleni Katsantoni	Greece	www.bioacademy.gr	Omics, bioinformatics, biomarkers discovery					
	Regenerative Medicine Insitute (REMEDI), National University of Ireland Galway, Ireland	Prof Tim O'Brien, Prof Frank Barry	Ireland	http://www.nuigalway.ie/remedi/	Translational research, Cell Therapy, Phase 1/2 Clinical Trials					
	Centre for Cell Manufacturing Ireland (CCMI), National University of Ireland Galway, Ireland	Prof Tim O'Brien, Andrew Finnerty	Ireland	http://www.nuigalway.ie/stem-cells/	GMP Cell Manufacturing, Phase 1/2 Clinical Trials				Possible	
	CCMI, National University of Ireland, Galway	Andrew Finnerty	Ireland	http://www.nuigalway.ie/stem-cells/	Cell Therapy				Possible	
	Pluristem Ltd. Israel	Zami Aberman	Israel	Pluristem.com	Cell therapy	300	Critical Limb Iscemia, Muscle Injury, Bone marrow deficienecies, GvHD		No	
	Medical Genetics, Dept Medical Biotechnologies University of Siena	Pr. Alessandra Renieri	Italy		Gene therapy (gene editing)	0	CDKL5, FOXG1, IQSEC2), Parkinson (LRRK2), Pompe disease			No
	Istituto di Ricerche Farmacologiche Mario Negri	Dr Elisa R Zanier	Italy	https://www.marionegri.it/eng/home	Cell therapy	0	Traumatic brain injury, chronic neurodegenerative diseases	Spynal cor injury		
	Istituto Scientifico Romagnolo per lo studio e la Cura dei Tumori IRCCS	Dott. Massimiliano Petrini	Italy	http://www.irst.emr.it	Cell Therapy	74	Melanoma, Mesothelioma, Sarcoma, Colorectal cancer	Acute lymphoblastic leukemia	Yes	Yes
	Fondazione IRET	Prof Dr Laura Calza	Italy	https://iret-foundation.org/en/	Tissue engineering, biomarkers		Lesion and degeneration of the nervous system; Chronic skin ulcers	rare diseases	Yes	
	TransMed Research (GLP-certified CRO	Prof Dr Laura Calza	Italy	https://transmed-research.com/	Tissue engineering, biomarkers					
	Department Research, Innovation & Technology, IRCCS Istituto Ortopedico Rizzoli & University of Bologna	Prof. Nicola Baldini	Italy	http://www.ior.it/ricerca-e-innovazione/dipartimento-rizzoli-rit	Cell therapy, Tissue engineering, Bioprinting					
	Candiolo Cancer Institute IRCCS	Dr. Luca Crotto	Italy	https://research.fpoircc.it/	Gene therapy, Cell therapy		Oncologic diseases		Possible	No
	Center of Molecular Biotechnology and Translational Medicine	Prof. Dr. Fiorella Altruda	Italy	https://x027-unito.prod.cineca.it/en	Cell therapy, cell factory		Thoracic Oncology, Cancer Immunology, anti-angiogenetic		Possible	No
	A.O. Nazionale SS. Antonio e Biagio e Cesare Arrigo, Struttura Complessa di Ematologia		Italy	https://www.ospedale.al.it/sc-ematologia/	Cell therapy (CAR-T)		Hematology		No	No
	AOU Città della Salute e della Scienza – Torino		Italy	https://www.cittadellasalute.to.it/	Cell therapy (CAR-T)		Oncoematologic diseases		No	No
	Bioair (Euroclone spinoff)	Dr . Cristina Zanini	Italy	https://www.bioair.it/	Cell and gene therapy solutions					No
	RAMSES, Research & Innovation technology Department, Istituto di Ricerca Codivilla Putti, Istituto Ortopedico Rizzoli	Dr. Brunella Grigolo	Italy	http://www.ior.it	Cell therapies; biological compounds, 3D bioprinting; nutraceuticals; biomarkers; musculoskeletal tissues; preclinical in vitro studies		Degenerative and inflammatory musculoskeletal diseases (osteoarthritis; rheumatoid arthritis; traumatic lesions)	metabolic bone diseases	Yes	No
	Laboratorio Studi Preclinici e Chirurgici, Research & Innovation Technology Department (Rizzoli RIT) IRCCS Istituto Ortopedico Rizzoli Istituto di Ricerca Codivilla Putti	Dr. Milena Fini	Italy	http://www.ior.it	Ciomaterials, medical devices, scaffolds, biocompatibility, preclinical in vitro and in vivo models, innovative surgical technologies, regenerative medicine, histology, histomorphometry, biomechanics		Acute, degenerative, infective and oncologic diseases of the musculoskeletal system	soft and mineralized tissue defects, osteoarthritis, osteoporosis, bone metastases, bone implant infections	Yes	No
	IRCCS Ospedale San Raffaele	Prof. Lorenzo Piemonti	Italy	https://research.hsr.it/en/index.html	Cell therapy, gene therapy		Oncology, autoimmune disesase, neurological disorders, genetic diseases		Yes	Yes
	Center for iPS Cell Research and Application	Prof. Shynia Yamanaka	Japan	http://www.cira.kyoto-u.ac.jp/e/index.html	Parkinson's disease, amyotrophic lateral sclerosis (ALS)					
	Leiden University Medical School	Prof. Dr. Frank JT Staal	Netherlands	www.lumc.nl	Cell nad Gene Therapy	100s	GvHD, Type I diabetes, SCID,, Thalassemia, Lysosomal storage diseases	XLA	Yes	Yes
	Radboud University Medical Center	Dr. Mangala Srinivas	Netherlands	https://www.multiscaleimaging.com/	Cell therapy	100s	Imaging agents for various applications; dept has established clinical trials with cell therapy in melanoma		No	No
	Cenya Imaging B.V.	Dr. James Simon	Netherlands	https://www.cenyaimaging.com/	Cell therapy		imaging agents, primarily for cell therapies		Possible	No (but approved for clinical trial)
	3B's Research Group at the University of Minho	Prof. Rui Reis	Portugal	www.3bs.uminho.pt	Tissue Engineering, Stem cell therapy		Degenerative and inflammatory musculoskeletal diseases (osteoarthritis; rheumatoid arthritis; traumatic lesions), bone, tendon, skin, intervertebral disk, cancer, metabolic bone diseases		No	No
	Expertissues EEIG	Prof. Rui Reis	Portugal	https://expertissues.eu	Tissue Engineering, Stem cell therapy		Musculoskeletal diseases (osteoarthritis; rheumatoid arthritis; traumatic lesions), bone, cartilage		No	No
	National Center for Stem Cell and Regenerative Medicine - KCDC -		Republic of	http://www.cdc.go.kr/						
	Fundación para la Investigación Biomédica Hospital Infantil Universitario Niño Jesús	Dr. Manuel Ramírez	Spain	http://fibhnjs.org/	Cell therapy, gene therapy, tissue enginering therapy	200	Advanced cancers, graft versus host disease, osteonechrosis, brain damage, epidermolisis bullosa		Yes	No
	Translational Research and Advanced Therapies Unit. Pediatric Hemato-Oncology Service. Hospital Universitario La Paz	Dr. Antonio Pérez Martínez	Spain	https://www.comunidad.madrid/hospital/lapaz/profesionales/hospital-materno-infantil/hemato-oncologia-pediatrica	Cell and gene therapy	60	Relapsed pediatric leukemias and solid tumors (advanced sarcomas, central nervous system tumors), graft versus host disease and avascular necrosis			No
	Biodonostia Health Research Institute	Dr. Ander Izeta	Spain	www.biodonostia.org	Somatic cell therapy, tissue engineering	0	Urinary Incontinence	Muscle degenerative diseases	Possible	No
	Vall d'Hebron Research Institute (VHIR)		Spain	http://en.vhir.org/portal1/homepage.asp?	Gene therapy, Cell therapy	40	Neuromuscular diseases; cancers	Rare diseases	Yes	Yes

	Andalusian Network for the design and translation of Advanced Therapies	Roke Iñaki Oruezabal	Spain	https://www.sspa.juntadeandalucia.es/terapiasavanzadas/index.php/en/	Cell Therapy, Gene Therapy, Tissue Engineering	600	Critical Limb Ischemia, Acute Myocardial Infarction, Dilated Miocardiopathy, Chronic Ischemic Cardiopathy, Stroke, Multiple Sclerosis, Amiotrophic Lateral Sclerosis, Chronic Graft versus Host Disease, Acute Graft versus Host Disease, Extended Liver Resection, Faecal Incontinence, Corneal Ulcers, Skin Burns, Skin Tumours, Rectum Cancer, Hidradenitis Suppurativa, Cleft Palate	Liver Surgery, Dry Eye Disease, Macular Degeneration, Intestinal Anastomosis, Acute Bone Marrow Lesion, CNS Developmental Disorders, Wiskott-Aldrich Syndrome, Pompe Disease	Possible	Yes
	at the Faculty of Medicine and Health Science of the University of Barcelona	Josep M. Canals Coll	Spain	http://www.ub.edu/creatio/	Cell Therapy		Huntington Diseases, neurological diseases		Yes	
	Advanced Therapies Unit - OSI Donostialdea	Dr. Ander Izeta	Spain	www.osakidetza.euskadi.eus/portada-osi-donostialdea/	Gene therapy, somatic cell therapy, tissue engineering	0	Blood cancers		Possible	No
	Karolinska Universitetssjukhus Huddinge		Sweden	www.karolinska.se/kcc						
	Wyss Zurich, University and ETH Zurich	Prof. Dr. Dr. Simon P.	Switzerland	https://www.wysszurich.uzh.ch	Tissue engineering, cell therapy, gene therapy					
	LLC "Medical Center "HEMAFUND"	Yaroslav Issakov	Ukraine	https://international.hemafund.com/	Somatic cell therapy	15000 of related units, 600	Autistic spectrum disorders, Spina bifida, CorD program to correct complex critical congenital heart defects	Oncohematological diseases, Solid tumors, Aplastic anaemia, Juvenile rheumatoid arthritis, Primary immunodeficiencies		
	Public cord blood bank Bank of Life	Yaroslav Issakov	Ukraine	http://www.bankof.life/uk/	Somatic cell therapy	103 of unrelated units	Oncohematological diseases	Planned	Yes	No
	QR Health Solutions	Dr. Sergii Isaev	Ukraine	https://qr-clinic.com/	Somatic cell therapy	2	Demyelinating CNS diseases, Post stroke and post-TBI conditions, Autistic spectrum disorders, Spinal cord injury,	Planned	Yes	Clinical trials
	LLC "Medical Biotech Company "HEMAFUND"	Yaroslav Issakov	Ukraine	https://international.hemafund.com/	Somatic cell therapy, tissue engineering or combined	Currently GMP	R&D	Planned	Yes	No
	CHDSCR, Faculty of Medicine, Univewrsity of Southampton	Prof ROC Oreffo	United Kingdom	www.stemcells.org.uk	Tissue Engineering, Cell therapy	17	Bone reconstruction (3D Printed Hip reconstruction with autologous cells)		No	No
	Sonoma Biotherapeutics	Jeff Bluestone	USA	https://www.sonomabio.com	Treg cell engineering and adoptive immunotherapy	dozens with polyclonal Tregs	autoimmune diseases, organ transplantation		Yes	No
	Wake Forest Institute for Regenerative Medicine (WFIRM)	Prof. Anthony Atala	USA	https://school.wakehealth.edu/Research/Institutes-and-Centers/Wake-Forest-Institute-for-Regenerative-Medicine	Tissue Engineering for different organs such as blood vessels, bladder, kidney, liver, ear, prenatal treatment, cancer, military health applications		Burn injuries, traumatized limbs, facial and hand reconstruction, genital and urinary organs		Yes	No

3. Challenges and Limitations

As mentioned previously, this list of institutions and facilities is not exhaustive, since it is biased towards the participants and supporters of the RESTORE project. This list can and should be complemented by obtaining further information from international stakeholders, industry organizations and also international scientific societies.

4. Putative solutions

The incomplete information about existing facilities and resources and expertise compromises the possibility to have synergies between similar efforts being performed in other regions of the world in the development of ATMPs. Therefore, further information should be sought from international stakeholders, industry organisations and international scientific societies to complement the list made here.

It is recommended that the members of RESTORE join efforts to complete this registry and to foster collaborations and synergies with other ATMP-based institutions worldwide to promote faster progress of those therapies into the clinic for the benefit of the society.

5. Challenges for RESTORE

RESTORE will ensure a unique opportunity to not only establish links within the EU but also internationally to facilitate the mapping of ATMP products approved and in use worldwide but also to create a network of international resources, stimulate collaboration between different institutions and best practices at all the levels of the development and translation into the clinic of ATMPs.

It is important to complement the information herein generated with data about approved, ongoing and finished ATMP clinical trials that for sure involve the use of GMP-compliant facilities with capacity to both develop and produce ATMPs. An example of such sources of information is a recent publication by the Alliance for Regenerative Medicine [1] where the trends in ATMP development are compared in different regions of the globe. Indeed, this publication shows that Europe is lagging behind in terms of clinical trials launched in the period 2014-2018 for ATMPs when compared with US and ASIA. In fact, only 1 in each 6 clinical trials of ATMPs in this period were performed in Europe.

Other sources of useful information include technology forecast analysis [2] publications in which clinical trials, market authorizations and even differences in the landscape of regulations are analysed in detail for different countries in Europe.

RESTORE will generate unique opportunities to bring together the ATMP stakeholders in Europe, creating the needed conditions to overcome the current fragmentation and to generalize the best practices and successes of treating patients with ATMPs in Europe.

6. Summary

The MAP of ATMP facilities and institutions herein listed is currently incomplete, particularly in other regions, taking into consideration the larger numbers of clinical trials launched in USA and Asia in comparison with Europe in the last years.

It is clear from the data herein presented that Europe has a considerable number of facilities that are active in the development, production and clinical application of ATMPs. Therefore, there are opportunities to establish synergies between those institutions to foster and promote a faster development of ATMPs to facilitate the access of patients in Europe to advanced and potentially curative treatments for many chronic and highly debilitating diseases.

7. References

[1] Alliance for Regenerative Medicine, Recent Trends in ATMP Development, 2019

[2] Eder C., Wild C., Technology forecast: advanced therapies in late clinical research, EMA approval or clinical application via hospital exemption, J. Market Access & Health Policy, 2019, 7, 1600939