

# ADMAIORA

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**Project title:** ADvanced nanocomposite MAterIals fOr in situ treatment and  
ultrASound-mediated management of osteoarthritis

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**Project website:** [www.admaiora-project.com](http://www.admaiora-project.com)

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## D7.2

# Preliminary report of the preliminary dissemination, communication and exploitation plan

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<b>PP</b>	Restricted to other programme participants (including the Commission Service)	
<b>RE</b>	Restricted to a group specified by the consortium (including the Commission Service)	
<b>CO</b>	Confidential, only for members of the consortium (including the Commission Service)	

## Document History

Version	Date	Author	Summary of Main Changes
1	15/03/2019	Leonardo Ricotti, SSSA	First version of the template for project Deliverables
2	10/04/2019	Michele Nardini, SSSA	First draft of the Deliverable concerning communication and dissemination activities
3	14/04/2019	Roni Wechsler	First draft of the Deliverable concerning exploitation activities
4	16/04/2019	Leonardo Ricotti	Integrated Deliverable draft, circulated to the partners for revisions and integrations
5	23/04/2019	Gilbert Nessim	Check on dissemination activities
6	25/04/2019	Leonardo Ricotti	Second integrated Deliverable version integrated with partners' contributions
7	30/04/2019	Leonardo Ricotti	Final Deliverable version and Deliverable submission

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## 1 Executive summary

This document presents the preliminary dissemination, communication and exploitation plan of the project (to be updated and refined through the entire project time-frame) and reports the activities carried out by the Consortium in the initial period, from the kick-off meeting (February 4-5, 2019) to the Deliverable due date (April 30, 2019).

The specific aim of dissemination activities is to share the research and pilot experiences with European and international leaders in regenerative medicine, medical devices, biomaterials and nanotechnologies. This will be pursued through different lines of action, namely: (1) the development of a project website, to be continuously improved and updated during the project. It will play a key role in the dissemination of the non-confidential partners' outcomes; (2) project brochures and leaflets, which will be used to promote the project at international conferences, fairs, symposia, exhibitions, workshops, but also in non-scientific events (e.g. with stakeholders); (3) graphic renderings and videos, guaranteeing an easy-to-understand representation of the ADMAIORA approach and outcomes; (4) presentations at international scientific and technological events; (5) lectures and seminars given by the academic partners involved in the proposal and (6) publications in peer reviewed, international scientific journals in the different ADMAIORA fields of research. In the Deliverable, expected performances and planned strategies are reported, for all these dissemination activities.

The specific aim of communication activities is to increase the project visibility and the awareness of end-users, stakeholders and general population that the project exists and that produces potentially game-changing results. Communication activities have been planned from the outset and will continue throughout the entire project lifetime. They are based on clear objectives and aim to reach different target groups, thus to complement the dissemination activities. This will be pursued through different lines of action, namely: (1) extensive use of the project website; (2) external links to the project website; (3) social network profiles, managed with constant updates almost on a daily basis; (4) communication events on media (press, internet, TV, radio, etc.); (5) non-specialistic presentations at conferences and fairs dealing with osteoarthritis, medical devices, tissue regeneration, etc., allowing non-specialistic presentations to the general public or to policy makers; (6) development of promotion material, such as roll-up, posters, one page project descriptions, infographics, project gadgets, etc.; (7) Newsletters, focused and adapted depending on the groups of interest; (8) non-technical project workshops to healthcare system actors, stakeholders, OA patients and elderly people; (9) ADMAIORA elderly marathon; (10) informative workshop co-organized with a professional soccer society and (11) communication event co-organized with CONI, at the Olympic games of Tokyo 2020. In the Deliverable, expected performances and planned strategies are reported, for all these communication activities.

The aim of exploitation activities is to pave the way to a future clinical and commercial translation of the project outcomes, by defining an exploitation roadmap for the expected main project outcomes, but also from possible lateral ones. In the Deliverable, a general strategy is depicted, with two main products that could arise from the project efforts. A preliminary main business plan is presented for the *RegenCart kit* (a nanocomposite

hydrogel for cartilage regeneration, added with enabling technologies boosting its action). A secondary business plan is also reported for the *ArthroPrint tool* (a handheld 3D bioprinting medical device). Finally, further lateral business opportunities are mentioned, for the different SMEs involved in the Consortium.

## 2 Planned dissemination activities

Dissemination of knowledge will be carried out by all the ADMAIORA partners and will be addressed not only at scientific level but also towards industrial and public arenas. In order to meet this goal, each project participant will put effort into disseminating ADMAIORA outcomes and achievements. More in detail, each partner will carry out public presentations of the project progress and results at different public meetings in their own country and also by exploiting pre-existing scientific networks.

All dissemination activities will be agreed among the partners of the Consortium. This will be done for any actions, ranging from communication through specialized media to selected scientific journals, magazines, conferences, courses, seminars, fairs and websites.

ADMAIORA Results will be boosted following two main strategies:

1. The dissemination of information about the project and the achievements towards the larger lay public, ensuring the awareness of results and use of EC funding in this key research area.
2. The disseminations of the best practices developed in the project towards the scientific community, making available the tools and methodologies, thus allowing other researchers the access for use in other domains.

From this perspective, the two strategies will be implemented under the Open Access research data and the Open Access for publications policies, which will play a complementary role in the dissemination of the results.

ADMAIORA preliminary dissemination plan includes different levels of dissemination, focused on the following:

- Dissemination of information through project website, brochure and leaflets, graphic renderings and videos;
- National and international conferences or workshops;
- Forums and exhibitions;
- National and European showrooms.
- Lectures and seminars
- Journal publications

### 2.1 Project website

Table 1 reports the specific actions/features and the quantitative targets concerning the project website.

Public dissemination tool	Specific actions/features	Quantitative targets
Project website	An official website will be set up and continuously improved and updated during the project. It will play a key role in the dissemination of the non-confidential partners' outcomes. The Website will be not used as a management	Expected number of visits: at least 350/month. Expected location of the visits: at least 25

	<p>tool (actually no private areas have been included): indeed, the Consortium decided to rely on different tools (more flexible ones) for project management. Thus, the Website is exploited as a platform to maximise the dissemination and communication potential of the Consortium.</p> <p>All website sections will be fully public, aesthetically attractive and containing official documents (e.g. logo, leaflet and brochure, public presentations, etc.) of the project, general introduction, latest achievements (e.g. videos) and news, the dissemination activities that are scheduled and past events (e.g. registered talks, etc.). Such information will be published and updated on a regular basis.</p> <p>The website will be managed by SSSA, through the ADMAIORA Communication Manager, also after the end of the project. The website will be posted to all major search engines and will hold a maximum of 100 keywords to facilitate visibility of the project throughout the Internet.</p>	<p>different countries in 4 years.</p> <p>The expected contacts through the website, will include academic/industrial players, policy makers, etc. However, the different categories accessing the website will not be registered, to avoid the need of filling questionnaires that would be counterproductive in terms of website attractiveness.</p>
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**Table 1:** Description of the planned specific actions and features and expected targets for the project website.

The website [www.admaiora-project.com](http://www.admaiora-project.com) is on-line from the end of March. The website is based on WordPress platform, a free and open-source content management system (CMS) based on PHP & MySQL. A specific website template has been purchased: Codeus — Multi-Purpose Responsive Wordpress Theme (<https://themeforest.net/item/codeus-multipurpose-responsive-wordpress-theme/6906054>).

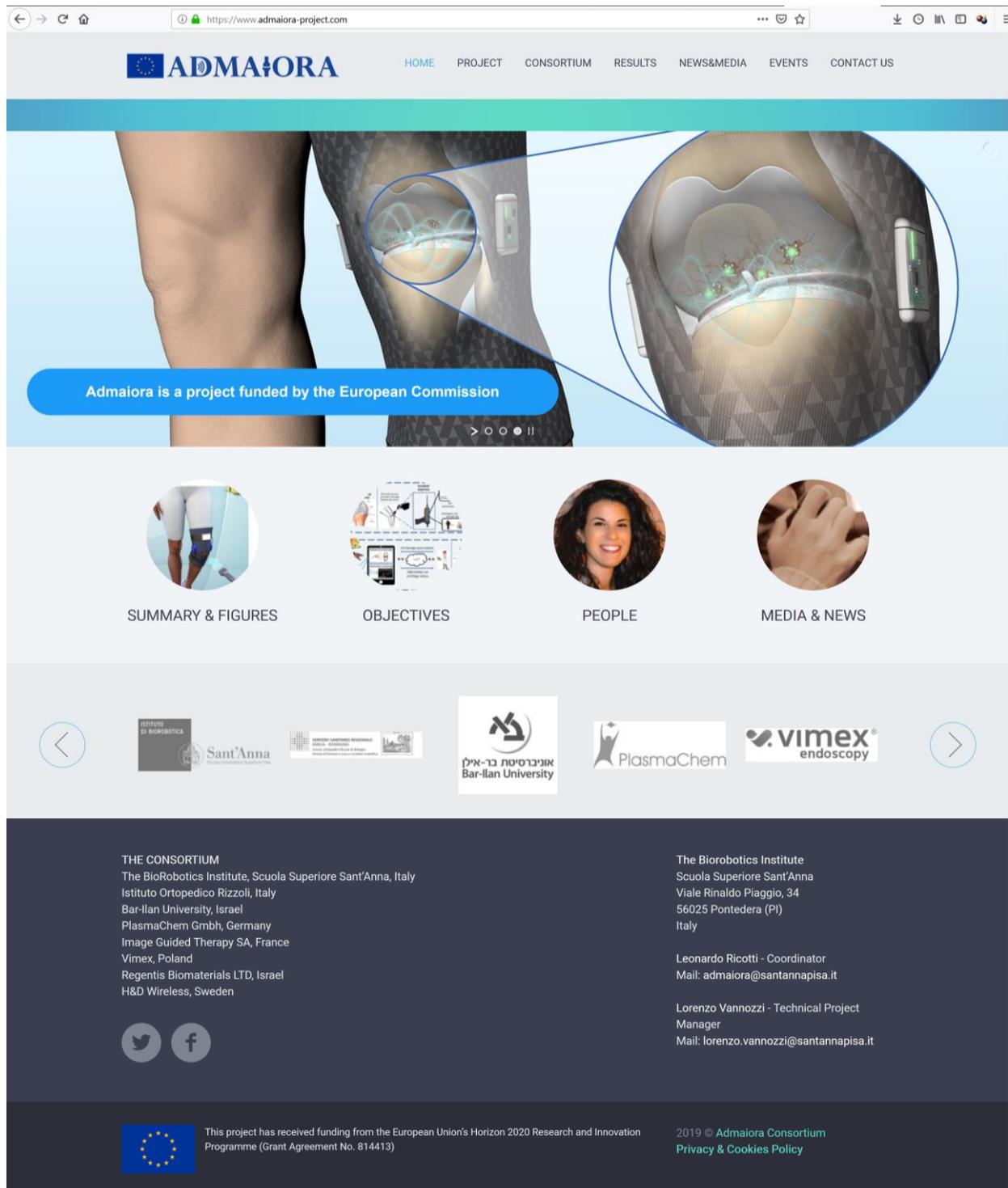
The structure of the ADMAIORA website (main menu and secondary sections) is shown in Figure 1:



**Figure 1:** ADMAIORA website structure.

The website contains official information about the goal of the project, the ongoing research efforts, the project impact and perspectives, the events and news, etc. The website information will be updated on a regular basis by the project Communication Manager, appointed at SSSA.

The home page is shown in Figure 2.



**Figure 2:** Current screenshot of the ADMAIORA website Home page.

According to the EU policy, “the EU emblem and reference to EU funding must be displayed in a way that is easily visible for the public and with sufficient prominence”. In our case, the emblem is well visible both at the top (together with the project logo) and the bottom of the page. The sentence to acknowledge the EU funding and to evidence the Grant Number is shown at the bottom of the page in a well-visible position. The EU emblem and EU funding information appears in all the website pages, thus to guarantee an appropriate visibility.

The strategy planned to maximize the website visibility includes:

- Promotion of the ADMAIORA website on other network platforms (e.g. the institutional websites of the eight partners involved in the project), as well as international and local media, in association with project-related news;
- Diffusion of the website contents on the Facebook and Twitter profiles associated with the ADMAIORA project, in an organic and dynamic communication strategy managed by the project Communication Manager.
- Continuous updating of contents. Such update will concern not only the project results and events, but also other projects funded in the same ADMAIORA Call (H2020-NMBP-TR-IND-2018) and in general worldwide news dealing with the ADMAIORA field that can be of general interest for people along the whole value chain;
- Promotion of the ADMAIORA website (through brochures and other documents) in the events, international conferences, fairs and forums, meetings with stakeholders, etc.;
- The traffic on the website is supervised by Google Analytics. As an initial result, from April 10 to April 30, the visits to [www.admaiora-project.com](http://www.admaiora-project.com) have been **246** (visitors were from **24** different countries: Italy, United States of America, Sweden, Spain, China, Greece, Israel, German, Poland, Japan, Pakistan, Mexico, Australia, Czech Republic, France, Croatia, Georgia, South Korea, Latvia, Netherlands, Oman, Portugal, Thailand and Turkey).

## 2.2 Project brochure and leaflets

Table 2 reports the specific actions/features and the quantitative targets concerning the project brochure and leaflets.

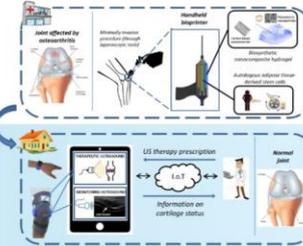
Public dissemination tool	Specific actions/features	Quantitative targets
Project brochure and leaflets	Project leaflets and brochures with general information about objectives, consortium and final goals of the research will be prepared and distributed during all dissemination events. A copy of these documents in different languages will be made for ensuring the widest dissemination of the project and also for allowing local dissemination and communication activities. During the project time-frame, dedicated leaflets or brochures will be prepared for disseminating both intermediate and final results.	Expected academic/industrial players, policy makers and end-users reached through brochures and leaflets: at least 100/year

**Table 2:** Description of the planned specific actions and features and expected targets for the project brochure and leaflets.

The official ADMAIORA brochure will be used in all main dissemination events (participation in international conference, fairs, symposia, exhibitions and workshops, etc.). It will be also useful for promoting the project in other contexts, such as in meetings with stakeholders. It will contribute to promote the project website and social network profiles. The first draft of the ADMAIORA brochure (still to be refined) is shown in Figure 3.

**ADMAIORA** will target a ground-breaking paradigm that may revolutionize OA treatment. Within the project time-frame (4 years) the target is to achieve a 60% reduction of degeneration in OA animal models treated with the ADMAIORA technologies, with respect to control (untreated) ones, after 4 weeks, and a 90% reduction after 3 months. To achieve this ambitious objective the Consortium will evolve and merge technologies that already showed a high potential as experimental proof of concepts and will bring them at a preclinical level.

The **ADMAIORA Consortium** will develop biosynthetic hydrogels embedded with carbon-based nanomaterials, conferring higher mechanical and lubrication properties, and piezoelectric nanoparticles enabling responsiveness to remote wireless ultrasound waves. Stem cells derived from autologous adipose tissue, which already demonstrated anti-inflammatory and regenerative properties, will be entrapped in the hydrogels. Materials and cells will be delivered in situ through an innovative handheld 3D bioprinter, embedded in an arthroscopic tool. A custom brace will be designed and equipped with ultrasound probes for both monitoring the joint status and stimulating the implanted piezoelectric nanobiomaterial. A dedicated App will allow a direct connection between patient and physician in an Internet of Things framework.



**The Consortium**



**Project Coordination**  
**Scuola Superiore Sant'Anna - The BioRobotics Institute, Italy**  
**Leonardo Ricotti (Coordinator)**

**Partners**

- Istituto Ortopedico Rizzoli, Italy - Principal Investigator (PI): Gina Lisignoli
- Bar-Ilan University, Israel - PI: Gilbert Daniel Nessim
- PlasmaChem GMBH, Germany - PI: Carsten Jost
- Image Guided Therapy SA, France - PI: Erik Dumont
- Vimex Endoscopy, Poland - PI: Tomasz Gapinski
- Regentis Biomaterials LTD, Israel - PI: Aharon Wechsler
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## ADMAIORA



[www.admaiora-project.com](http://www.admaiora-project.com)

**ADMAIORA** (Advanced nanocomposite Materials for in situ treatment and ultrasound-mediated management of osteoarthritis) is a research project funded under the Horizon 2020 EU Framework Programme (Call: H2020-NMBP-TR-IND-2018, Research and Innovation action), coordinated by The BioRobotics Institute of Scuola Superiore Sant'Anna (Pisa, Italy). The aim of the project is to explore alternative treatments for Osteoarthritis (OA), able to reduce the healthcare costs and to improve patients' quality of life and their healthy and active lifespan in the long-term.

**WHAT IS THE OSTEOARTHRITIS?**  
 Osteoarthritis (OA) is a major burden that affects ~ 40 million of EU citizens, with enormous direct and indirect costs for the European healthcare systems. This disease involves the degeneration of cartilage and other joint structures and is one of the most common causes of pain and disability in middle-aged and elderly people.  
 Over the next decade, the number of people affected by OA is expected to double due to population ageing and increased rate of obesity (a risk factor for OA), resulting in a significant burden at the society level. According to the United Nations, by 2050, 130 million people will suffer from OA worldwide, of whom 40 million will be severely disabled by the disease. This represents an issue that is largely unsolved, at present.

**THE PROJECT**  
 ADMAIORA aims, in the long-term, at increasing the healthy and active lifespan of people affected by OA, by considerably slowing down or even stopping the degeneration process, thus delaying by several years or even avoiding surgical interventions for total joint replacement. To make this challenging objective a reality, the project partners will collaborate in the investigation of nanotechnologies, advanced materials, remotely physical stimulation, advanced manufacturing, wearable devices and cloud platforms into a unique workflow. ADMAIORA will explore the potential of smart nanocomposite materials and stem cells, in synergy with external physical stimuli (based on low-intensity ultrasound), for stopping the degeneration of cartilage during OA at early stages. Within the project time-frame (4 years), the target is to demonstrate the ground-breaking potential of such a regenerative approach, at a preclinical level.

**ADMAIORA will achieve its ambitious target by tackling the following scientific and technological problems:**

- Development of a biosynthetic hydrogel with carbon-based and piezoelectric nanomaterials embedded;
- Use of stem cells derived from autologous adipose tissue, to reduce inflammation and to regenerate cartilage;
- Development of a system for highly controlled ultrasound stimulation of scaffolds and cells;
- Development of an innovative handheld 3D bioprinter, embedded in an arthroscopic tool



**Figure 3:** First draft of the ADMAIORA project brochure.

In the project course, further material will be produced, as follows:

- National versions of the brochure, translated into Italian, French, German, Polish, Swedish and Hebrew (the languages of the partners involved). This will help to more effectively reach some end-users (elderly people, who may hardly understand English);
- Specific brochure versions, focusing on the project intermediate/final objectives and results (approximately, one new version at each reporting period: month 19, month 37 and month 49);
- Dissemination materials for selected audiences (companies, investors, universities, foundations, policy makers, etc.): roll ups, small/large-format posters and presentations of the project, with objective-focused contents;

## 2.3 Graphic renderings and videos

Table 3 reports the specific actions/features and the quantitative targets concerning the project graphic renderings and videos.

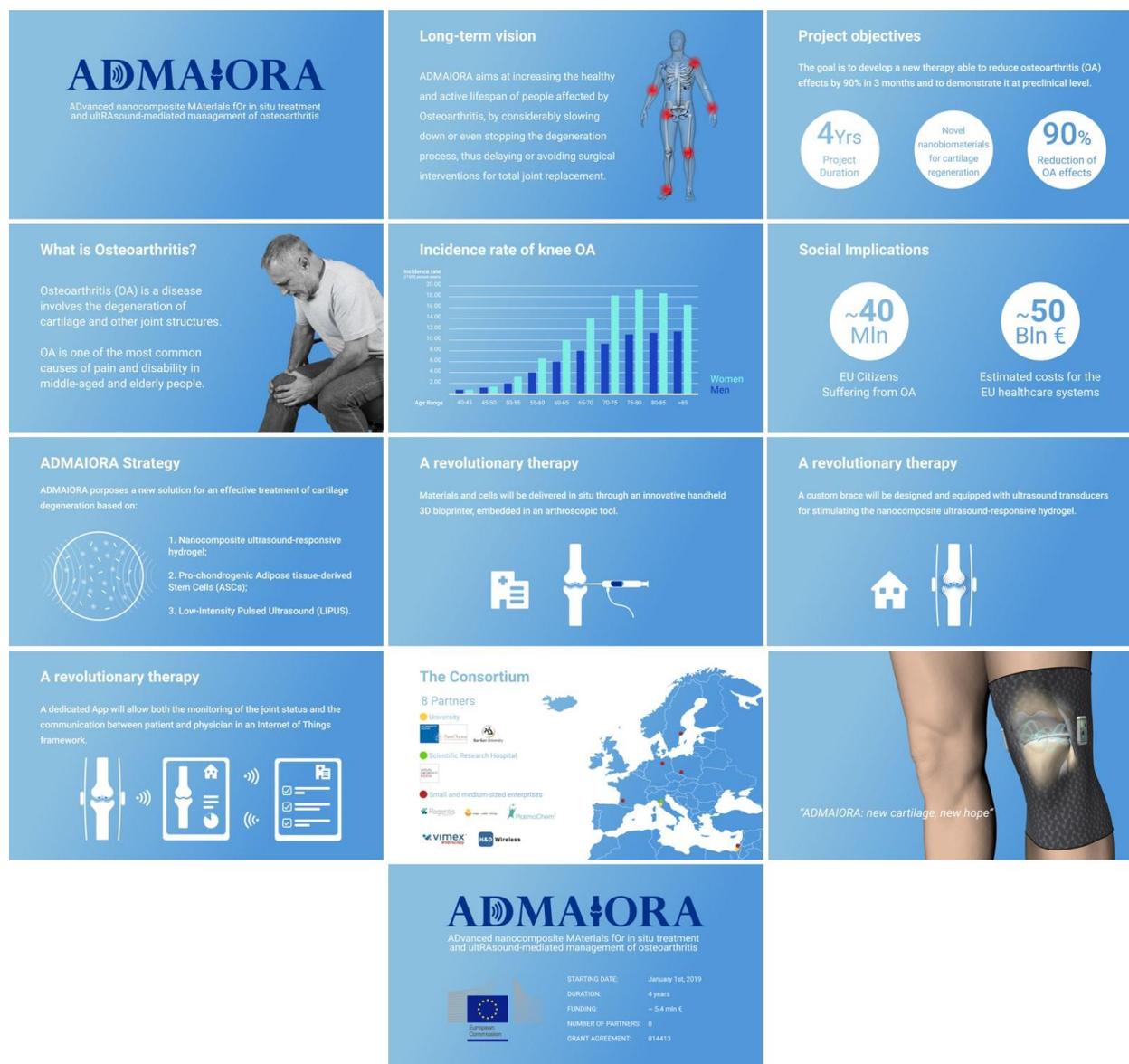
Public dissemination tool	Specific actions/features	Quantitative targets
Graphic renderings and videos	Both static images and animations will provide an easy-to-understand representation of the ADMAIORA technological components and targeted project outcomes, in order to guarantee a wide and effective dissemination process among researchers, industrial players and policy makers. Based on users' feedbacks and following the system re-design, the graphic rendering will be enhanced during all the project lifetime.	Expected academic/industrial players or policy makers reached through images and videos: at least 100/year. Expected feedbacks (online comments): at least 35/year.

**Table 3:** Description of the planned specific actions and features and expected targets for the project brochure and leaflets.

To promote graphic renderings, videos and static images, the ADMAIORA strategy includes three types of initiatives that will maximize visibility and dissemination efficacy:

- Dissemination of multimedia material at international conferences: the videos will be integrated in some presentations delivered to the audience, in closed-loop presentations shown at workshops, stands at fairs and other dissemination events;
- Dissemination of multimedia material on interactive channels such as Youtube, social networks (ADMAIORA Facebook and Twitter accounts), official project website, institutional websites of the Consortium partners and research/professional portals (ResearchGate and LinkedIn);
- Dissemination of multimedia material through press releases and other media events.

Different videos, animations and images will be produced in the project course, following the evolution of the technical activities. At present, a 1 min and 50 s - long preliminary version of the project infographic has been produced. It aims at describing the project long-term vision, approach and impact in a simple way. Figure 4 shows a collection of screenshots describing the different information reported in the infographic.



**Figure 4:** Screenshots of the preliminary ADMAIORA infographic.

## 2.4 Presentations at scientific and technological events

The dissemination plan also includes presentations at scientific and technological events. In particular:

- National and international conferences or workshops to share information with other research groups about relevant aspects of the project research. One dedicated ADMAIORA workshop per year is foreseen with the purpose of presenting the project results to a broader audience of potential users, stakeholders and scientists. Whenever possible and appropriate, such events will be concerted and co-organized with the Coordinators of the other projects funded in the NMBP-22-2018 call. Official reports about the workshop results are included in the WP7 deliverables list.

The ADMAIORA Project Coordinator (Leonardo Ricotti) has already contacted both Dr. Meriem Lamghari (University of Porto, Portugal) and Prof. Chiara Vitale-Brovarone (Polytechnic of Turin, Italy) that coordinate two projects in the NMBP-22-2018. The three project coordinators are going to organize joint dissemination events, in agreement with the Project Officer.

- Forums and exhibitions to identify the latest technology in the ADMAIORA research fields and to share ideas and developments with industries, e.g. through *ad hoc* demonstrations. Such dissemination initiatives will also foster exploitation ones.
- National and European showrooms directed to the public administrations and policy makers, as well as clinical and healthcare communities at large.

A preliminary list of such dissemination events, with corresponding expected targets, is reported in Table 4.

NAME	DESCRIPTION	COUNTRIES AND DATES	PARTNERS INVOLVED	TARGET GROUPS / OBJECTIVES
<b>Conferences and meetings with a broad scope</b>				
IEEE/EMBS Engineering in Medicine and Biology Conference (EMBC)	<p>Interdisciplinary conference on the applications of engineering in medicine and biology.</p> <p><b>ALREADY CONFIRMED FOR 2019</b></p> <p>SSSA will participate in the 2019 edition of this conference with the following contributions:</p> <ul style="list-style-type: none"> <li>• Leonardo Ricotti (ADMAIORA Project Coordinator) is the organizer of a Mini-Symposium – already accepted by the Conference organizers - focused on a scientific topic closely adherent to the ADMAIORA scope. Title of the event: <i>“Physical triggers and nano-biomaterials for tissue regeneration”</i></li> <li>• A paper on the design of a low-intensity ultrasound stimulation system by F. Fontana et al. has been accepted for presentation (still to be decided if oral or poster one). Title: <i>“Highly controlled and usable system for Low-Intensity Pulsed Ultrasound Stimulation of Cells”</i></li> <li>• A paper on the development of piezoelectric nanocomposites by L. Vannozzi et al. has been accepted for presentation (still to be decided if oral or poster one). Title: <i>“Nanocomposite thin films based on polyethylene vinyl acetate and piezoelectric nanomaterials”</i></li> <li>• A paper on the preliminary behaviour of stem cells on substrates by F. Iberite et al. has been accepted for presentation (still to be decided if oral or poster one). Title: <i>“Influence of substrate stiffness on human induced</i></li> </ul>	Germany, July 23–27, 2019 (next editions: to be decided)	SSSA	<p>Target group: clinicians, technicians, researchers, industrial players and policy makers in bioengineering</p> <p>Organization of at least 1 large workshop/year. Expected audience: 200/event</p> <p>At least other 7 presentations/year. Target audience: at least 100 people/event</p>

	<i>pluripotent stem cells: preliminary results"</i>			
TERMIS EU and World Congress	<p>Leading conference in tissue engineering and regenerative medicine, integrating industry, governmental and academic realities in this field.</p> <p><b><u>ALREADY CONFIRMED FOR 2019</u></b></p> <p>SSSA will participate in the 2019 edition of this conference with the following contribution:</p> <ul style="list-style-type: none"> <li>A paper on the development of a hydrogel for cartilage regeneration by L. Vannozzi et al. has been accepted for presentation (still to be decided if oral or poster one). Title: "<i>Gellan gum/poly (ethylene glycol) di-acrylate hydrogels with tunable mechanical properties for articular cartilage engineering</i>"</li> </ul> <p>IOR will participate in the 2019 edition of this conference with the following contribution:</p> <ul style="list-style-type: none"> <li>A paper on a new hydrogel type for bone regeneration by G. Lisignoli et al. has been accepted for oral presentation. Title: "<i>Calcium-Functionalized 3D Silk Gelatin Bioink Promotes Osteogenesis of Mesenchymal Stromal Cells: Perspectives For Orthopaedic Surgery</i>"</li> <li>A paper on advanced in vitro tissue models by M. Maglio et al. has been accepted for oral presentation. Title: "<i>Advanced in vitro tissue models: current status, feasible scenarios, limits to overcome</i>"</li> </ul>	Greece, May 27-31, 2019 (next editions: to be decided)	IOR,SSSA	
SMIT (Society for Medical Innovation and Technology)	One of the most important events for technological innovation in medicine.	(next editions: to be decided)	VIMEX, HDW	
European Conference on Biomaterials (ESB)	Leading event on biomaterials for biomedical applications, organized by the European Society for Biomaterials.	(next editions: to be decided)	REGENTIS, IOR	
ESAO Congress	Interdisciplinary event organized by the European Society for Artificial Organs.	(next editions: to be decided)	SSSA	
World Congress on Functional Materials and Nanotechnology (WCFMN-2019)	<p>This conference focuses on recent trends of research and applications of functional materials and nanotechnology.</p> <p><b><u>ALREADY CONFIRMED FOR 2019</u></b></p> <p>SSSA will participate in the 2019 edition of this conference: Leonardo Ricotti has been invited as Keynote</p>	Spain, May 13-14, 2019 (next editions: to be decided)	SSSA	

	Speaker with a talk focused on the ADMAIORA topics, entitled: <i>"Ultrasound and responsive materials for biomedical applications: direct and indirect effects"</i>			
<b>Technical/scientific focused conferences</b>				
MRS Fall Meeting & Exhibit	One of the largest conferences focused on innovative materials and their applications (including healthcare). The call for abstracts will open on May 13, 2019 and the accepted abstracts will be communicated by September. <b><u>ALREADY CONFIRMED FOR 2019</u></b> Since 2007, Prof. Nessim and his group at BIU presented 3 invited talks and 18 contributed talks in this Conference. BIU will surely participate in the 2019 edition.	USA, December 1-6, 2019 (next editions: to be decided)	BIU	Target group: technical communities concerning biomedical and biomechanical devices, chemistry and biomaterials, nanotechnologies, stem cell biology, ultrasound systems, IoT.  At least 6 presentations/year. Target audience: at least 50 people/event
Nature conference on engineering biology for medicine	Conference on strategies for probing, diagnosing and combating human diseases. <b><u>ALREADY CONFIRMED FOR 2019</u></b> SSSA will participate in the 2019 edition of this conference with the following contribution: <ul style="list-style-type: none"> <li>A paper on the ADMAIORA concept and approach by L. Ricotti et al. has been accepted for presentation. Title: <i>"A groundbreaking approach for cartilage regeneration and osteoarthritis treatment: the ADMAIORA project"</i></li> </ul>	USA, May 19-22, 2019 (next editions: to be decided)	SSSA	
International Conference on Biomedical Robotics and Biomechanics (BIOROB)	International biannual conference that covers both theoretical and experimental challenges posed by the application of robotics and mechatronics in medicine and biology.	(next editions: to be decided)	SSSA	
Design of Medical Devices Conference	World's largest premiere medical devices conference.	(next editions: to be decided)	VIMEX, IGT, HDW	
Annual ACS (American chemical society) meeting	Platform to present, publish, discuss and exhibit the most exciting research discoveries and technologies in chemistry and its related disciplines.	(next editions: to be decided)	REGENTIS, BIU	
Gordon Research Conferences (GRC)	International forum for the presentation and discussion of frontier research in the biological, chemical, and physical sciences, and their related technologies.	(next editions: to be decided)	REGENTIS	
ISN2A (International Symposium on Nanoparticles/Nano materials and	Important event on nanotechnology and nanocomposites for different purposes, included medical/biomedical ones.	(next editions: to be decided)	SSSA, IOR, BIU, PLASMACHEM	

Applications)				
International conference & exhibition on Nanotechnology	The largest technology, networking and matchmaking annual event in Europe.	(next editions: to be decided)	PLASMACH EM, BIU	
Applied Nanotechnology and Nanoscience Conference - ANNIC	Annual event that hosts high-profile plenary speakers, world class researchers, oral and poster presentations, workshops, sponsor exhibits and afterworks. It is a great opportunity to share research findings with a wide audience, promote knowledge exchange, and networking.	(next editions: to be decided)	PLASMACH EM, BIU	
IEEE International Ultrasonics Symposium	Symposium dedicated to ultrasound-related topics, but open to medical and biological applications and insights.	(next editions: to be decided)	IGT	
International Society for Therapeutic Ultrasound - ISTU Conference	Event to increase and diffuse knowledge of therapeutic ultrasound to the scientific and medical community, and to facilitate the translation of therapeutic ultrasound techniques into the clinical arena for the benefit of patients worldwide.	(next editions: to be decided)	IGT, SSSA	
International Conference on Internet of Things (IoT) Technologies for HealthCare	Global event on healthcare support for the elderly, real-time monitoring systems, emerging e-Health IoT applications, smartphones as a healthy thing, machine learning, deep learning, and cloud computing.	(next editions: to be decided)	HDW	
<b>Fairs and Forums (also towards exploitation)</b>				
MEDICA fair	World Forum for medical devices and technologies. <b><u>ALREADY CONFIRMED FOR 2019</u></b> VIMEX will participate in the 2019 edition of this fair with a stand of the company in which the ADMAIORA activities will have visibility.	Germany, November 18-21, 2019 (next editions: to be decided)	REGENTIS, VIMEX, IGT, HDW, SSSA	Target groups: public hospitals and private clinics representatives, physicians, companies and policy makers.
COMPAMED fair	High-Tech solutions for Medical Technology Fair.	(next editions: to be decided)	IGT, REGENTIS, HDW	At least 3 presentations or stands/year. Target audience: at least 100 people/event or stand
EuroNanoForum	The EuroNanoForum is a meeting point for industry, science and policy. Organised biannually since 2003, it has grown into the most significant European networking conference focusing on innovations in the various nanotechnology fields and associated industrial sectors.	(next editions: to be decided)	PLASMACH EM, BIU	
FIME Fair	Medical trade fair. <b><u>ALREADY CONFIRMED FOR 2019</u></b> VIMEX will participate in the 2019 edition of this fair. The ADMAIORA	USA, June, 26-28, 2019 (next	VIMEX	

	activities will have visibility.	editions: to be decided)		
Hospitalar Fair	Medical trade fair. <b><u>ALREADY CONFIRMED FOR 2019</u></b> VIMEX will participate in the 2019 edition of this fair. The ADMAIORA activities will have visibility.	Brasil, May 21-24, 2019 (next editions: to be decided)	VIMEX	
CMEF Fair	International Medical Equipment Fair. <b><u>ALREADY CONFIRMED FOR 2019</u></b> VIMEX will participate in the 2019 edition of this fair. The ADMAIORA activities will have visibility.	China, May 14-17, 2019 (next editions: to be decided)	VIMEX	
Africa Health Exhibition	Largest gathering of healthcare companies, technology, products and services in the African continent. <b><u>ALREADY CONFIRMED FOR 2019</u></b> VIMEX will participate in the 2019 edition of this fair with a stand of the company. The ADMAIORA activities will have visibility.	South Africa, May 28-30, 2019 (next editions: to be decided)	VIMEX	
<b>Medical Congress</b>				
World Congress of the Osteoarthritis Research Society International (OARSI)	Global forum for people involved in OA research and treatment from academia and industry. <b><u>ALREADY CONFIRMED FOR 2019</u></b> IOR will participate in the 2019 edition of this conference. The following contribution has been submitted by Manferdini C. et al. and accepted as poster presentation. Title: " <i>Osteoarthritic milieu and hypoxia exert specific effects on adipose mesenchymal stromal cell migration and cytokine receptor expression</i> ".	Canada, May 2-5, 2019 (next editions: to be decided)	IOR	Target groups: physicians, associations and stakeholders.  At least 2 presentations/year. Target audience: at least 75 people/event
World Congress of the International Cartilage Regeneration & Joint Preservation Society (ICRS)	Congress to advance science and education in the field of cartilage repair and regenerative medicine involving industry, surgeons and scientists. <b><u>ALREADY CONFIRMED FOR 2019</u></b> IOR will participate in the 2019 edition of this conference. The following three contributions have been submitted: - A paper by F. Veronesi et al. Title: " <i>The n-acetyl phenylalanine glucosamine derivative on the inflammatory/catabolic osteoarthritic joint environment as reproduced by both an in vitro and an in vivo model</i> "; - A paper by F. Veronesi et al. Title:	Canada, October 5-8, 2019 (next editions: to be decided)	REGENTIS , IOR	

	<p>"Modulation of the typical inflammatory environment of OA in the chondrogenic differentiation of MSCs from two type of sources (bone marrow and adipose tissue): an in vitro study";</p> <p>- A paper by F. Veronesi et al. Title: "Amniotic epithelial stem cells (AECs) Vs adipose-derived mesenchymal stem cells (ADSCs): translational potential as biological injective treatment for osteoarthritis"</p>			
<p>Congress of the European Society for Sports Traumatology, Knee Surgery and Arthroscopy (ESSKA)</p>	<p>Event that brings together orthopaedic surgeons, clinicians and scientists in Europe, along with their various societies. It fosters the sharing of research, of practical techniques and experience.</p> <p><b><u>ALREADY CONFIRMED FOR 2019</u></b></p> <p>VIMEX will participate in the 2019 edition of this fair. The ADMAIORA activities will have visibility.</p>	<p>Spain, May 9-12, 2019 (next editions: to be decided)</p>	VIMEX	

**Table 4:** Preliminary list of ADMAIORA dissemination events, with details and expected targets.

## 2.5 Lectures and seminars

The techniques and technologies developed in ADMAIORA will be also object of lectures and seminars by the academic partners involved in the proposal (SSSA, BIU and IOR). Target groups: Master and PhD students in bioengineering, biorobotics, nanotechnology, materials science and stem cell biology. Objective: at least 50 h/year of lectures on the ADMAIORA topics (considering all the partners' efforts), with an overall audience of at least 200 students/year. The lectures may catch the interest of Master and PhD students in future research stays at different partners' sites. This will foster students' exchanges between partners.

Lectures already given by the participants on ADMAIORA topics:

- SSSA: 10 h lectures on methods on milli, micro and nanosystems for targeted therapies. Given by Leonardo Ricotti, in the framework of the Master of Science in Bionics Engineering (Course: "Micro-nano robotics and biomaterials"), jointly managed by University of Pisa and Scuola Superiore Sant'Anna (Pisa, Italy). Number of students: 20 (the Master Degree is highly selective and admits a fixed number of students – 20 - each year).
- SSSA: 1 h seminar on the ADMAIORA topics planned by Lorenzo Vannozzi, in the framework the workshop "Innovative approaches for label-free manipulation and monitoring of biological cells and tissues", organized at University of Rome Tor Vergata, School of Engineering (Rome, Italy), on 23/05/2019. Seminar title: "Biomaterials and wireless stimuli for cell/tissue regeneration".
- BIU: Introducing concepts on the synthesis of carbon nanotubes and 2D layered nanomaterials within the courses of Kinetics of Materials 1 (solid state diffusion) and Kinetics of Materials 2 (phase transformations). Each course includes 20 hours of classes

and 13 hours of recitations and is attended by 10 to 20 students in the chemistry department who are focused on materials science.

- IOR: 2 h Round Table on Mesenchymal stromal cells in translational medicine, in the framework of research prospective at the DIBINEM Department of University of Bologna, given by Gina Lisignoli and Riccardo Meliconi. Number of participants: 100.

## 2.6 Journal publications

All partners have a recognized tradition in publishing in peer reviewed, international scientific journals in their different fields of research; ISI papers are indeed an important means for timely demonstrating and sharing the project results at global level. Medical and technical progresses will be published in selected top international journals with high impact factor to guarantee that important findings through the project are disseminated rapidly and efficiently to the relevant scientific research communities. Open access policy will be pursued. "Gold" publishing policy (immediate publishing and open access) will be preferred over "green" one (self-archiving and embargo).

The ADMAIORA website includes a section where scientific publications will be downloadable. Furthermore, a project citation map will be prepared, pointing out the published papers that cite ADMAIORA project in its entirety, or for single results. The whole consortium will contribute in the updating of the project references/citations, for covering all the research fields involved in the project.

Table reports a tentative project publication plan.

Project year	Expected number of publications	Possible target journals
1	≥ 3	Nature Communications, Advanced Science, PNAS, Science Advances, Scientific Reports, Cell Reports, Cells Stem Cells, eLife, JACS, Materials Today, Advanced Materials, Advanced Healthcare Materials, Biomaterials, Biofabrication, Journal of Materials Chemistry A, Chemistry of Materials, Small, ACS Nano, PLoS Medicine, Osteoarthritis and Cartilage, Journal of Tissue Engineering and Regenerative Medicine, IEEE Transactions on Biomedical Engineering, Ultrasound in Medicine & Biology, Ultrasonics, IEEE Transactions on Biomedical Circuits and Systems, IEEE Internet of Things Journal
2	≥ 5	
3	≥ 5	
4	≥ 8	

**Table 5:** Preliminary publication plan for the ADMAIORA partners.

Open access to research data will be also promoted. This means that during the project, all data will be managed following the FAIR (*Findable, Accessible, Interoperable and Re-usable*) model, in agreement with the terms and conditions stated in the ADMAIORA Data Management Plan (DMP), currently in progress. The opt-in option will be pursued whenever possible: this means that Research Data will be available in a chosen open repository (e.g. Zenodo platform), directly linkable on the ADMAIORA website. The DMP will also include the opt-out conditions (e.g. in case of needs related to patients' personal data protection, or IP-sensitive data). In any case, the DMP will contribute to the purposes included in this Dissemination Plan, following a fully coordinated strategy aimed at boosting the effectiveness of the ADMAIORA dissemination results.

## 3 Planned communication activities

ADMAIORA communication activities have been planned from the outset and will continue throughout the entire project lifetime. They are based on clear objectives and aim to reach different target groups, thus to complement the dissemination activities.

Communication initiatives allow to increase the project visibility and the awareness of end-users, stakeholders and general population that the project exists and that produces potentially game-changing results. The ADMAIORA target groups have been identified along the whole value chain, as follows: public and private hospitals, clinical community, healthcare systems, research community, students (including children), industry community, decision makers and public entities, possible future stakeholders, OA patients, sports practitioners, elderly people and the general public.

Communication tools will be used to: communicate the project vision to EU citizens; engage researchers/stakeholders/end-users; empower dissemination and exploitation events.

### 3.1 Traditional communication tools and activities

Table 6 reports a list of communication tools that will be used to both communicate the project vision to EU citizens and to engage researchers/stakeholders/end-users, also to empower dissemination and exploitation events.

WHAT Communication activities and target groups	HOW MANY Expected level of performance	HOW TO Strategy and planned actions
Project website, number of visits – Target groups: all	Expected number of visits: at least 350/month. Expected location of the visits: at least 25 different countries in 4 years.	<p>The strategy to increase the website visibility will include:</p> <ul style="list-style-type: none"> <li>• Promotion of ADMAIORA website on other network platforms (e.g. the institutional websites of the eight ADMAIORA partners;</li> <li>• Diffusion of the website contents on the Facebook and Twitter profiles associated with the ADMAIORA project, in an organic and dynamic communication strategy managed by the project Communication Manager.</li> <li>• Continuous updating of contents. Such update will concern not only the project results and events, but also other projects funded in the same ADMAIORA Call (H2020-NMBP-TR-IND-2018) and in general worldwide news dealing with the ADMAIORA field that can be of general interest for people along the whole value chain;</li> <li>• Promotion of the ADMAIORA website (through brochures and other documents) in the events, international conferences, fairs and forums, meetings with stakeholders, etc.;</li> <li>• Promotion of ADMAIORA website through the international and local media (TVs, radio, web);</li> <li>• Share of the link on other web portals.</li> </ul>

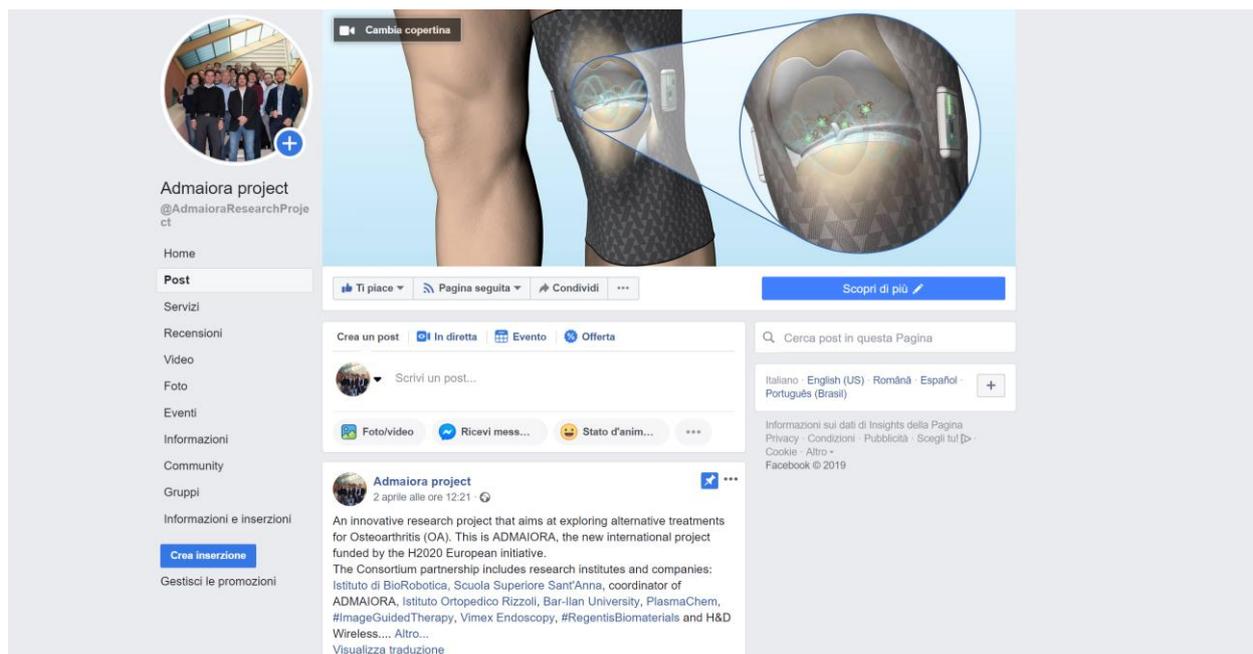
		<p>The website <a href="http://www.admaiora-project.com/">http://www.admaiora-project.com/</a> is online. Further details on the website are described in section 2.1.</p> <p>As an initial result, from April 10 to April 30, the visits to <a href="http://www.admaiora-project.com">www.admaiora-project.com</a> have been <b>246</b> (visitors were from 24 different countries: Italy, United States of America, Sweden, Spain, China, Greece, Israel, German, Poland, Japan, Pakistan, Mexico, Australia, Czech Republic, France, Croatia, Georgia, South Korea, Latvia, Netherlands, Oman, Portugal, Thailand and Turkey).</p>
N° of external links to the project website - Target groups: all	At least 15 per year	<p>The strategy to maximize the number of external links will include:</p> <ul style="list-style-type: none"> <li>• Promotion of the ADMAIORA website through traditional and new digital media (e.g. newspapers, specialized magazines, social networks, H2020 communication channels);</li> <li>• Diffusion of the website contents on the Facebook and Twitter profiles associated with the ADMAIORA project, in an organic and dynamic communication strategy managed by the project Communication Manager. This, in addition to give visibility to the website itself, will foster people to share its contents through external links;</li> <li>• Network of contacts with universities and companies working on similar research topics, willing to share the ADMAIORA contents.</li> </ul>
N° of contacts or followers within the social network profiles - Target groups: general public	At least 1,000 followers/social network	<p>ADMAIORA will ground on two main social network profiles: a Facebook and a Twitter one (see section 3.2 for a more detailed description). The communication plan includes an almost daily updating of contents through the following lines of action:</p> <ul style="list-style-type: none"> <li>• Frequent (almost daily) updates and key elements on the project (brief descriptions of the partners, of the single researchers; of the objectives, of the long-term vision, on research results, when available, etc.);</li> <li>• Deployment of videos, photos, static images and graphics renderings;</li> <li>• Information about projects focused on research lines close to the ADMAIORA ones.</li> </ul> <p>At the end of April, the ADMAIORA social network profiles have 125 followers.</p>
N° of communication events on media (press, internet, TV, radio, etc.) - Target groups: all	At least 10 per year	<p>A press release was organized in correspondence to the project start and kick-off meeting at Scuola Superiore Sant'Anna, on February 1, 2019. This had significant resonance in Italy (see section 3.3). The Consortium will pursue:</p>

		<ul style="list-style-type: none"> <li>joint international press releases;</li> <li>selected TV/radio interviews to the project partners' PIs, in different phases of the project, also depending on the intermediate results achieved;</li> <li>internet news, designed to be complementary to the previously mentioned communication initiatives and empowering them.</li> </ul>
Non-specialistic presentations at conferences, fairs, etc. - Target groups: clinical community, industry community, decision makers and public entities, possible future stakeholders	At least 2 per year, with at least 50 participants/event	Such events will be organized by carefully selecting scientific and industrial events, dealing with osteoarthritis, medical devices, tissue regeneration, etc., which allow non-specialistic presentations, to the general public or to policy makers. Once identified such events, specific requests will be done to the organizers, asking for: <ul style="list-style-type: none"> <li>the possibility to organize a stand or a similar dedicated space, to highlight the ADMAIORA vision and scopes;</li> <li>the possibility to advertise the ADMAIORA participation through the official event website (this will be complemented by reporting the event and the corresponding link also on the ADMAIORA website);</li> <li>the use of promotion material (see below), such as leaflets or gadgets, to be used during the events.</li> </ul>
Promotion material - Target groups: all	At least 200 leaflets and brochures, 5 roll-up stands, 5 posters and 1 video/infographics per year	The following materials have been planned for: <ul style="list-style-type: none"> <li>Leaflets and brochures showing the basic features of project: objectives and expected results, standard presentation for EU and local project communication gathering key messages;</li> <li>roll-up, posters and one page project descriptions, to support project communication at target events;</li> <li>infographics, videos and other multimedia pieces;</li> <li>other ADMAIORA gadgets (see section 3.4)</li> </ul>
Newsletters focused and adapted depending on the groups of interest - Target groups: OA patients, sports practitioners, public and private hospitals, clinical community and healthcare systems	At least 1 newsletter per year	The strategy is to focus, initially on two possible types of newsletters with a certain priority, to differentiate the information and the targets as follows: <ul style="list-style-type: none"> <li>1<sup>st</sup> priority: newsletter for end-users: developed to inform and engage elderly people affected by osteoarthritis;</li> <li>2<sup>nd</sup> priority: newsletter for clinicians: developed to inform and engage orthopaedic surgeons and other clinicians potentially interested in the project application and medical tools.</li> </ul>

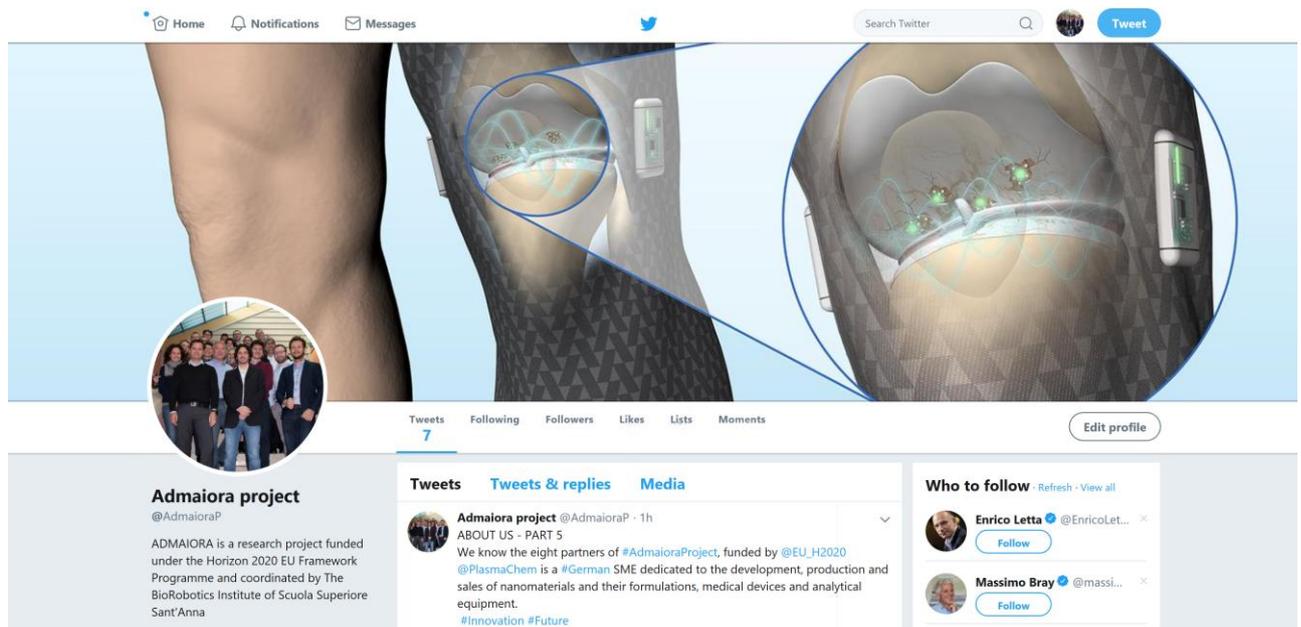
**Table 6:** Traditional communication activities and tools employed in ADMAIORA, expected levels of performance and envisaged strategy.

### 3.2 ADMAIORA social networks

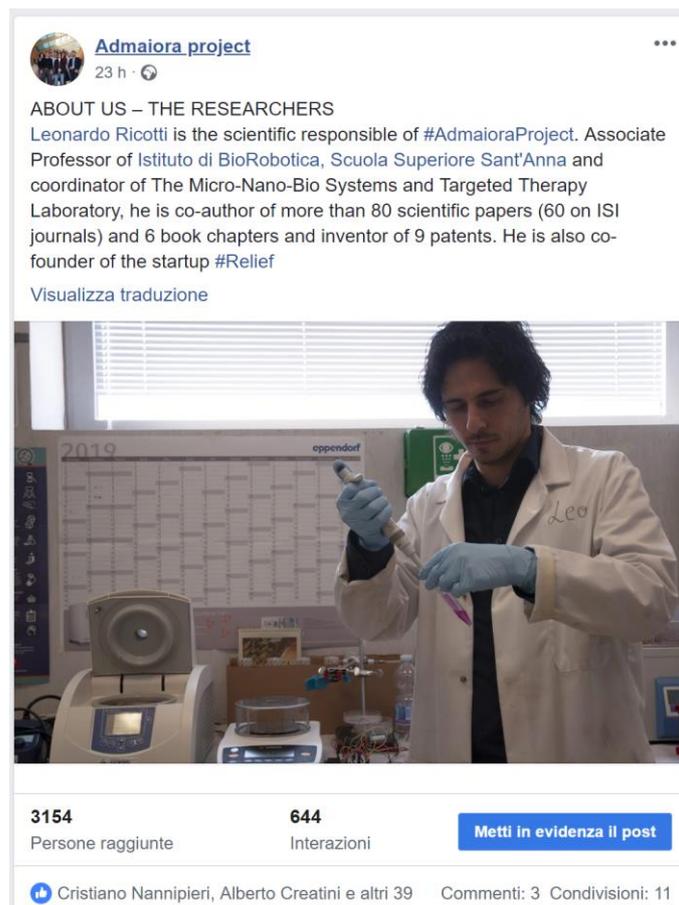
The key social networks used to promote ADMAIORS are Facebook and Twitter. Two dedicated ADMAIORA profiles have been created (Figure 5 and Figure 6). On April 30, the two profiles have a total of **125** followers. A total of **16** posts on Facebook and **15** tweets on Twitter have been created. Together, they have collected a total of 152 likes, 9 comments and have been shared 51 times. Figure 7 reports an example of Facebook post that reached 3154 people, fostered 644 interactions received 40 likes, 3 comments and 11 shares.



**Figure 5:** Screenshot of the ADMAIORA Facebook profile.



**Figure 6:** Screenshot of the ADMAIORA Twitter profile.



**Figure 7:** Example of a post published on the ADMAIORA Facebook profile.

### 3.3 Press releases and internet news

Figure 8 shows an internet news published by SSSA on its Institutional website, concerning the ADMAIORA project start and the correspondent kick-off meeting, held at the BioRobotics Institute.

SANT'ANNA MAGAZINE  
**NEWS**

< SANT'ANNA MAGAZINE

SANT'ANNA SCHOOL BIROBOTICS INSTITUTE RESEARCHERS OF EU-FUNDED ADMAIORA PROJECT OFFER A NEW PARADIGM FOR THE TREATMENT OF OSTEOARTHRITIS



Researchers of the EU-funded **ADMAIORA** (*ADvanced nanocomposite MAterials fOr in situ treatment and ulTRAsound-mediated management of osteoarthritis*), project through the **H2020** initiative are working under the supervision of Professor **Leonardo Ricotti** to combine regenerative therapy and ultrasound mediated targeted therapy as a novel strategy that has the potential to restore structure and function of damaged cartilage.

The kick-off meeting of four-year project **ADMAIORA** is bringing together the European partners to explore alternative treatments for Osteoarthritis (OA). Traditional pharmacologic therapies are incapable of reversing cartilage damage, which is the leading cause of disability in elderly people (15 million people in Europe aged 50 years and older). Current research focuses on the development of regenerative therapies and tissue engineering involving bioactive factors, adipose-derived stem cells implantation and ultrasound effects in cells migration.

Overall, the **ADMAIORA** *healthy and active ageing* paradigm, after validation in OA disease pre-clinical models, has the potential to reduce the OA-related healthcare costs: estimated

Osteoarthritis-related direct medical costs are 50 billion euros annually.

The Consortium partnership includes research institutes and companies **Istituto Ortopedico Rizzoli** - Bologna, **Bar-Ilan University** – Israel, **Regentis** (Israel), **IGT** (France), **PlasmaChem** (Germany), **Vimex** (Poland), and **HD Wireless** (Sweden).

"Our research team is developing a new system for ultrasound-mediated stimulation" – commented Leonardo Ricotti, as the **Micro-Nano-Bio Systems and Targeted Therapies** Lab. scientific coordinator. "Our investigators will perform cartilage regeneration in vitro studies in cooperation with researchers from the Istituto Ortopedico Rizzoli".

**Figure 8:** Internet press release on the ADMAIORA kick-off meeting.

The news fostered the interested of several website news and TVs, as described in the following clickable Web Press Review and demonstrating the efficacy of the ADMAIORA communication strategy:

[ANSA ITALIA](#)

[IL MESSAGGERO](#)

[SKY TG24](#)

[IL SECOLO D'ITALIA](#)

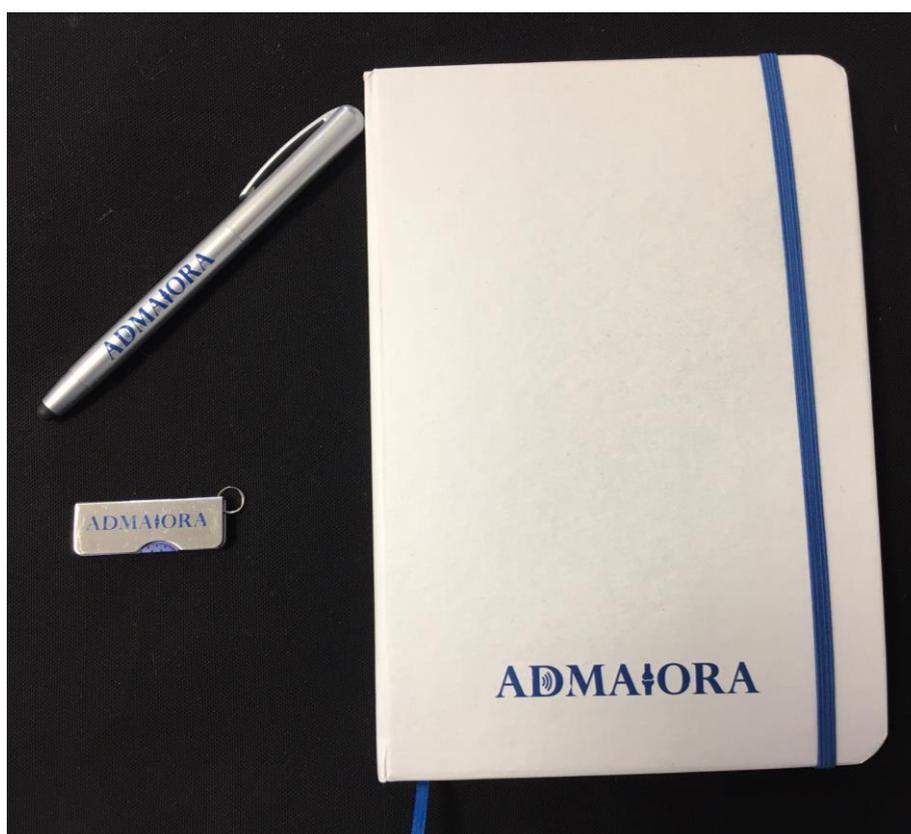
[LA NAZIONE](#)

[HEALTH ITALIA](#)

[IN SALUTE NEWS](#)

### 3.4 ADMAIORA gadgets

In addition to brochures, leaflets, posters, etc., SSSA already developed some ADMAIORA gadgets that will be used in targeted non-technical communication events (e.g. with end-users). They include notebooks, pens, USB drivers, etc. (Figure 9)



**Figure 9:** Examples of ADMAIORA gadgets produced by SSSA.

### 3.5 Special communication activities

In addition to the previously mentioned activities, less traditional ones have been also devised, in order to maximize the ADMAIORA communication efficacy. A list of such events, with corresponding targets groups and quantitative targets, is reported in Table 7.

Initiative	Description and tools	Target group(s)	Quantitative targets	How to
Non-technical project workshops	Four workshops organized to promote results to healthcare system actors and stakeholders (2) and to train OA patients and elderly people to the technologies under development, with <i>ad hoc</i> demos (2), thus to decrease the barriers for adoption of the project results. The stakeholder will have the opportunity of clarify doubts and ask questions in an open dialogue.	Healthcare system actors and stakeholders (2 events), OA patients and elderly people (2 events), general public (1 final event)	4 project workshops (1 per year), 120 attendees/workshop, 1 final event, with at least 400 attendees	For the first year of the project the goal is to organize an event on osteoarthritis and the potential benefits of this research theme on the European healthcare system. The venue of the event could be Pisa. The hope is to involve not only the universities and the world of scientific research, but also the decision makers, the health sector companies, the public institutions such as the Tuscany Region. For some of these

	A final event will allow the partners to communicate project results and experiences to the general public and to describe the possible pathways for future translation into the clinics of the project research.			activities, the Consortium will be supported by society engaged in the project, such as the S.I.G.A.S.C.O.T (Italian Knee Society Arthroscopy Sport Cartilage Orthopaedic Technologies, the ESCEO (European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Disease, the AMRER (Associazione malati Reumatici Emilia Romagna), and other ones.
ADMAIORA elderly marathon	An international marathon reserved to "over 60" will be organized. The event will properly followed by media.	Elderly people, sports practitioners, general public	Media coverage: at least 3 national (from different countries) and 1 international top-level TV channels, 7 newspapers and 45 web posts	Such event will be concerted with policy makers, once decided the precise location. The project logo, website, etc. will be displayed over the whole path. An informative press conference also concerning the project activities will be organized at the end of the marathon.
Informative workshop co-organized with a professional soccer society	Informative event on the ADMAIORA potential for both young top-level athletes and elderly people, co-organized with the a professional soccer society.	Clinical community, healthcare systems, sports practitioners, general public	Media coverage: at least 1 national and 1 international top-level TV channels, 5 newspapers and 25 web posts	This communication event will be initially pursued by leveraging a collaboration between SSSA and the chief physician of the Napoli soccer team (Prof. Alfonso De Nicola). The Napoli professional soccer society is one of the top Italian soccer teams, enrolled in the "Serie A" and participating in European leagues. This event is thought to give an important international visibility to the project.
Communication event co-organized with CONI, at the Olympic games of Tokyo 2020	Communication event to be held in conjunction with the CONI (Italian Olympic Committee).	General public	Media coverage: at least 15 national and 5 international top-level TV channels, 25 newspapers and 150 web posts	CONI has been engaged by the Project Coordinator through Dr. Diego Nepi Molineris (CONI Marketing and Development Director). The ADMAIORA Project Coordinator already met the CONI representatives (Figure 10) on November 12,

				2018. In the following months, a preliminary informal agreement has been concerted, for the organization of a communication event during the Olympic games of Tokyo 2020. This event is thought to receive a capillary media coverage.
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**Table 7:** Special communication events devised for ADMAIORA.



**Figure 10:** Preliminary meeting between the ADMAIORA Project Coordinator and CONI managers.

## 4 Preliminary exploitation plan

This preliminary Exploitation Plan is intended to provide an overview of the strategy through which the ADMAIORA Consortium intends to pave the way towards commercialization for the technologies developed in the project course. Together with a main business plan led by REGENTIS, ADMAIORA plans to enable the growth of a series of lateral business opportunities for the SMEs involved in the project.

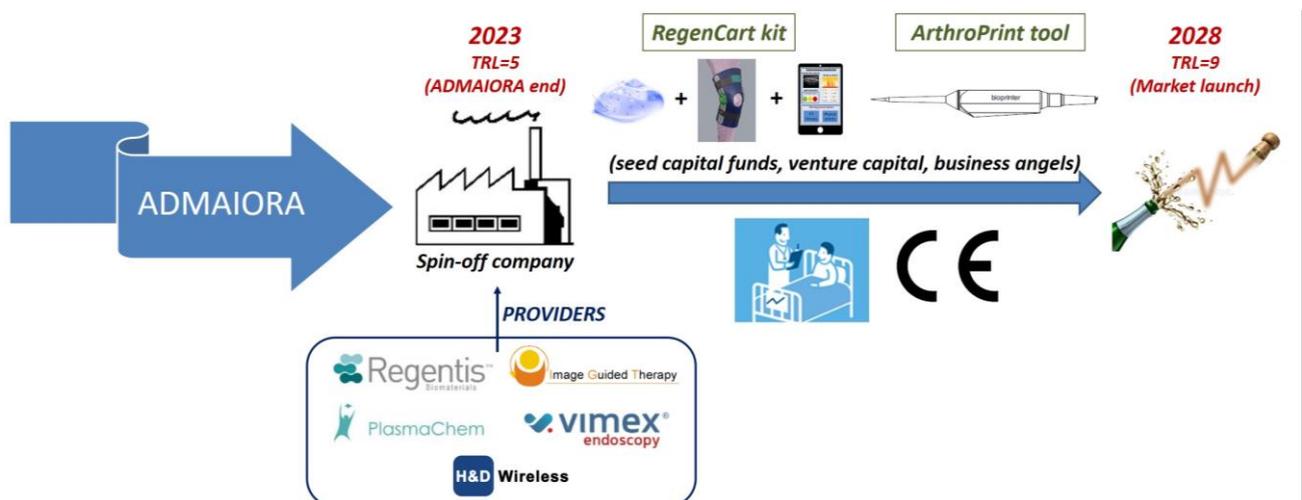
### 4.1 Main outcomes and general roadmap

After the project end, the ADMAIORA technologies will be at a TRL of 5. Such technologies will consist of separate components, whose exploitation could be led by different industrial players, such as:

1. a biosynthetic hydrogel (REGENTIS) with embedded responsive nanoparticles (PLASMACHEM);
2. a stimulation/monitoring brace (IGT);
3. a software App and an Internet-of-Things (IoT) framework connected with the brace (HDW);
4. a handheld 3D bioprinting arthroscopic tool for hydrogel delivery into the joint in a minimally invasive way (VIMEX).

All these elements will be designed *ad hoc* for the final ADMAIORA objective and will thus possess specific and application-driven characteristics. From a commercial exploitation viewpoint, the first three components (nanocomposite hydrogels, stimulation/monitoring brace and software/IoT architecture) are intimately connected and must be considered a single product. In the following we will refer to such product as the **RegenCart kit**. The fourth element (the handheld bioprinting tool) is still connected to the nanocomposite hydrogel, but it can be considered a more general-purpose tool, which may find exciting applications also in other medical/surgical domains. This is referred to as the **ArthroPrint tool**.

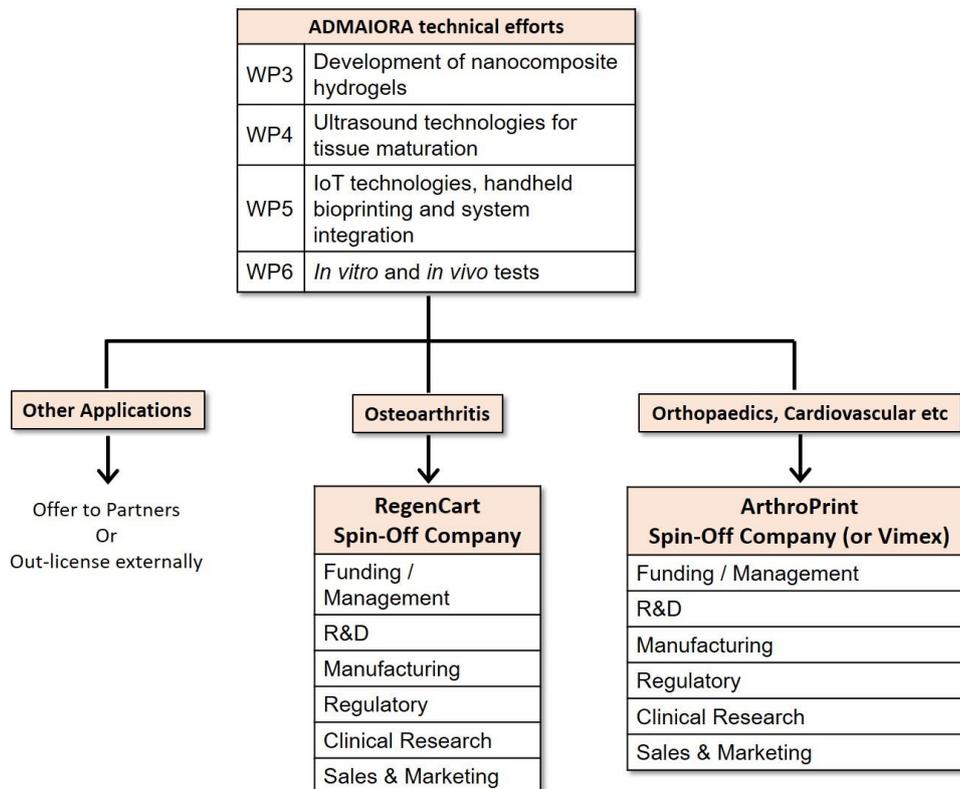
Concerning these two elements, the planned roadmap for maximizing the exploitation is depicted in Figure 11:



**Figure 4:** Pathway towards commercialization envisaged after the project end.

After the project end, the creation of a spin-off company (“NewCo”) is expected. The mission of such company will be to bring to the market and to commercialize the two mentioned products: the *RegenCart* kit and the *ArthroPrint* tool. All partners (academic and industrial ones) will evaluate their possible participation in such a company, and the correspondent conditions. The Cosortium Agreement, signed by all partners, details all the conditions regulating partnership shares and IP rights. The SMEs included in the ADMAIORA Consortium will be commercial providers of the spin-off company, concerning the key technologies to be brought on the market. Thanks to external funding (seed capital funds, venture capital, business angels, etc.), the spin-off company is expected to perform appropriate clinical trials, to receive the CE mark and to launch the products on the market in 2028.

A preliminary business plan has been devised for “NewCo”, to bring the *RegenCart* product from the laboratory to the market (section 4.2). Additionally, a second spin-off company may be created to commercialize the *ArthroPrint* technology (or VIMEX could take the leadership for the exploitation of this tool). Such a handheld printing tool could find application across a wider field of surgical specialties than just osteoarthritis (section 4.3). Any IP and know-how developed during the course of the project that will be outside the primary focus of ADMAIORA (*i.e.* not associated with the treatment of early/moderate osteoarthritis) will be first presented to partner organizations for potential sub-licensing or, failing that, offered to other companies. This plan is depicted in Figure 12:



**Figure 5:** Possible exploitation strategies for the different technologies, IP and know-how developed in the project.

## 4.2 Preliminary business plan for the RegenCart kit

The primary objective of the spin-off company NewCo will be to commercialize *RegenCart* and *ArthroPrint* for the treatment of early to moderate osteoarthritis. NewCo will achieve this by utilizing the knowledge and IP developed during the course of the ADMAIORA project as the basis for a stand-alone company with the necessary capabilities to obtain CE mark clearance in the EU. Once approved for sale, these products may be marketed either directly by NewCo or in conjunction with a strategic partner.

### Market need:

Osteoarthritis (OA) is the most common chronic joint disease involving a progressive damage and loss of cartilage, remodeling of subchondral bone, osteophyte formation, weakening of periarticular muscles and thickening of the joint capsule (Figure 13)<sup>1</sup>. OA most commonly affects the knees since the knees are the major weight bearing joint, however it is also prevalent in the hips, and to less extent the shoulders, feet, spine and other joints<sup>2</sup>.



**Figure 6:** Depiction of a healthy knee (left) and a knee affected by osteoarthritis (right).

In early stages, arthritis of the knee is treated with nonsurgical conservative approach such as changes in activity level, weight reduction, pain relievers such as ibuprofen or nonsteroidal anti-inflammatory drugs (NSAIDs), along with physical therapy and corticosteroid injections<sup>3,4</sup>. Extended use of NSAID and corticosteroid treatments may produce serious side effects, specifically elderly patients are at heightened risk for serious gastrointestinal and cardiovascular events.

Inter-articular visco-supplements is a treatment option for early to moderate OA when other methods of non-surgical pain relief have failed to provide sufficient pain relief. In this procedure, hyaluronic acid (HA), the lubricating component of synovial fluid, is injected into the knee joint in order to replenish the original HA that was diluted and abolished in the inflamed joints. Visco-supplements have a good safety record; however, their efficacy is marginal and has been questioned in several placebo-controlled trials<sup>5,6</sup>.

The unmet need is for a true disease modifying treatment that could slow or even reverse joint structural destruction and thus either delay or prevent the occurrence of late-stage OA which eventually leads to joint replacement and huge socio-economic burden<sup>7, 8</sup>. Notably, the cost of OA in Europe is currently estimated at 0.5% of gross national product<sup>9</sup>.

<sup>1</sup> R. F. Loeser, *et al.* Osteoarthritis: a disease of the joint as an organ. *Arthritis Rheumatoid*. 64: 1697 (2012)

<sup>2</sup> <https://www.oarsi.org/which-joints-does-osteoarthritis-affect>

<sup>3</sup> G. Filardo, *et al.* Non-surgical treatments for the management of early osteoarthritis. *Knee Surgery, Sports Traumatology, Arthroscopy*. 24(6) 1775-1785 (2016)

<sup>4</sup> H. S. Kan, *et al.* Non-surgical treatment of knee osteoarthritis. *Hong Kong medical journal* (2019).

<sup>5</sup> D.C. Crawford, *et al.* Conservative management of symptomatic knee osteoarthritis: a flawed strategy? *Orthopedic Reviews*. 5: 1 (2013)

<sup>6</sup> D. Jevsevar, *et al.* Viscosupplementation for osteoarthritis of the knee: a systematic review of the evidence. *Journal of Bone and Joint Surgery*. 97(24): 2047-2060 (2015)

<sup>7</sup> M. A. Karsdal, *et al.* Disease-modifying treatments for osteoarthritis (DMOADs) of the knee and hip: lessons learned from failures and opportunities for the future. *Osteoarthritis and Cartilage*. 24(12) 2013-2021 (2016)

### Target patients and overall market:

OA affects nearly 10% -15% of the population over the age of 60 worldwide<sup>10,11</sup>. It is estimated that it affects about 30 million Americans, mainly adults over age 45, while in Europe this number is estimated around 40 million<sup>11</sup>. This number is rapidly growing, with estimates suggesting that this number will almost double in the next decade. To calculate the target population, among those subjects affected by OA, only ~ 20% of them accepts to undergo a treatment based on injectable materials (internal estimate based on surgeons' feedback). A study on the patient's preference between oral and injectable treatment for rheumatoid arthritis supports for this internal estimate of 20% acceptance of injectable therapy<sup>12</sup>.

Thus, NewCo's target population is 8 million people in Europe and a further 6 million people in the US.

According to a recent report by Persistence Market Research (PMR)<sup>13</sup>, the global non-surgical OA treatment market was valued at \$ 7.9 billion and is expected to rise to a valuation of \$ 11.6 billion by the end of 2025, with a CAGR of 4.8%. In addition, the surgical joint replacement market is estimated at a further \$ 15 billion and to grow at 4% per year<sup>14</sup>. Key market drivers are the aging population, rising obesity rates and demand for active lifestyles among the older as well as younger generations. In addition, there is an increase in OA in the Millennial generation caused by sports-related injuries.

### NewCo Products

The RegenCart kit will include the following elements:

1. a prefilled vial or syringe containing the biosynthetic nanocomposite hydrogel to be administered in hospital setting (Figure 14-1). This hydrogel will contain carbon-based nanofillers for enhanced strength and higher lubrication and piezoelectric nanoparticles for indirect electric stimulation of encapsulated cells by low-intensity ultrasound. The hydrogel injection as a paste will ease its in-situ bio-printing. Appropriate instructions will be provided about its mixing with autologous stem cells (density needed, modality, etc.) and UV exposure parameters to crosslink the hydrogel construct. The mixing/crosslinking will be automatic, if the clinician will use the *ArthroPrint tool*, or manual if the clinician will use an open surgery approach or traditional arthroscopic tools;
2. A stimulation/monitoring brace (Figure 14-2) provided with two low-intensity pulsed ultrasound (LIPUS) transducers dedicated to stimulation, one TELEMED ultrasonic probe

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<sup>8</sup> P. S. E. Davies, et al. Disease-modifying osteoarthritis drugs: in vitro and in vivo data on the development of DMOADs under investigation. *Expert opinion on investigational drugs*. 22(4): 423-441 (2013)

<sup>9</sup> P. G. Conaghan, et al. Osteoarthritis research priorities: a report from a EULAR ad hoc expert committee. *Annals of the rheumatic diseases*. 73(8): 1442-1445 (2014)

<sup>10</sup> Priority Medicines for Europe and the World 2013 Update ([https://www.who.int/medicines/areas/priority\\_medicines/Ch6\\_12Osteo.pdf](https://www.who.int/medicines/areas/priority_medicines/Ch6_12Osteo.pdf))

<sup>11</sup> Arthritis Foundation. Arthritis By the Numbers / Book of Trusted Facts & Figures. 2018; v2; 4100.17.10445 (<https://www.arthritis.org/Documents/Sections/About-Arthritis/arthritis-facts-stats-figures.pdf>)

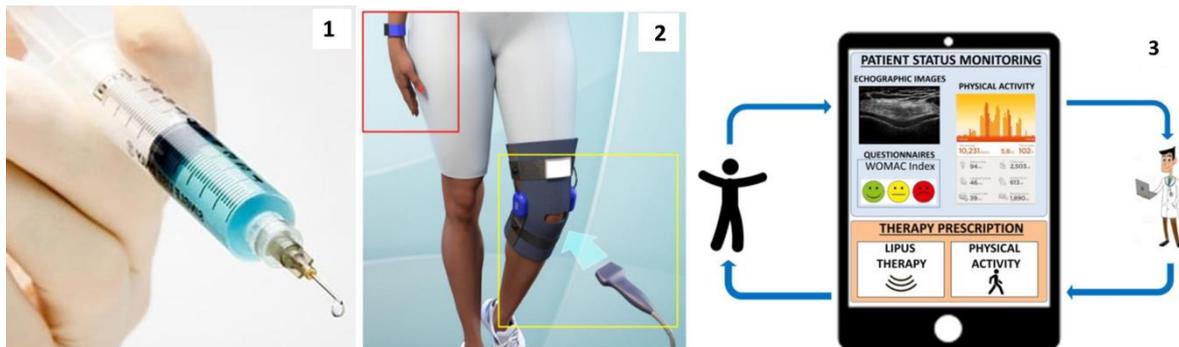
<sup>12</sup> N. Barclay, et al. Patient preference for oral versus injectable and intravenous methods of treatment for rheumatoid arthritis. *Value in Health*. 16(7): A568 (2013)

<sup>13</sup> Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025), published on March 2018

<sup>14</sup> US and European markets for joint arthroplasty products. Meddevice tracker (2016)

for US imaging and a bracelet with an embedded IMU. This element will be rented to the patient and used at home for a limited period.

3. A software App (Figure 14-3), allowing a bidirectional communication between the stimulation/monitoring brace, the patient's smartphone and an IoT architecture connecting the patient to the clinician. This element will be used at home for a limited period: it will be activated in correspondence to the brace rental and will expire at the end of the brace rental period.



**Figure 7:** Components of the *RegenCart* kit.

### Intellectual Property:

#### a) Knowledge management and protection:

IP Rights (IPR) is ruled by the Consortium Agreement (CA). Here, all provisions related to the management of IPR including ownership, protection and publication of knowledge, access rights to knowledge and pre/existing know-how as well as issues of confidentiality, liability and dispute settlement are laid down in detail and agreed. The IPR management strategy has been defined in accordance with the indication provided by the Guide to Intellectual Property Rules for European projects available on the H2020 website and customized taking into account the peculiarities of the project approach and expected results.

As a first step, the partners identified background and foreground knowledge at the beginning of the project. Background knowledge includes all intellectual property that partners possess, that will be used in the project and may be accessed by the Consortium for the sole purpose of project collaboration; foreground knowledge will be generated by the project activities and its ownership will be assigned to specific partners or will be subjected to a default joint ownership regime, and it will be protected as agreed by the Consortium in the CA.

The ADMAIORA partners' intention is to guarantee an exclusive license to the spin-off company that will be established at the end of the project, concerning the patents related to the *RegenCart* product. Any lateral results may be commercialized by a single ADMAIORA SME. A royalties-based policy will be adopted to compensate such *a priori* exclusive license. Specific conditions and royalty percentages will be defined at a later stage.

#### b) IP Current status:

In the first months of the ADMAIORA project, the following patent application has been submitted:

- Patent application No. 102019000002697 titled "*Materiale e sistema per il trattamento terapeutico di articolazioni (Material and system for the therapeutic treatment of joints)*" submitted in Italy in the name of all ADMAIORA partners on February 25<sup>th</sup>, 2019.

This patent refers to the key elements of the ADMAIORA approach and will be essential to protect and commercialize the *RegenCart* product.

In addition, the ADMAIORA Consortium is conducting a continuous intellectual property landscaping search through selected patent attorneys. Furthermore, a due-diligence of the ADMAIORA patent portfolio has been recently performed by an Italian IP consultant. The conclusion of this due-diligence program was that the ADMAIORA approach as described in the proposal and/or grant agreement does not appear to pose obstacles for patentability.

### Competition:

The market competition for treating osteoarthritis can be broken down into the following segments:

- Physical Therapy:  
Most patients suffering from OA are initially treated with a course of physical therapy intended to improve joint function through strengthening the primary muscles around the knee. Typically, these treatments, at best, only delay subsequent, more aggressive approaches and provide limited long-term benefits.
- Viscosupplements:  
The use of hyaluronic acid (HA) viscosupplements is currently the most prevalent therapeutic approach for moderate knee osteoarthritis patients who are either non-responders to NSAIDs and corticosteroid injections or which have developed adverse side effects as a result of treatments with these non-specific pharmacological agents<sup>15</sup>. HA is the natural lubricant in joints and so inter-articular injections of HA aim to replenish the natural HA present in synovial fluid and so restore normal joint lubrication. Viscosupplement products are classified as Class III devices in Europe and considered high-risk devices. There is considerable controversy about the efficacy of HA injections with a number of double-blind clinical studies questioning the long-term benefits. However, the lack of effective, alternative treatments has caused many surgeons to continue using these products, regardless of the literature.  
The viscosupplementation market is comprised of a dozen or more HA manufacturers providing products that are based on either standard or modified HA. Key players are: Sanofi (France), Anika Therapeutics, Inc. (US), Ferring B.V. (Switzerland), Ferring Pharmaceuticals (Switzerland), Fidia Farmaceutici (Italy), Lifecore Biomedical LLC (US), Seikagaku Corporation (Japan), Smith & Nephew Plc (UK), Zimmer Biomet (US), Allergan (Dubai), F. Hoffmann-La Roche (Switzerland), HTL Biotechnology (France). The global viscosupplementation market was estimated at 3.2 B\$ in 2017 and is expected to reach 5.3 B\$ by 2023 at a CAGR of 8.9% during the forecast period<sup>16</sup>. The Sanofi

<sup>15</sup> N. Arden, et al., Atlas of Osteoarthritis Second edition (2018), Springer Healthcare in collaboration with the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO).

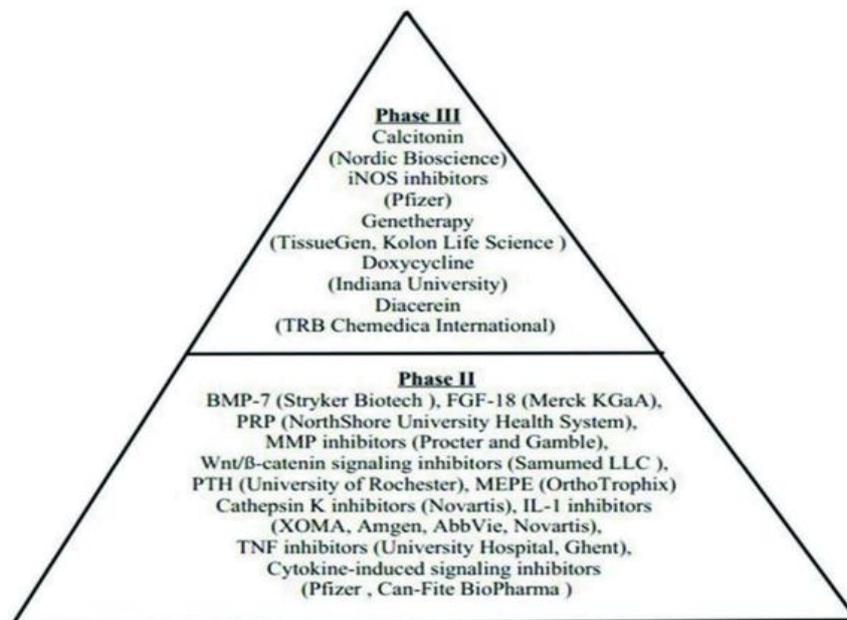
<sup>16</sup> Market Search Future Report: <https://www.medgadget.com/2019/02/viscosupplementation-market-estimated-usd-5-34-bn-till-2023-by-sanofi-ferring-pharmaceuticals-zimmer-biomet-allergan-etc-mrfr.html>

products, Synvisc and Synvisc-One (Figure 15), share alone 56% of the viscosupplementation market <sup>17</sup>.



**Figure 8:** SynviscOne (Sanofi) Hyaluronic acid single injection viscosupplementation product.

- **Drugs:**  
Various Disease-modifying OA drugs (DMOAD), *i.e.* those that aim to induce structural changes in the joints leading to either slow-down of the degenerative process or even to regenerate tissues are currently in clinical development. Figure 16 lists some of these emerging therapies.

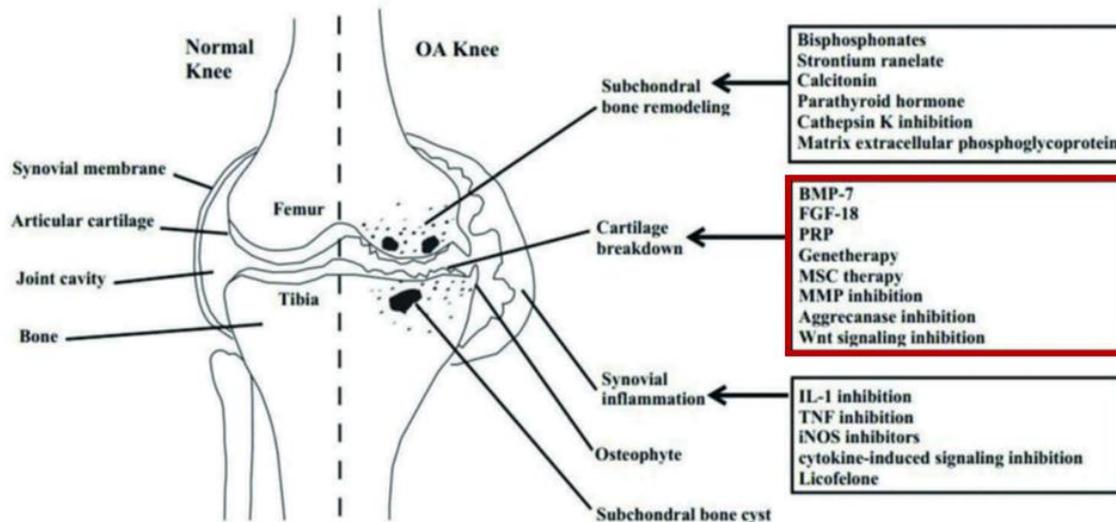


**Figure 96:** DMOAD that are in clinical development (Phase II or III).

The DMOAD target 3 major tissues: sub-chondral bone, cartilage and synovium. Figure 17 shows the various DMOAD and their target tissues. The DMOAD currently in clinical phase that target cartilage include (1) Growth factors: BMP-7 (Phase II, Stryker), FGF18 (Phase II, Merck), (2) Platelet-rich plasma (PRP; Phase II), (3) Gene therapy (Phase III, TissueGen and Kolon Life science), (4) Small molecules/protease inhibitors: MMP inhibitors (Phase II;

<sup>17</sup> Medtech Insight Report on U.S. Markets for Orthopedic Biomaterials -2013

Procter & Gamble), Wnt-catenin inhibitor (Samumed LLC) and (5) Stem cells therapy (e.g ADIPOA2 EU-funded project-Injection of Adipose Derived Stem Cells for OA- Phase IIb).



**Figure 107:** DMOAD divided based on their target tissue. DMOAD designed to alt/reverse cartilage degeneration are shown in the red frame.

- **Joint Replacement:**  
Once alternative low-invasiveness treatments have failed, many patients undergo joint replacement surgery. This involves surgically excising the diseased joint and typically replacing it with a metal-on-plastic prosthesis. This procedure is now recognized as one of the most successful innovations of the 20<sup>th</sup> century. However, for all its success, total knee replacement surgery is extremely invasive and requires extensive post-operative physical therapy before any benefits can be achieved. Recent attempts to introduce less invasive designs of prosthesis and the use of robots have been introduced but still require extensive excision of the underlying bone, leading to pain and abnormal joint kinematics. The current worldwide market for total joints is estimated at around \$17 billion, growing at 3.8% a year and that for knees at around \$9 billion and growing at 4.9% per year<sup>18,19</sup>. In the OECD countries, the number of total knee replacement surgeries each year is 163 per 100,000, with 190 in Germany, 145 in France, 141 in UK and 226 in the United States<sup>20</sup>.

#### Competitive Advantages of the NewCo Technology:

The primary advantages of the ADMAIORA approach to regenerating cartilage damaged by osteoarthritis are:

<sup>18</sup> Major Orthopedic Joint Replacement Implants Market Global Opportunities And Strategies To 2022

<sup>19</sup> Joint Reconstruction Market by Type (Ankle Replacement, Digit Replacement, Elbow Replacement, Hip Replacement, Knee Replacement, Shoulder Replacement), by Geography (North America, Europe, Asia-Pacific, Rest of the World) - Global Analysis & Forecast to 2019

<sup>20</sup> I. Papanicolas, et al. Health care spending in the United States and other high-income countries. *Journal of American Medical Association*. 319(10): 1024-1039 (2018)

- A multi-approach therapy: a unique combination of smart nanomaterial, autologous efficacious stem cells, efficient surgical procedure, external pro-regenerative stimulus (LIPUS) and online monitoring of treatment;
- Grounded on 'personalized' treatment: (1) Precise filling of any shape/geometry of defect by smart hydrogel, (2) application of the patient own stem cells (autologous), (3) online, continuous monitoring of the individual patient using smart brace/IoT, (4) enhancement of treatment by LIPUS according to patient needs;
- Double action: (A) immediate pain relief through the use of strong, elastic and lubricious hydrogel which will shield the exposed bony parts of the joints from rubbing against each other, (B) disease-modifying action through the inclusion of autologous stem cells and continuous stimulation of these cells to produce cartilage matrix thus to regenerate the missing cartilage. To date, none of the disease-modifying OA drugs has immediate pain relief capabilities. Likewise, the HA viscosupplement products that aim to reduce pain, do not address the unmet need for cartilage regeneration.

### Management:

At this preliminary status of the development plan, it is not possible to identify specific members of the NewCo's management team. However, at the appropriate time, a strong, experienced group of medical device executives will be appointed in all key departments of the company. There are numerous potential candidates for these roles, thus these positions will be probably easily filled.

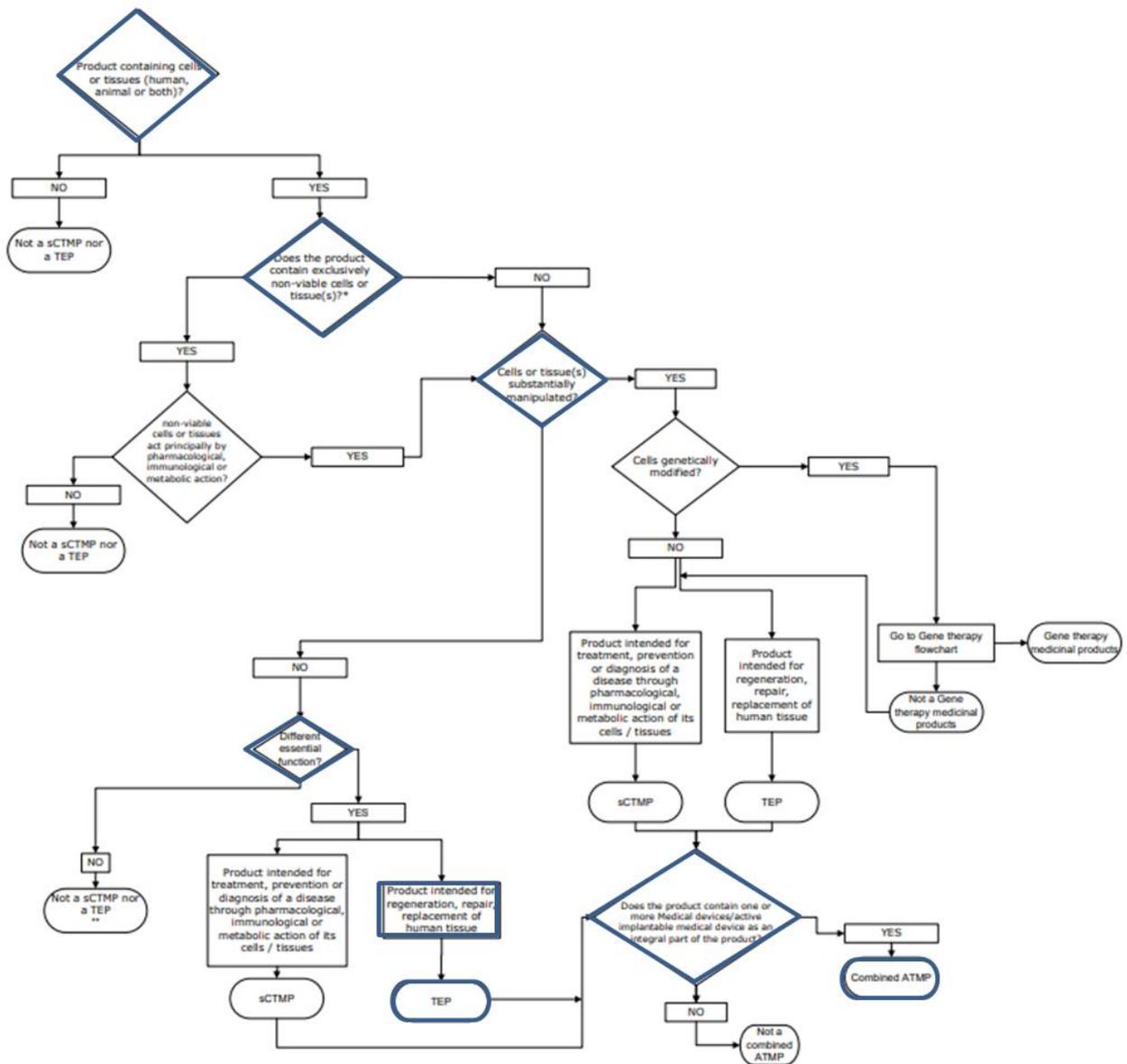
### Development Plan:

#### a) Regulatory Status and Procedure

At this stage of development and given the role of the autologous adipose stems cells in conjunction with ultrasound stimulation, the product will likely be considered a Combined Advanced Therapy Medicinal Product (ATMP), according to 'Procedural advice on the evaluation of combined advanced therapy medicinal products and the consultation of Notified Bodies in accordance with Article 9 of Regulation (EC) No. 1394/2007'. The use of the adipose stem cells, even without a hydrogel carrier, will be regulated under ATMP since according to the regulations "*adipose cells transplanted to other than fat tissue are considered to be ATMPs*"<sup>21</sup>. Specifically, within ATMPs, the adipose stem cells fall under Tissue Engineering product (TEP): "*TEPs are used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue*". The use of cells with the hydrogel will lead to regulation as Combined ATMP - see the flow chart in Figure 18.

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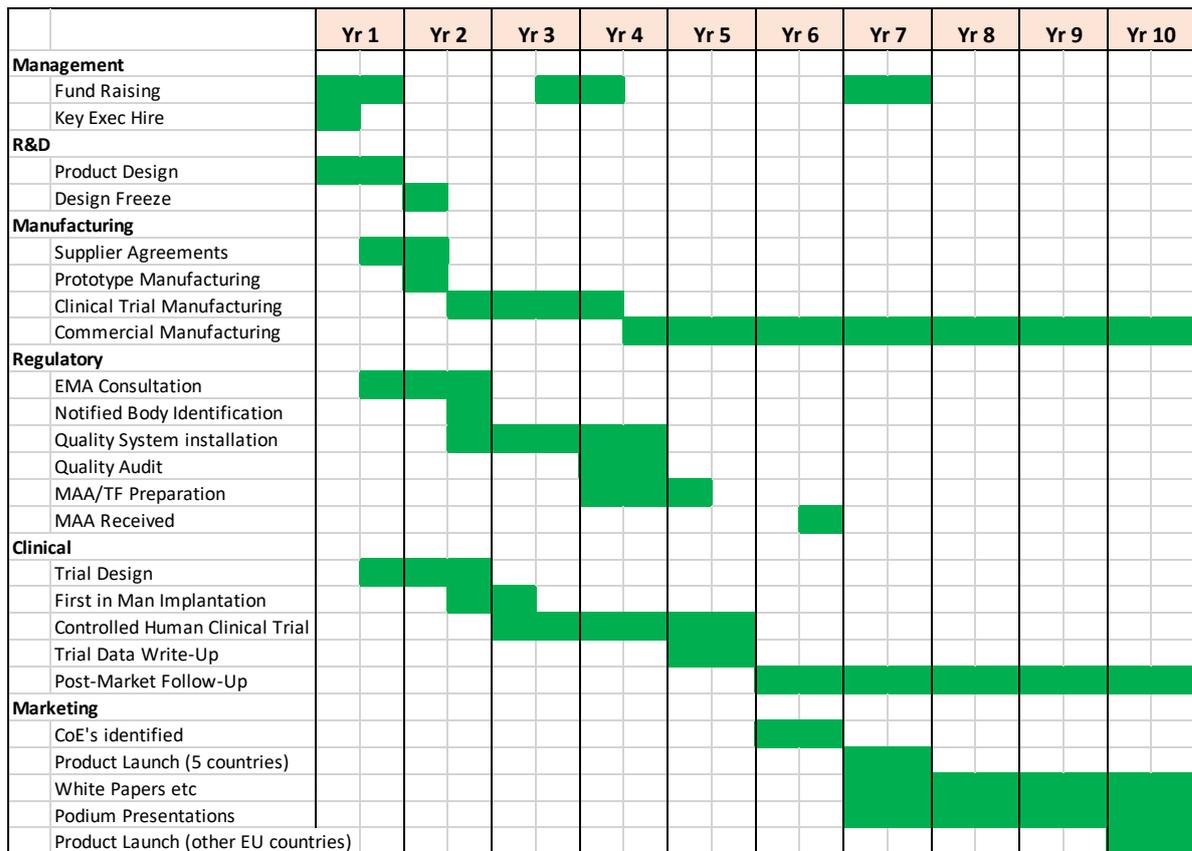
<sup>21</sup> [EMA/CAT/600280/2010 rev.1: Reflection paper on classification of advanced therapy medicinal products - https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-classification-advanced-therapy-medicinal-products\\_en-0.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-classification-advanced-therapy-medicinal-products_en-0.pdf)



**Figure 118:** Flow chart to select the most appropriate regulation criteria.

As such and in order to win approval to market in the member EU states, companies are required to submit to EMA for an initial consultation which determines the appropriate regulatory procedure, including the need for involvement of an appropriate Notified Body. Once the development process will be complete and the necessary preclinical and clinical data will be generated, NewCo will submit a Marketing Authorization Application (MAA) to the Committee for Advanced Therapies (CAT), as shown in Figure 19:





**Figure 20:** Timetable for NewCo Development and Marketing.

Pricing Projection:

Overall, reimbursement will be the object of negotiation with the various country health authorities. However, taking into account the risk/benefit profile of the treatment and its related expected improvement in terms of quality of life and savings in overall healthcare (pain killing drugs, physical therapy, home care, etc.), it is likely that the ADMAIORA-derived product will be appraised in a positive way by Health Technology Assessment (HTA) agencies for both its valuable cost-effectiveness and cost per quality adjusted life years (QALY). Once in commercial release, an average price for the *RegenCart* of €4,000 is projected. This pricing hypothesis does not include the instruments/kits needed to obtain the stem cells (these are currently commercially available and therefore will be not produced and marketed by NewCo).

Marketing Plan:

The initial target market for *RegenCart* is the EU, in particular France, Germany, Italy, Spain and UK, which together correspond to 43% of the target population (thus, 1.61 million potential patients). In the long-term, the USA market will be also targeted. Initial sales and marketing efforts in the targeted countries will be focused on developing key Centers of Excellence (CoE) which can both utilize the product and act as learning centers for other surgeons. These CoEs will be chosen from the sites conducting the clinical trial and thus the surgeons will have extensive experience of using *RegenCart*. Additional marketing efforts will be focused on presenting data at both local and international surgeon meetings (ESKA,

AAOS, ICRS etc). Sales support for *RegenCart* will be provided by a network of direct NewCo sales employees where ever appropriate with additional assistance from local distributors when necessary. A preliminary Profit & Loss plan for NewCo is shown in Figure 21.

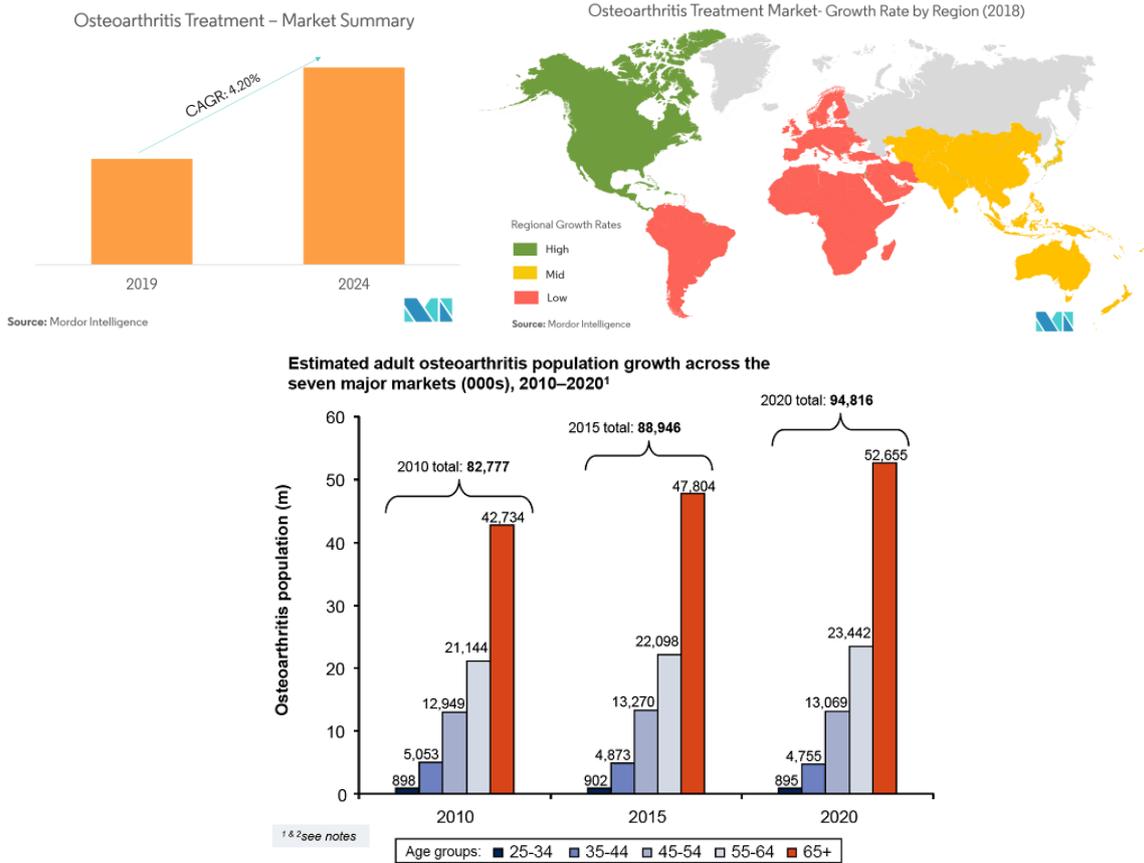
	Yr 1	Yr 2	Yr 3	Yr 4	Yr 5	Yr 6	Yr 7	Yr 8	Yr 9	Yr 10
<b>Potential Number of Patients (F, D, S, I, UK)</b>	1,600,000	1,600,000	1,600,000	1,600,000	1,600,000	1,600,000	1,600,000	1,600,000	1,600,000	1,600,000
<b>Penetration (%)</b>	-	-	-	-	-	-	0.5%	1.0%	1.3%	1.5%
<b>Procedures</b>	-	-	-	-	-	-	8,000	16,000	20,000	24,000
<b>Average Sales Price</b>	€4,000	€4,000	€4,000	€4,000	€4,000	€4,000	€4,000	€4,000	€4,000	€4,000
<b>Revenues (,000)</b>	-	-	-	-	-	-	€32.0	€64.0	€80.0	€96.0
<b>Cost of Goods Sold</b>	-	-	-	-	-	-	€12.8	€22.4	€24.0	€24.0
Gross Margin	-	-	-	-	-	-	€0.6	€0.7	€0.7	€0.8
<b>Gross Profit</b>	-	-	-	-	-	-	€19.2	€41.6	€56.0	€72.0
<b>Expenses</b>										
Sales							€9.6	€19.2	€24.0	€28.8
Marketing							€4.8	€9.6	€12.0	€14.4
R&D	€5.0	€5.0	€10.0	€12.0	€12.0	€12.0	€12.0	€12.0	€12.0	€12.0
Admin	€1.5	€1.8	€2.2	€2.6	€3.1	€3.4	€3.8	€4.1	€4.6	€5.0
<b>TOTAL</b>	€6.5	€6.8	€12.2	€14.6	€15.1	€15.4	€30.2	€44.9	€52.6	€60.2
<b>EBITDA</b>	-€6.5	-€6.8	-€12.2	-€14.6	-€15.1	-€15.4	-€11.0	-€3.3	€3.4	€11.8
<b>Cumulative Profit /(Loss)</b>	-€6.5	-€13.3	-€25.5	-€40.1	-€55.2	-€70.6	-€81.5	-€84.9	-€81.4	-€69.6

**Figure 21:** Expected Profit & Loss plan for the *RegenCart* product.

### 4.3 Lateral business plan for the ArthroPrint tool

A second spin-off company may also be set up to commercialize the *ArthroPrint* product (but Vimex could also decide to take the leadership of the tool exploitation, being already in this market segment). Since the potential application of *ArthroPrint* extends far beyond its initial use in conjunction with *RegenCart*, there exists a significant opportunity for *ArthroPrint* across a wide spectrum of surgical fields.

The main potential market for the device will be orthopedics, in particular osteoarthritis treatment. The initial customers of this tool will be orthopaedic surgeons at both public and private hospitals and its success is expected to be partly connected with the efficacy and market adoption of the *RegenCart* product as the main result of ADMAIORA project. According to the World Health Organization, around 10% to 15% of all adults aged over 60 have some degree of osteoarthritis, with high prevalence among women than men. According to the UN, by 2050, people aged over 60 will account for more than 20% of the world population (Figure 22). Of this 20%, a conservative estimate of 15% will have symptomatic osteoarthritis, and one-third of this population will be severely disabled. Consequently by 2050, 130 million people will suffer from osteoarthritis globally. Osteoarthritis accounts for more than 50% of the entire musculoskeletal diseases. According to the Global Burden of Disease 2010 study, Osteoarthritis is 11<sup>th</sup> highest contributor to global disability.



**Figure 22:** Epidemiological forecasts for osteoarthritis.

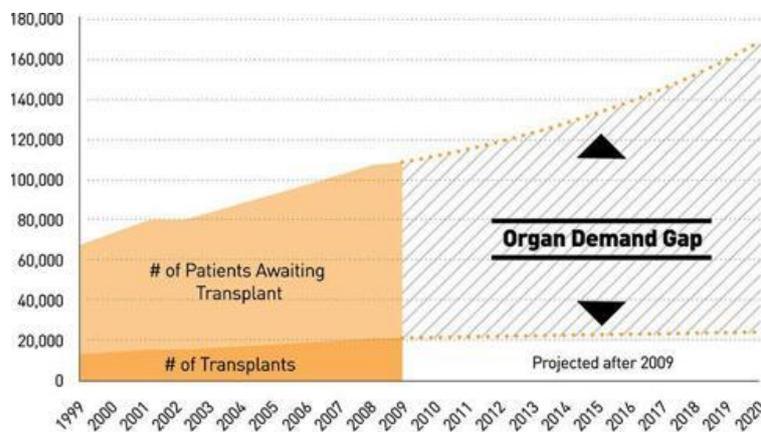
However, the handheld instrument is also expected to find additional application domains, especially in cardiovascular and gastrointestinal surgery. A controlled handheld bioprinting of UV-crosslinkable materials (eventually loaded with stem cells) could be desirable, for example, in organ regeneration (liver, kidney, etc.) as well as to treat valvular abnormalities and congenital heart defects, aortic disorders, ischemic heart diseases and fistulas etc., and many others laparoscopic procedures for example innovative hernia treatment. Table 8 shows the market size for the different segments that could be addressed by the *ArthroPrint* product and the envisioned market penetration starting from 2028 (assuming similar considerations to the ones made above for certification issues and clinical trials).

Market Area	Key competitors	Addressable market size analyzers	Target Market Share in 2028	Target Market Share in 2034
Surgical tools for OA treatment (connected with the use of the <i>RegenCart</i> product)	Arthrex, Conmed, Johnson & Johnson, Karl Storz, Aesculap. (B. Braun), Smith & Nephew	€ 4.17 billion (CAGR: 6.1%)	0.5%	4%

Surgical tools for cardiovascular procedures	Becton, Dickinson and Company, B. Braun Melsungen, Teleflex, Medline Industries, KLS Martin Group	€ 1.16 billion (CAGR: 7.1%)	0.25%	0.75%
Surgical tools for gastrointestinal tract interventions	Boston Scientific, Johnson & Johnson, Karl Storz	€ 0.9 billion (CAGR: 10.53%)	0.1%	0.5%

**Table 8:** Preliminary analysis of business opportunity for the ArthroPrint product.

The *ArthroPrint* product is promising in terms of possible future market opportunities. The *ArthroPrint* will be a device which can be used in the wide area of 3D Bioprinting Market, which is valued at around USD 484.50 Million in 2017 and is evaluated to achieve USD 3250.60 Million before the finish of 2024, developing at a CAGR of 31.25% in the vicinity of 2018 and Forecasting 2024 (BMRC MD 116, 23-Jun-2018). The pivotal factors contributing to the growth of the 3D Bioprinting Market includes rising incidences of lifestyle oriented diseases, massive demand for organ & tissue transplants and improvement in life expectancy rate. Limited number of organ donors has also attributed towards the growth of the 3D bioprinting market. According to U.S. Department of Health & Human Services, in every 10 min an individual is added to the national transplant waiting list. The growth in the waiting list of transplants (Figure 23) has created a potential for the 3D bioprinted implants and organs.



**Figure 23:** Trend of patients awaiting organ transplant in recent years.

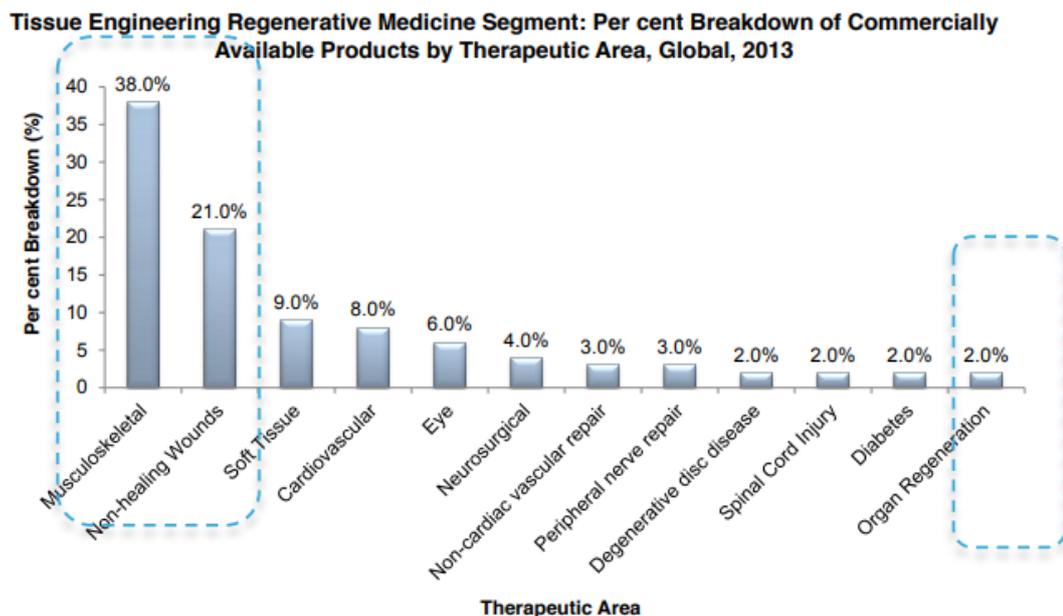
Interest in 3D bioprinting has been gaining momentum in recent years. Between 2014 and 2015, the market welcomed numerous 3D bioprinting companies, and new start-ups, spin-outs, and subsidiaries are continuing to emerge. Though investment in the field has been driven on by the futuristic goal of providing solutions for regenerative by way of fabricating organs for transplant, more realistic applications in product development and testing have shown great promise and are already being marketed. Over 2016, several 3D bioprinting companies saw a doubling of revenue, and comparable results are anticipated for the next

few years. Given these market trends, IDTechEx forecasts that the global market for 3D bioprinting will reach a value of \$1.9 billion by the year 2028. In 2014, there were more than 30 companies worldwide having a business directly related to 3D bioprinting and bioprinted products. IDTechEx has defined 3D bioprinting as the deposition of living cells in a spatially controlled manner in the absence of any pre-existing scaffold and in more than a single layer. Under this definition, 3D bioprinters are currently based on four main printhead technologies: Inkjet, Extrusion, Laser-induced forward transfer Microvalve<sup>22</sup>.

The *ArthroPrint* product will be probably grounded on an extrusion-based technology. The global syringe based 3D bioprinting market is anticipated to reach 923.5 million by 2024, at a CAGR of 17.8% from 2016 to 2024<sup>23</sup>.

Special attention is paid to regenerative medicine, as not only does it have the potential to be the largest application for 3D bioprinting in the future, but also one with the highest impact. 3D bioprinting can be applied to regenerative medicine, and focuses on the following tissue types: bone and cartilage, skin, dental, vasculature complex organs.

The *ArthroPrint* might be use as an alternative to existing procedures in various application areas that have a large market potential, such as regeneration of musculo-skeletal tissues, wounds/skin, etc. (Figure 24).



**Figure 24:** Main therapeutic areas of tissue engineering and regenerative medicine market segments.

The strongest feature of the *ArthroPrint* will be most probably its versatility. It could be adapted to the repair of hard tissues, such as bone and cartilage, but also of soft ones. Below, a preliminary SWOT analysis is reported for this product.

<sup>22</sup> <https://www.idtechex.com/research/reports/3d-bioprinting-2018-2028-technologies-markets-forecasts-000592.asp>

<sup>23</sup> <https://marketresearchinsightssite.wordpress.com/tag/3d-bioprinting-market-share/>

<p><b>Strengths:</b></p> <ul style="list-style-type: none"> <li>→ Tissues and even organ parts could be printed</li> <li>→ Easy to build own custom machine</li> <li>→ Easy to fill the decrease with desired amount of bioink</li> <li>→ Huge market potential</li> </ul>	<p><b>Weakness:</b></p> <ul style="list-style-type: none"> <li>→ Its success strongly depends on the quality of the bioink</li> <li>→ Production time</li> <li>→ Technology in premature state</li> <li>→ Expensive</li> </ul>
<p><b>Opportunities:</b></p> <ul style="list-style-type: none"> <li>→ Several research efforts are focusing on the development of effective bioinks</li> <li>→ Possibility to scale reduction of the bioprinter parts cost</li> <li>→ Possibility to improve the printing speed</li> </ul>	<p><b>Threats:</b></p> <ul style="list-style-type: none"> <li>→ Printing time</li> <li>→ OR conditions</li> <li>→ Sterility</li> </ul>

For now Vimex considers different solutions for the *ArthroPrint* device commercialisation (production in Vimex facility and introduction to the Vimex Endoscopy portfolio - the main interesting option, licence sale or IP disposal, creating of a new spin-off company), depending on the ADMAIORA project directions and results.

A future detailed business plan will be developed that will consider the introduction of the product into the medical devices market, the manufacturing technology optimization, the pricing and marketing strategy etc. Different markets respect to the 3D bioprinting one will be considered, since depending on its features, the tool may compete not really with 3D bioprinters, but rather with surgical instruments used in different districts.

#### 4.4 Additional lateral exploitation opportunities

Aside from the two main products (*RegenCart* and *ArthroPrint*) and the two possible spin-off companies described above, there may be other opportunities for commercial exploitation of the technologies developed during ADMAIORA, either as stand-alone companies or within the partner organizations. Examples of these are reported below, for the different companies involved in the project.

##### Regentis Biomaterials Ltd.

REGENTIS has a specific core business, in the development of biomaterials for cartilage healing/regeneration. Thus, it is fully aligned with the ADMAIORA objectives. The main revenue opportunities for this company will derive from being a provider for the future spin-off company of biosynthetic hydrogels (NewCo). Further, the chemical hydrogel modification planned in the project course and their integration with nanoparticles are expected to further widen the possible business opportunities, by allowing REGENTIS to enter other markets, as summarized in Table .

Market Area	Addressable market size analyzers in 2018	Addressable market size analyzers in 2028	Company Market Share in 2018	Target Market Share in 2028
Hydrogels for cardiovascular applications (possibly connected with the <i>ArthroPrint</i> product)	20.7 B€	37 B€	-	0.25%
Hydrogels for wound healing	23 B€	35 B€	-	0.1%

**Table 9:** Short summary of exploitation opportunities for REGENTIS.

### Image Guided Therapy SA

IGT R&D efforts concern both high-intensity and low-intensity ultrasound technologies, for both stimulation and monitoring. Part of the future IGT revenues will derive from being a provider of the future spin-off company, concerning the stimulation/monitoring brace and some of its components. However, the knowledge acquired in the project course will generate further market opportunities for the company, in the fields of ultrasound monitoring systems for orthopaedic applications focused on bone healing and on *in vitro* platforms for LIPUS stimulation of cells and materials, for biomedical applications. A short summary of lateral business opportunities is reported in Table .

Market Area	Addressable market size analyzers in 2018	Addressable market size analyzers in 2028	Company Market Share in 2018	Target Market Share in 2028
Ultrasound monitoring systems for orthopaedic applications related to bone	1 B€	1.8 B€	-	0.25%
<i>In vitro</i> platforms for LIPUS stimulation of cells and materials	100 M€	200 M€	0.1%	3%

**Table 10:** Short summary of exploitation opportunities for IGT.

### PlasmaChem GmbH

PLASMACHEM grounds its business on the production and sale of nanomaterials and medical products. The participation in the ADMAIORA project will allow the commercial exploitation of project outcomes, concerning the increase of the palette of nanomaterials sold through the catalogue by inclusion of novel materials to the R&D customers. PLASMACHEM will also be manufacturing the particles developed in the project for the direct medical applications on OEM basis. Table 11 shows the market size for different segments, the current market penetration of the company and the one envisioned in 10 years.

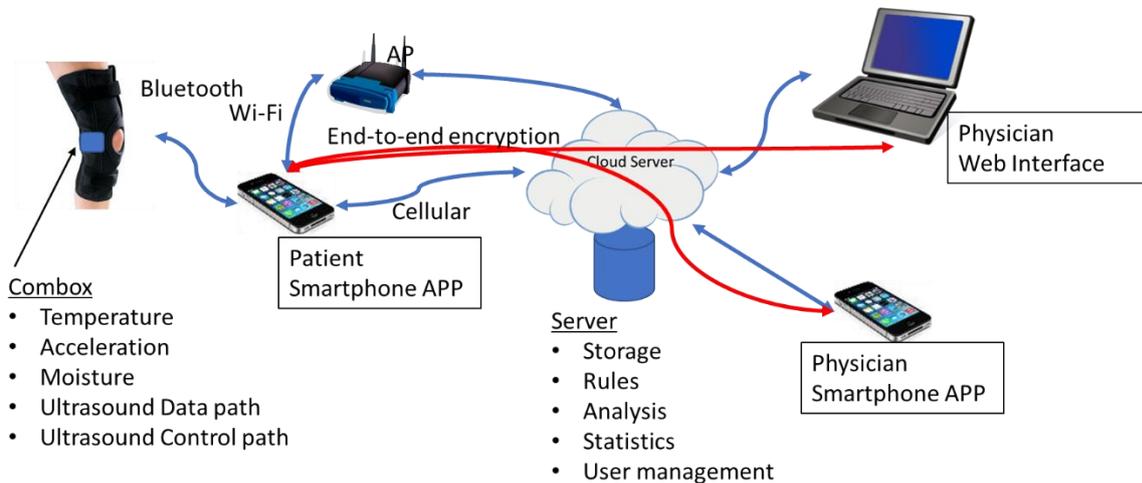
Market Area	Addressable market size analyzers in 2018	Addressable market size analyzers in 2028	Company Market Share in 2018	Target Market Share in 2028
Piezoelectric nanomaterials for R&D use	1 M€	5 M€	40%	65%

**Table 11:** Short summary of exploitation opportunities for PLASMACHEM.

## H&D Wireless AB

HDW is a fast growing company in the field of IoT technologies, especially for industrial applications. The company will benefit from participating in the ADMAIORA project both in terms of future revenues as a provider for App and IoT framework for the future spin-off company and in terms of new expertise gained to widen the company interests in the medical/biomedical field.

In the project an IoT architecture will be implemented following the privacy by design and privacy by default approaches, as required by the current EU Regulation 2016/679 for the multi-input of data from the patient that utilizes data exchange and secure storage using a cloud server in EU, allowing the physician to monitor the data and provide feedback to the patient. The feedback to the patient will consist of both information to patient and control data for the ultrasound stimulation (Figure 25).



**Figure 25:** IoT architecture planned by H&D Wireless.

A short summary of HDW future business opportunities is reported in Table 3.

Market Area	Addressable market size analyzers in 2018	Addressable market size analyzers in 2028	Company Market Share in 2018	Target Market Share in 2028
General-purpose IoT frameworks (with the proprietary cloud-based software platform) for hospitals and other healthcare structures	14 B€	35 B€	-	0.1%
Custom wireless communication systems for medical devices	3.58 B€	24.5 B€	-	0.1%

**Table 3:** Short summary of exploitation opportunities for HDW.

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## 5 Conclusions

*This Deliverable outlines the preliminary dissemination, communication and exploitation plans of the project. These will be continuously updated and refined through the entire project time-frame, led by the responsible partners and with the contribution of the whole Consortium. In the Deliverable, the activities carried out by the Consortium in the initial period, from the kick-off meeting (February 4-5, 2019) to the Deliverable due date (April 30, 2019) are also mentioned.*

*The preliminary dissemination plan is ambitious and aims at reaching the scientific as well as the clinical community in an effective way. Communication activities are also challenging and aim at completing and empowering the dissemination ones, by reaching the general public. Several tools (e.g. the website, the social network profiles, the brochures, etc.) will be used in a synergetic way for both initiatives, under the careful and continuous monitoring of the project Communication Manager, appointed at SSSA. An almost daily update of project website/social network contents and other initiatives will help to keep the momentum of ADMAIORA in terms of overall visibility. This will also facilitate the organization of the different types of events planned for the project dissemination and communication and will facilitate to reach the quantitative targets set for each of them.*

*The preliminary exploitation plan draws how the future clinical and commercial translation of the project outcomes shall be carried out. A general strategy is depicted, with two main products arising from the project efforts: the RegenCart kit and the ArthroPrint tool. The initial strategy is based on the creation of spin-off companies that will be dedicated to the commercialization of such products. An important achievement of the Consortium in this first period was the filing of a patent on the general ADMAIORA approach/method. This will maximize future exploitation opportunities. Further lateral business opportunities by the different SMEs involved in the Consortium are also mentioned in the Deliverable and will be described more in detail in the next months.*