

## A new network for the advancement of marine biotechnology in Europe and beyond

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# A new network for the advancement of marine biotechnology in Europe and beyond

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### *Conflict of interest statement*

The authors declare a potential conflict of interest and state it below

Francesco Bertoni: institutional research funds from Acerta, ADC Therapeutics, Bayer AG, Cellestia, CTI Life Sciences, EMD Serono, Helsinn, ImmunoGen, Menarini Ricerche, NEOMED Therapeutics 1, Oncology Therapeutic Development, PIQUR Therapeutics AG; consultancy fee from Helsinn, Menarini; expert statements provided to HTG; travel grants from Amgen, Astra Zeneca, Janssen-Cilag AG, Jazz Pharmaceuticals, PIQUR Therapeutics AG

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

### *Author contribution statement*

AR designed the article concept and drafted the manuscript. All authors read, commented, improved and approved of the final version of the manuscript.

### *Keywords*

marine biotechnology, Marine Natural Products, Blue growth, marine biodiversity and chemodiversity, Responsible Research & Innovation, stakeholder engagement, science communication, sustainability

### *Abstract*

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Marine organisms produce a vast diversity of metabolites with biological activities useful for humans, e.g. cytotoxic, antioxidant, anti-microbial, insecticidal, herbicidal, anticancer, pro-osteogenic and pro-regenerative, analgesic, anti-inflammatory, anti-coagulant, cholesterol-lowering, nutritional, photoprotective, horticultural or other beneficial properties. These metabolites could help satisfy the increasing demand for alternative sources of nutraceuticals, pharmaceuticals, cosmeceuticals, food, feed, and novel bio-based products. In addition, marine biomass itself can serve as the source material for the production of various bulk commodities (e.g. biofuels, bioplastics, biomaterials). The sustainable exploitation of marine bio-resources and the development of biomolecules and polymers are also known as the growing field of marine biotechnology. Up to now, over 35,000 natural products have been characterized from marine organisms, but many more are yet to be uncovered, as the vast diversity of biota in the marine systems remains largely unexplored. Since marine biotechnology is still in its infancy, there is a need to create effective, operational, inclusive, sustainable, transnational and transdisciplinary networks with a serious and ambitious commitment for knowledge transfer, training provision, dissemination of best practices and identification of the emerging technological trends through science communication activities. A collaborative (net)work is today compelling to provide innovative solutions and products that can be commercialized to contribute to the circular bioeconomy. This perspective article highlights the importance of establishing such collaborative frameworks using the example of Ocean4Biotech, an Action within the European Cooperation in Science and Technology (COST) that connects all and any stakeholders with an interest in marine biotechnology in Europe and beyond.

### *Contribution to the field*

Dear colleagues, The co-authors (Rotter et al.) are submitting a perspective article with the general aim of highlighting the emerging importance of this exciting field of marine biotechnology. This field is an excellent example of how science and innovation collaborations should be conducted nowadays as science is rapidly evolving, not only in terms of scientific content but also in its mode of conduct. Interdisciplinary (and even transdisciplinary) teams are today mandatory, and, on top of that, research and innovation development must include industrial policy making and general public representatives. This is especially true in newer fields such as marine biotechnology. This perspective article highlights the importance of all mentioned partners to bridge the communication gap between science-industry-society (the latter including policy makers and general public). Only the inclusion of all relevant actors can guarantee an innovative and sustainable society. One of the few inclusive, transdisciplinary and participatory network is a recently established COST Action »European transdisciplinary networking platform for marine biotechnology« (Ocean4Biotech), joining together all interested actors from the marine biotechnology field, from biological, chemical experts, to experts in communication, ethics and Responsible Research and Innovation.

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84 **communication, sustainability.**

85 **Abstract**

86 Marine organisms produce a vast diversity of metabolites with biological activities useful for  
87 humans, e.g. cytotoxic, antioxidant, anti-microbial, insecticidal, herbicidal, anticancer, pro-  
88 osteogenic and pro-regenerative, analgesic, anti-inflammatory, anti-coagulant, cholesterol-lowering,  
89 nutritional, photoprotective, horticultural or other beneficial properties. These metabolites could help  
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91 cosmeceuticals, food, feed, and novel bio-based products. In addition, marine biomass itself can  
92 serve as the source material for the production of various bulk commodities (e.g. biofuels,  
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94 of biomolecules and polymers are also known as the growing field of marine biotechnology. Up to  
95 now, over 35,000 natural products have been characterized from marine organisms, but many more  
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97 unexplored. Since marine biotechnology is still in its infancy, there is a need to create effective,  
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103 importance of establishing such collaborative frameworks using the example of Ocean4Biotech, an  
104 Action within the European Cooperation in Science and Technology (COST) that connects all and  
105 any stakeholders with an interest in marine biotechnology in Europe and beyond.

### 106 **Introduction**

107 During four billion years of evolution in the ocean, marine organisms have evolved in their  
108 environment to biosynthesize a plethora of biopolymers and biomolecules. These include the unique  
109 secondary metabolites that are produced in response to environmental stimuli. They play important  
110 biological roles in improving competitiveness, providing chemical defense against predators or  
111 competitors and facilitating reproductive processes. These biomolecules are not always essential for  
112 the growth and development of the organism, but they are important for the survival and well-being  
113 in its environment. Furthermore, some compounds such as marine enzymes have properties essential  
114 for industrial applications like thermostability or tolerance to a diverse range of pH and salinity  
115 conditions. These properties are being utilized in various industries such as in the food, animal feed,  
116 leather, textile and horticulture industries, and in bioconversion and bioremediation processes (Rao et  
117 al., 2017). Marine biotechnology appeared in the 1960s and 1970s when scientists realized the  
118 potential of living organisms and their natural products for industrial exploitation (Dias et al., 2012).  
119 Initially, the investigation of marine ecosystems relied on the easily accessible organisms like corals  
120 and sponges as well as macroalgae that have high biomass levels and were representative of targeted  
121 ecosystems (Greco and Cinquegrani, 2016). Therefore, most of the known natural products deriving  
122 from the marine environment were initially isolated from macro-organisms. On realizing that marine  
123 microbial biodiversity is vast, largely underexplored and unexploited, the application of marine  
124 microbial biotechnology aiming to valorize marine resources is a natural step forward in the  
125 development of the biotechnology sector.

126 For a long time, it has been considered that only around 1% of the whole marine microbial  
127 population could be cultured under laboratory conditions (Vartoukian et al., 2010). However, recent  
128 findings suggest the percentage of culturable microbial population is higher; an estimated 13% - 78%  
129 of genera are cultured, depending on the environment (Lloyd et al., 2018). For example,  
130 environments with high human engagement and disease-driven research benefit from greater  
131 culturing effort (Steen et al., 2019; Lloyd et al., 2018). Since many cells in nonhuman environments  
132 belong to novel phyla, new culturing approaches and innovations will increase the percentage of  
133 uncultured microbes (Steen et al., 2019). Culture-independent methods using omics approaches are  
134 nowadays used to detect microorganisms that are yet uncultured. These methods include high-  
135 throughput sequencing, metagenomics, transcriptomics, proteomics, metabolomics and  
136 bioinformatics resources for the identification of organisms and elucidation of metabolic pathways  
137 responsible for production of chemical compounds, as well as DNA-based or heterologous  
138 expression systems. Microbial identification is only an initial step and additional research is essential  
139 to develop cultivation techniques to obtain the necessary biomass in a sustainable manner. Next,  
140 biochemical and genetic engineering methods are required for the production of high quantities and  
141 quality of proteins, marine oils and other secondary metabolites of interest. Figure 1 provides a  
142 schematic representation of parameters that should be considered for the whole bioprospecting



143 process, starting from the selection of marine organisms, for their cultivation prior to their utilization  
144 for the biosynthesis of high-value bio-components and for investigation of their biological potential  
145 in various industries.

146 Natural products are currently the most common source of therapeutic agents. The World Health  
147 Organization estimates that approximately 80% of the world's population uses remedies based on  
148 natural products to treat their basic health problems. Over 35,000 bioactive compounds have been  
149 isolated and chemically characterized from marine organisms since the 1960s (Lindequist, 2016).  
150 While before 1985 less than 100 natural products were discovered annually, in the late 1990s, this  
151 number rose to over 500 new products discovered yearly up to over 1,000 since 2008, mainly due to  
152 the advances in analytical methods (Carroll et al., 2019; Lindequist, 2016). The application of new  
153 dereplication strategies using mass spectrometry (MS) and the use of high-resolution Nuclear  
154 Magnetic Resonance (NMR) spectrometers with cryoprobes have enabled the discovery of new  
155 natural products even at the nanomole scale (Klitgaard et al., 2014). The most common approach  
156 used for the discovery of new marine bioactive chemical entities involves the screening of crude  
157 extracts or partially purified fractions of similar polarities against selected test organisms or  
158 therapeutic targets, followed by the purification and the structure elucidation of the active  
159 ingredients. The purification of metabolites is usually performed by means of chromatographic  
160 separation techniques combined with high-resolution MS based approaches that allow a rapid and  
161 accurate identification of the molecular mass and formulae of bioactive compounds. These methods  
162 are becoming a gold standard for the rapid and reliable dereplication of natural product extracts or  
163 fractions (Gaudêncio and Pereira, 2015).

164 The unique structural architecture and broad range of activities exhibited by marine metabolites have  
165 caught the attention of the scientific community. This has resulted in the development of research  
166 programs promoting innovation and industrial uptake along with the creation of new jobs and of a  
167 competitive environment for biotechnology-oriented enterprises as stated in the Blue Growth  
168 Strategy of the European Union (EU). This orientation is in line with the strategy for "A sustainable  
169 bioeconomy for Europe: strengthening the connection between economy, society and environment"  
170 which is a 2018 update from the original 2012 Bioeconomy Strategy by the European Commission  
171 (EC). The strategy aims to create a more innovative, resource-efficient and competitive society that  
172 will reconcile drug discovery and food security with the sustainable and economically viable use of  
173 renewable resources for industrial purposes while ensuring environmental protection.

## 174 **Prerequisites for marine biotechnology (Figure 2)**

175 **Sustainability.** There are two sustainability levels that must be considered to effectively implement  
176 marine biotechnology in practice: (i) environmental and (ii) supply sustainability. (i) Environmental  
177 sustainability tackles the main sources of marine biomass which come either from species harvested  
178 in nature or from those that can be cultivated. It is especially relevant when wild stocks are the only  
179 source of supply and they are over-harvested, or where targeted marine species are rare, in the deep,  
180 or difficult to re-sample. The harvesting/sourcing of any target species should thus not threaten  
181 marine biodiversity and the future availability of target species. To minimize the environmental  
182 impact, the biotechnology community should consider valorizing side and waste streams and co-  
183 products, target sustainably cultured marine organisms and those that are sufficiently productive to  
184 supply specific high added-value biomolecules. (ii) Sustainable supply of biomolecules represents  
185 key bottlenecks, as they are usually present in trace amounts. To guarantee a sustainable sourcing and  
186 production of target compounds, biologically active molecules or whole organisms should therefore  
187 be considered in a life cycle assessment and a multi-risk environmental analysis context. This will

188 attain a global evaluation including environmental, health and economic aspects for both the  
189 biological (sourcing) and technical (supplying) cycle. Industrial symbiosis and circular economy  
190 approaches must therefore be applied to find sustainable ways for utilization of marine bioresources  
191 (blue growth) using green production techniques that economize on exhaustible resources (green  
192 growth, Rodrik, 2014).

193 **Industry.** Marine biotechnology generates various products and services, from the production of  
194 biofuels, food, feedstuffs and products for use in agriculture (high-volume, low-value and low-risk  
195 products), to the discovery of new biomaterials, cosmetics, nutraceuticals and pharmaceuticals (low-  
196 volume, high-value and high-risk products). Research and development investments for the discovery  
197 of marine-derived drugs entail high levels of capital expenditure and risk tolerance, as they require  
198 the use of state-of-the-art infrastructures and many years of basic and applied research. Despite some  
199 limitations, there are successful examples, as to date there are ten approved drugs, one example being  
200 trabectedin (ET-743), a product isolated from a Caribbean sea squirt *Ecteinascidia turbinata*, which  
201 is used for the treatment of advanced soft tissue sarcoma. This product first reached the market in  
202 2007, after 20 years of research (Cuevas and Francesch, 2009). In practice, out of every 2,500  
203 analogs from the marine environment that enter preclinical testing, only one may be safe and  
204 effective enough to reach clinical use (Gerwick and Fenner, 2013). There is a collaboration and  
205 communication gap between raw ideas and materials and their potential laboratory innovation and  
206 commercialization (Datta et al., 2014). This is being tackled by adopting three different strategies. (i)  
207 Firstly, by stimulating public-private partnerships in consortia that apply for research and innovation  
208 funding (such as Horizon 2020 and Horizon Europe, Europe's biggest research and innovation  
209 funding resource). (ii) Another alternative are the business incubators (such as Rocket57 in Northern  
210 Europe<sup>1</sup>), think tanks or stakeholder events that are often regionally financed to answer strategic  
211 regional developmental priorities and present a contact point for joining researchers, small and  
212 medium enterprises, industrial representatives and investors. (iii) Financial stimulation of networking  
213 activities (the example of COST Action Ocean4Biotech is presented in the next chapter of this  
214 article). The global marine biotechnology market is expected to reach ~\$6.4 billion by 2025<sup>2</sup> and it  
215 currently represents only ~1% of the whole biotechnology market. Noteworthy, the oceans cover  
216 over 70% of the Earth's surface and contain an estimated 25% of the world's species (Mora et al.,  
217 2011), of which most are unknown and undervalored. Hence, the marine biotechnology market is  
218 expected to expand at a much higher pace when high-throughput techniques and the collaboration  
219 between industry, science, general public and policy makers will be routinely used. The predominant  
220 players in the European marine biotechnology consist of some 140 micro SMEs (estimated by Ecorys  
221 in 2014) and academia that lack the financial stability necessary for sustained and long-term cutting-  
222 edge research.

223 **Scientific community.** To fully explore the ocean and its biota, the current screening and/or  
224 cultivation approaches of marine organisms of interest for biotechnological applications need to be  
225 optimized. High-throughput techniques produce vast amounts of data and can uncover the  
226 biodiversity and the metabolic potential of marine organisms. Hence, knowledge on data  
227 management, processing and data analysis to maximize the quality and quantity of resulting  
228 information needs to be advanced. Experts from the field of statistics, bioinformatics and  
229 chemometrics are essential in biotechnology research groups nowadays and their pipelines and

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<sup>1</sup> <https://rocket57.co/en/>

<sup>2</sup> <https://www.smithers.com/resources/2015/oct/global-market-for-marine-biotechnology>

230 databases should be integrated, harmonized and publicly available to prevent duplication of efforts,  
231 reduce the overall costs and support the discovery process.

232 **General public.** While the world population is rising and is expected to reach over 8.5 billion by  
233 2030, bioresources and available areas for cultivation and manufacture are declining. Hence, there is  
234 a growing demand for additional sources of food, drugs and chemicals. Marine biotechnology has the  
235 potential to mitigate these needs both by increasing the current production and by introducing new  
236 products in the food, feed, pharmaceutical, nutraceutical, healthcare, welfare, biomaterials and energy  
237 sectors. Nowadays, consumers expect innovative, efficient, safe, sustainable, ethical, financially and  
238 environmentally friendly solutions. We need to raise public awareness and improve communication  
239 to a broad audience regarding the benefits of marine biotechnology products to gain consumers'  
240 interest in eco-friendly products that meet high standards of sustainability.

241 **Policy makers.** Some national, regional and global strategies and guidelines are already in place to  
242 recommend investment into marine biotechnology and stimulate networking and transdisciplinary  
243 collaboration at the international level. These include the United Nations (UN) sustainable  
244 development goals<sup>3</sup>, national and EU legislation that must be developed and harmonized. The UN  
245 Convention on the Law of the Sea<sup>4</sup> sets the rules for the exploitation, conservation and management  
246 of living marine resources. The Nagoya Protocol on Access to Genetic Resources and Benefit  
247 Sharing provides a legal framework aimed at creating transparency for those interested in the  
248 production and exploitation of genetic materials. Marine biotechnology development needs also to  
249 comply with the Habitats Directive (92/43/EEC) on the conservation of natural habitats and of wild  
250 fauna and flora, the Marine Strategy Framework Directive (MSFD) (2008/56/EC, CD 2017/848)  
251 establishing a framework for community action in the field of marine environmental policy, the EU  
252 Water Framework Directive – WFD (Directive 2000/60/EC), and the Maritime Spatial Planning  
253 Directive (2014/89/EU) for the planning of multiple uses of the maritime and coastal areas.  
254 Biomolecules and their production processes must also comply with specific regulations related to  
255 the targeted application (e.g. EU 2015/2283 Novel Foods and Ingredients, EC No 1223/2009  
256 Cosmetic Regulation, EC No 1924/2006 Nutrition and Health Claims, EC No 1907/2006 REACH  
257 Regulation, among others). The widespread acceptance and certification of these novel compounds is  
258 a rigorous and time-consuming process where legislative documentation might need updating as  
259 novel compounds are being identified. It is thus necessary to encourage collaboration among  
260 scientists and policy makers, as outlined during the UNESCO High-Level Conference on the Ocean  
261 Decade (2018). Moreover, intellectual property strategies need to be established and agreed upon to  
262 conduct research in accordance with ethical recommendations for bioprospecting in the open ocean  
263 and beyond the national jurisdictions covered by the Nagoya protocol.

### 264 **The establishment of a collaborative network as a solution for advancing marine** 265 **biotechnology: COST Action Ocean4Biotech**

266 Efficient and sustainable exploitation of the ocean's potential is possible only if industrial actors,  
267 researchers, the general public, policy makers and environmental experts work together. This direct  
268 interaction among different stakeholders across different countries is not always possible and limited  
269 programs have been supported until today that allow a minimal direct transdisciplinary interaction  
270 (see more in Supplementary Table S1).

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<sup>3</sup> <https://sustainabledevelopment.un.org/>

<sup>4</sup> [https://www.un.org/depts/los/convention\\_agreements/texts/unclos/unclos\\_e.pdf](https://www.un.org/depts/los/convention_agreements/texts/unclos/unclos_e.pdf)

271 From this viewpoint, the EU COST program that was established in 1971 represents an excellent  
272 opportunity for the creation of research networks on diverse topics, called COST Actions. These  
273 networks offer an open space for collaboration among stakeholders across Europe (and beyond),  
274 thereby catalyzing research advancement and innovation<sup>5</sup>. One of the recently approved Actions is  
275 CA18238 – European transdisciplinary networking platform for marine biotechnology  
276 (Ocean4Biotech)<sup>6</sup>. The motivation behind creation of this network is included in the SWOT analysis  
277 (see Supplementary Table S2 and the discussion therein). Ocean4Biotech is an international, unique  
278 and inclusive network that gathers experts from transdisciplinary fields of exact and natural sciences,  
279 social sciences and humanities, giving the Action participants the opportunity to work together and  
280 share their experiences creating a spill-over effect to foster marine biotechnology and bioeconomy in  
281 a sustainable way. Ocean4Biotech will apply the Responsible Research and Innovation Roadmap  
282 (Theodotou Schneider, 2019) involving scientists, citizens, policy makers and industry in the co-  
283 creation of knowledge and in the establishment of sustainable collaborative networks.

284 Notably, Ocean4Biotech builds upon existing knowledge from current and past projects and  
285 initiatives (see Supplementary Table S1). It aims to establish strong collaborations to avoid the  
286 duplication of efforts. The difference between Ocean4Biotech and the current and past efforts is this  
287 Action is envisaged as a “connecting-the-dots” funnel initiative that will gather scientists and  
288 professionals from all areas related to the marine biotechnology field. This enables a wider approach  
289 aiming to facilitate the circular economy in the marine biotechnology sector. Researchers from all  
290 fields and levels of expertise relevant to marine biotechnology will have the opportunity to  
291 participate in the Action and will be included in knowledge exchange activities (between the  
292 scientific fields as well as within, e.g. senior-to-junior knowledge transfer), establishing new  
293 collaborations and having an opportunity for career advancement. The developments from this COST  
294 Action can impact the industrial sector, and in turn will most likely influence governance boards.  
295 However, the efforts of Ocean4Biotech to establish connections between its members and linkages  
296 with other initiatives will not be possible without proactive science communication, extensive  
297 dissemination along with active engagement and outreach activities. Efficient communication will  
298 enable informing on the activities and objectives of the Action and will attract researchers to prepare  
299 and initiate new collaborations that will span beyond the lifetime of Ocean4Biotech.

### 300 **How will Ocean4Biotech foster advances in the field of marine biotechnology?**

301 There are five general objectives within the Ocean4Biotech COST Action:

302 **1. Description of marine biodiversity.** Knowledge of marine biodiversity is still limited. Moreover,  
303 there is a large interregional variability in species distribution and in their taxonomic knowledge. The  
304 lack of experts in marine species taxonomy, duplicates/redundancies/inconsistencies in the primary  
305 nucleotide databases, lack of type species and polyphyly of traditionally established taxa result in  
306 many misidentified or unidentified species/strains (many of which hold great potential for  
307 biotechnological applications). These are also important challenges to marine natural product  
308 programs. Hence, human resources, research effort, time and cost-efficient methods are needed to  
309 overcome the current gap in knowledge on biological and chemical diversity in marine ecosystems.  
310 These may be addressed by high-throughput methods that facilitate the discovery, classification and  
311 supply of organisms. However, high-throughput methods for biodiversity monitoring have not been  
312 routinely adopted and the methodology for biodiscovery is often not standardized. In fact,

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<sup>5</sup> <https://www.cost.eu/who-we-are/about-cost/>

<sup>6</sup> <https://ocean4biotech.eu>

313 bioinformatics pipelines and big data analyses are changing the landscape for marine biotechnology,  
314 as around 18,000 new species are uncovered yearly<sup>7</sup>. Ocean4Biotech will propose operating  
315 procedures for uncovering the biodiversity using high-throughput methods, such as DNA barcoding  
316 approaches (Leese et al., 2016). These methods can then be combined with a more quantitative  
317 assessment by *in situ* hybridization techniques that allow the quantification and localization of  
318 specific microbial clusters within the environmental matrices. Such biodiversity assessment provides  
319 crucial information for subsequent monitoring and exploitation of marine organisms. The  
320 environmental impacts of such biological prospecting are considered minimal at the early stages of  
321 sampling, where the size of samples collected is small. Moreover, the standardization of the  
322 biodiscovery process is necessary as chemodiversity, even in the same taxa, greatly varies along  
323 geographical and environmental gradients, as well as seasonally and timely along the life cycle of  
324 organisms.

325 **2. Natural product discovery** is a process involving separation techniques in parallel with biological  
326 screening, followed by structure elucidation of the pure bioactive metabolites. If the target compound  
327 from a given species shows biotechnological potential, scale-up production and supply will certainly  
328 increase the environmental impact. However, the organic synthesis of the compound (although time-  
329 consuming and expensive) and/or production of the compound of interest using biological synthesis  
330 generally overcome the need for repeated collection and over-exploitation of the natural ecosystem.  
331 Therefore, Ocean4Biotech will build a compendium of pipelines, i.e. methods and procedures,  
332 detailed on a case study basis, starting from the creation of marine biorepositories, the identification  
333 of the collected species using integrative systematics, screening for specific bioactivities for selected  
334 industries, identification of the bioactive metabolites and their sustainable production, business plan  
335 development, marketing strategy, where legal and ethical aspects to be considered along with  
336 adherence to strict guidelines for protection of the environment and sustainability. These pipelines  
337 will serve as guidelines and tutorials for future product development and will enable the transfer of  
338 knowledge between disciplines. These pipelines will highlight the complementary transdisciplinary  
339 aspect of marine biotechnology and as a link with other sectors of biotechnology. According to the  
340 principles sustainability the supply chain decision-making will require the inclusion of social and  
341 economic aspects together with environmental aspects. Thus, the Action will apply an integrated  
342 framework for Life Cycle Sustainability Assessment (LCSA). Wherever possible, it will combine  
343 physical LCA considering different environmental impact categories (e.g. climate change,  
344 eutrophication or acidification) at different life-cycle levels (partial LCA) with social LCA (SLCA)  
345 and Life Cycle Costing (LCC), based on UNEP/SETAC guidelines. The approach used in this Action  
346 will build on existing models (Perez-Lopez et al., 2018). It will also follow the methodological  
347 framework for conducting LCA as outlined by the International Standards Authority (ISO) 14040  
348 series.

349 **3. Sharing infrastructure.** There is an increasing need to create a bridge between research and  
350 innovation capabilities from the academia and business sectors. This includes the availability of the  
351 research infrastructure, thereby providing access to a range of new tools and facilities to allow marine  
352 biotechnology to thrive. Many of the tools and techniques used in marine biotechnology are widely  
353 used in other areas of science and technology. Engaging in collaborative research projects is one way  
354 of providing access to these facilities and encouraging multidisciplinary research. Ocean4Biotech  
355 will enable the diverse actors to share their expertise and infrastructure, mostly through short-term  
356 scientific missions and new collaborative activities. Preference will be given to users from the less

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<sup>7</sup> [https://www.eurekalert.org/pub\\_releases/2018-05/scoe-elt051718.php](https://www.eurekalert.org/pub_releases/2018-05/scoe-elt051718.php)

357 research-intensive countries<sup>8</sup> or early career investigators that need access to state-of-the-art  
358 analytical equipment, microbial cultures or screening facilities.

359 **4. Responsible Research and Innovation.** The ocean should be monitored, valorized and governed  
360 in a sustainable manner to generate the maximum benefit to science and society but limiting the  
361 negative footprints on the marine environment. This will be addressed within the Action by adopting  
362 the Responsible Research and Innovation (RRI) concept, which is based on six pillars.

363 (i) Ethics. We are all responsible for the stability and resilience of the Earth systems (Barbier et al.,  
364 2018). Accordingly, ethical issues and challenges will be identified, addressed and used to advocate  
365 for protection of marine ecosystems and promote responsible resource management and  
366 environmental policies together with societal awareness.

367 (ii) Open access. To efficiently co-create knowledge and capitalize from previous research, it is vital  
368 to consider transparency, efficiency, traceability, access to data, reciprocal relations, biosafety, nature  
369 conservation and transfer of knowledge to third countries.

370 (iii) Gender equality will be promoted throughout the Action by empowering especially early career  
371 and female colleagues to apply for managerial roles and in the future establish and lead consortia for  
372 valorization of marine biotechnology products.

373 (iv) Governance. Although the marine biodiversity has no borders, access to natural resources is  
374 framed under the Convention of Biological Diversity, promoting the conservation of biodiversity, the  
375 sustainable use of biological entities and their fair and equitable sharing. The latter is also covered in  
376 the Nagoya Protocol, which provides a legal framework for the fair and equitable sharing of benefits  
377 arising from the use of genetic resources which may sometimes delay or block certain research  
378 activities.

379 (v) Public engagement. Action participants will employ communication tools and different activities  
380 to further inform legislative authorities, researchers and industry with the aim of facilitating the  
381 regulatory requirements that are sometimes a bottleneck to transnational collaboration.

382 (vi) Science education. We will focus many of our activities into education of the next generation of  
383 researchers (i.e. early career investigators), with a special focus on the countries that are less research  
384 intensive, i.e. the so-called inclusiveness target countries<sup>9</sup>. These countries have developed their  
385 national strategic priorities in the frame of the EU Smart Specialization Strategy (S3), aiming to  
386 ensure a balanced development between regions<sup>10</sup>. Since marine biotechnology, including its  
387 products and applications, is well represented in all national S3 priorities, the timing is perfect to  
388 develop capacity-building educational opportunities that span beyond the traditional academic  
389 curricula. We will enable closing the educational gaps in three ways. (i) By short term scientific  
390 missions, which are mobility activities that involve a direct hands-on interaction and experience  
391 abroad. (ii) By offering financial opportunities for active participation in conferences that target any  
392 of the marine biotechnology related topics. (iii) Importantly, our trainings and workshops, that will  
393 be publicly promoted, will cover topics that integrate academy, technological centers and industry (as  
394 also promoted by the EuroMarine Working Group, 2019). By offering multidisciplinary skills, this

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<sup>8</sup> <https://www.cost.eu/who-we-are/cost-strategy/excellence-and-inclusiveness/>

<sup>9</sup> <https://www.cost.eu/who-we-are/cost-strategy/excellence-and-inclusiveness/>

<sup>10</sup> <https://ec.europa.eu/jrc/en/research-topic/smart-specialisation>

395 strategy will avoid the risk of training a marine-related workforce that the market may not absorb  
396 (EuroMarine Working Group, 2019).

397 **5. Knowledge co-creation and integration.** (i) The Action will be geographically inclusive as it will  
398 produce an open-access database of exploitable species for marine biotechnology in the  
399 Ocean4Biotech participating countries. In addition to the World Register of Marine Species  
400 (WoRMS<sup>11</sup>), this Action participants will focus on those species with putative biotechnological  
401 potential. (ii) The Action will be inclusive in the biological sense and include species regardless of  
402 the kingdom (from bacteria and algae to zooplankton and other species that are suitable for  
403 exploitation). (iii) Methodologically, the participants will integrate all levels of the biotechnological  
404 pipeline; from bioprospecting to cultivation, biological screening, compound isolation and  
405 optimization of the isolation process, and structure elucidation. (iv) This is a truly transdisciplinary  
406 Action, integrating expertise and including experts from various fields: marine (micro)biology,  
407 chemistry, food science, agriculture, pharmacology, medicine, environmental protection, engineering,  
408 energy, data science, omics techniques, statistics, law, policy making, economy, business planning,  
409 and more. The network will transfer knowledge from traditional academic institutions to exploitation  
410 industries leading to the elaboration of ecosystem services linked to policy makers' priorities,  
411 citizens, industry and SMEs.

### 412 **Conclusion**

413 This Ocean4Biotech COST Action will contribute to the implementation of the Bioeconomy Strategy  
414 and the European Green Deal<sup>12</sup>. It will also mainstream the responsible research and innovation  
415 principles among the scientific and industry communities to foster the interaction between marine  
416 scientists and other marine biotechnology stakeholders, including the general public. Such interaction  
417 will be multidirectional rather than top-down and co-creative instead of just being introduced by the  
418 authorities and/or knowledge holders. Outreach and communication activities will provide  
419 information to the broad community and improve their capacity to understand the challenges and  
420 opportunities to make appropriate decisions in the field of marine biotechnology. An inclusive,  
421 integrative approach is essential to catalyze the expansion of marine biotechnology in Europe and  
422 worldwide and to finally harvest the products of this promising field of research. Finally, the  
423 establishment of interdisciplinary connections and collaborations during Ocean4Biotech's lifetime  
424 will not only lead to future research collaborations that include industrial representatives as well, but  
425 also provide establishment of communication channels with policymakers, governments, and other  
426 stakeholders, including the public. This will eventually enable beneficial social and environmental  
427 impacts that will ultimately contribute to a more efficient and sustainable use of marine bioresources.

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<sup>11</sup> <http://www.marinespecies.org/>

<sup>12</sup> [https://ec.europa.eu/info/sites/info/files/european-green-deal-communication\\_en.pdf](https://ec.europa.eu/info/sites/info/files/european-green-deal-communication_en.pdf)

428 **Conflict of Interest**

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437 AR designed the article concept and drafted the manuscript. All authors read, commented, improved  
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469 **References**

470 Barbier, M., Reitz, A., Pabortsava, K., Wölfl, A.C., Hahn, T., Whoriskey, F. (2018). Ethical  
471 recommendations for ocean observation. *Adv. Geosci.* 45, 343-361

472 Carroll, A.R., Copp, B.R., Davis, R.A., Keyzers, R.A., Prinsep, M.R. (2019). Marine natural  
473 products. *Nat. Prod. Rep.* 36, 122-173

474 Cuevas, C., Francesch, A. (2009). Development of Yondelis (trabectedin, ET-743). A semisynthetic  
475 process solves the supply problem. *Nat. Prod. Rep.* 26(3), 322-337

476 Datta, A., Mukherjee, D., Jessup, L. (2014). Understanding commercialization of technological  
477 innovation: taking stock and moving forward. *R&D Management* 45(3), 215-249

478 Dias, D.A., Urban, S., Roessner, U. (2012). A historical overview of natural products in drug  
479 discovery. *Metabolites* 2(2), 303–336

480 Ecorys (2014). Study in support of Impact Assessment work on Blue Biotechnology, Revised Final  
481 Report FWC MARE/2012/06 – SC C1/2013/03. 214 pp. Available at  
482 [https://webgate.ec.europa.eu/maritimeforum/system/files/Blue%20Biotech%20-](https://webgate.ec.europa.eu/maritimeforum/system/files/Blue%20Biotech%20-%20Final%20Report%20final.pdf)  
483 [%20Final%20Report%20final.pdf](https://webgate.ec.europa.eu/maritimeforum/system/files/Blue%20Biotech%20-%20Final%20Report%20final.pdf)

484 EuroMarine Working Group (2019). Strategic agenda on enhancement of human resources to support  
485 blue growth sectors. Eds. M. Cappelletto, A. Cuttitta, B. Patti, National Research Council of Italy.  
486 ISSN: 2239-5172 n. DTA/28-2019. rev. 02 (March 2020).

487 Galanakis, C.M. (2019). *Carotenoids: Properties, Processing and Applications*. Elsevier

488 Gaudêncio, S.P., Pereira F. (2015). Dereplication: racing to speed up the natural products discovery  
489 process. *Nat. Prod. Rep.* 32 (6), 779-810

490 Gerwick, W.H., Fenner, A.M. (2013). Drug discovery from marine microbes. *Microb. Ecol.*, 65(4),  
491 800-806

492 Greco, G.R., Cinquegrani, M. (2016). Firms plunge into the sea. Marine biotechnology industry, a  
493 first investigation. *Front.Mar.Sci.*, 2. doi: 10.3389/fmars.2015.00124

494 Klitgaard, A., Iversen, A., Andersen, M.R., Larsen, T.O., Frisvad, J.C., Nielsen, K.F. (2014).  
495 Aggressive dereplication using UHPLC–DAD–QTOF: screening extracts for up to 3000 fungal  
496 secondary metabolites. *Anal Bioanal Chem*, 406(7), 1933-1943

- 497 Leese, F., Altermatt, F., Bouchez, A., Ekrem, T., Hering, D., Meissner, K. et al. (2016). DNAqua-  
 498 Net: Developing new genetic tools for bioassessment and monitoring of aquatic ecosystems in  
 499 Europe. RIO 2: e11321. doi:<https://dx.doi.org/10.3897/rio.2.e11321>
- 500 Lindequist, U. (2016). Marine-derived pharmaceuticals – challenges and opportunities. *Biomol. Ther.*  
 501 24(6), 561-571
- 502 Lloyd, K.G., Steen, A.D., Ladau, J., Yin, J., Crosby, L. (2018). Phylogenetically novel uncultured  
 503 microbial cells dominate earth microbiomes. *mSystems* 3(5): e00055-18.  
 504 doi:<https://dx.doi.org/10.1128/mSystems.00055-18>
- 505 Mora. C., Tittensor, D.P., Adl, S., Simpson, A.G.B., Worm, B. (2011). How many species are there  
 506 on earth and in the ocean? *PLoS Biol.* 9(8): e1001127.  
 507 doi:<http://dx.doi.org/10.1371/journal.pbio.1001127>
- 508 Perez-Lopez, P., Feijoo, G., Moreira, M. (2018). “Sustainability assessment of blue biotechnology  
 509 processes: addressing environmental, social and economic dimensions” in *Designing sustainable  
 510 technologies, products and policies*, eds. E. Benetto, K. Gericke, M. Guiton (Springer), 475-486
- 511 Rao, T.E., Imchen, M., Kumavath, R. (2017). Marine enzymes: production and applications for  
 512 human health. *Advances in food nutrition research* 80, 149-163
- 513 Rodrik, D. (2014). Green industrial policy. *Oxf. Rev. Econ. Policy* 30(3), 469–491
- 514 Steen, A.D., Crits-Christoph, A., Carini, P., DeAngelis, K.M., Fierer, N., Lloyd, K.G., et al. (2019).  
 515 High proportions of bacteria and archaea across most biomes remain uncultured. *ISME J* 13, 3126–  
 516 3130
- 517 Theodotou Schneider, X. (2019). Responsible Research and Innovation roadmap. [Report from the  
 518 MARINA Horizon 2020 project]. [https://www.xpro-  
 519 consulting.com/uploads/4/9/5/5/49557869/rri\\_roadmap\\_\\_online\\_single.pdf](https://www.xpro-consulting.com/uploads/4/9/5/5/49557869/rri_roadmap__online_single.pdf)
- 520 Vartoukian, S.R., Palmer, R.M., Wade, W.G. (2010). Strategies for culture of ‘unculturable’ bacteria.  
 521 *FEMS Microbiol. Lett.* 309, 1-7
- 522

523 **Supplementary Materials**

524 **Supplementary Table S1:** Examples of the past and current international initiatives in the field of  
525 marine biotechnology in Europe. The level column represents the targeted involvement within each  
526 initiative (industry, research community, legislative authorities, general public, environment  
527 protection; they are presented in Figure 2 and in the main text).

528 **Supplementary Table S2:** A SWOT analysis used to plan and assess the necessity of establishing  
529 marine biotechnology interdisciplinary networks such as COST Action CA18238 (Ocean4Biotech).

530

531 **Figure legends**

532 **Figure 1:** Schematic representation of a bioprospecting protocol for the extraction of valuable  
533 bioactive compounds from marine organisms (adapted from Galanakis, 2019).

534 **Figure 2:** Major prerequisites for the establishment of sustainable actions in marine biotechnology.

In review

Figure 1.TIF



