Project Acronym:
FUSVET (SEED/1221/0080)

Focused Ultrasound System for Veterinary Chemotherapeutic Applications for Oncology

Deliverable number: 4.3

Title: Report on the fund raising activities.

Prepared by:

Nikolas Evripidou (CUT)
Anastasia Antoniou (CUT)
Antria Filippou (VET-EX MACHINA)
Kyriakos Spanoudes (VET-EX MACHINA)
Christakis Damianou (CUT)

Date: 31/01/2025

Funded by the European Union NextGenerationEU
Cyprus tomorrow RECOVERY AND RESILIENCE PLAN
Republic of Cyprus
RESEARCH & INNOVATION FOUNDATION

The FUSVET project is funded by the Recovery and Resilience Facility of the NextGenerationEU instrument, through the Research and Innovation Foundation (RIF) of Cyprus.

Table of Contents

Executive Summary 3

Events 4

5th Annual Petcare Innovation Europe summit, Berlin, Germany 4

Entrepreneurial programmes 5

Beyond Pre-Accelerator programme, Junior Achievement Cyprus 5

European Innovation Council Accelerator programme 7

Provision of support services from the Central KTO of RIF 11

Appendix 1: Supplementary pitch deck presentation for EIC application 14

Appendix 2: EIC application 15

Cover page 15

First page 16

Appendix 3: Submitted proposal for provision of KTO support services 17

Appendix 4: Invention and Technology Disclosure Form 24

Executive Summary

This deliverable concerns the various fund-raising activities that were undertaken by the host organisation (VET-EX MACHINA) in an effort to attract the necessary financial support from potential investors for commercial exploitation of the system that was developed during the framework of the FUSVET project. In this sense, the end-product of the project was presented at a summit event dedicated to veterinary innovation wherein the main features of the robotic system and its major benefits over existing solutions were communicated to investors through personal meetings, while potential investment opportunities and pathways to the market were discussed.

Additionally, applications were made to different accelerator programmes as an alternate route for potentially acquiring the necessary funds for market deployment of the system. Specifically, an application was submitted to the Beyond Pre-Accelerator programme organized by Junior Achievement Cyprus, while a short proposal was made to the first stage of the European Innovation Council (EIC) Accelerator 2024 programme. In the framework of the former application, the developed system along with the potential benefits offered to veterinary oncology and the business model of the company were pitched in front of various experts, business people, and decision makers from the entrepreneurial world. The short proposal submitted to the EIC included a comprehensive description of the FUSVET system, highlighting its potential as a non-invasive, advanced therapeutic solution for veterinary oncology patients. It also outlined the need for financial resources to optimize and effectively market the device for commercial deployment.

To fully exploit the developed system and enhance its potential commercial impact, a request was also made to the Central Knowledge Transfer Office (KTO) of the Research and Innovation Foundation (RIF) for provision of commercialisation services for the developed technology. All required documents were appropriately completed and submitted in the form of a short proposal, commencing the company's journey in receiving the required support for the potential market deployment of the system. VET EX MACHINA, as the main beneficiary, received a comprehensive assessment focused on prior art search and IP protection strategy, presented in a detailed report containing findings, conclusions, and recommendations. A Freedom to Operate (FTO) analysis was conducted providing actionable insights on the viability of commercialization without infringement.

The various fundraising activities that were undertaken are presented in this deliverable according to the nature of the activity (i.e., events attended, applications to entrepreneurial programmes, and submission for provision of KTO services).

Events

5th Annual Petcare Innovation Europe summit, Berlin, Germany

Kyriakos Spanoudes (VET-EX MACHINA) attended the *5th Annual Petcare Innovation summit* that took place between the 3-4 May 2023 in Berlin, Germany; a summit dedicated to veterinary innovation, where investors and inventors from the European veterinary field meet. During the summit, he met with investors through numerous group and one-to-one meetings where he had the opportunity to talk about FUSVET as a product and discuss about investment opportunities and pathways to the market. Figure 1 shows photos taken during the summit, while Figure 2 shows the summits itinerary indicating scheduled 1-to-1 meetings with investors.

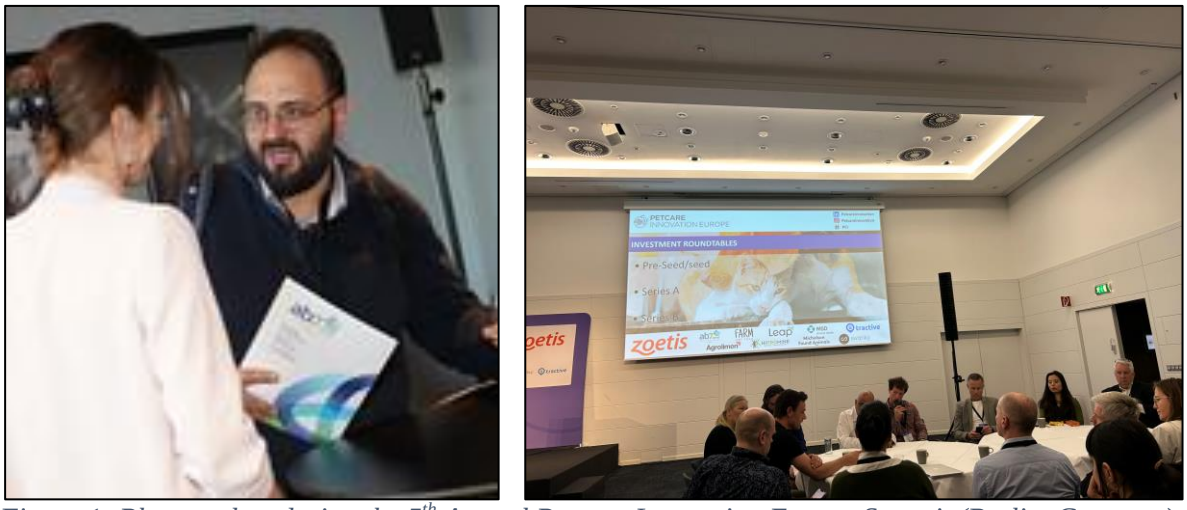

Figure 1: Photos taken during the 5th Annual Petcare Innovation Europe Summit (Berlin, Germany).

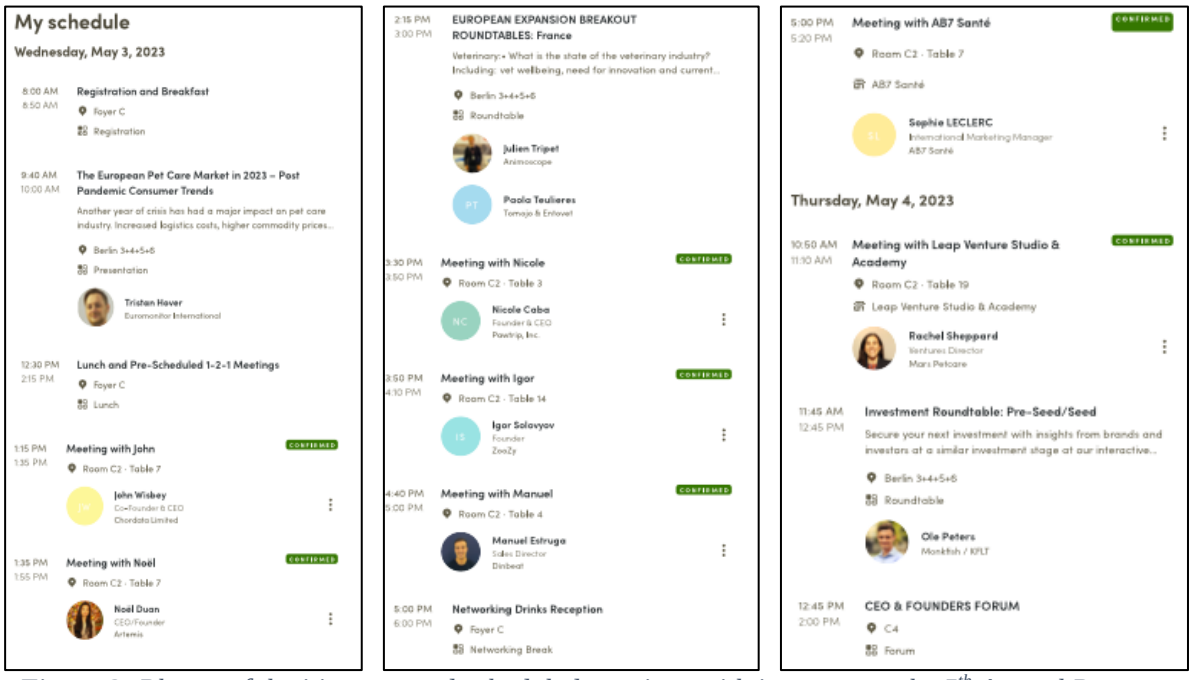

Figure 2: Photos of the itinerary and scheduled meetings with investors at the 5th Annual Petcare Innovation Europe Summit (Berlin, Germany).

Entrepreneurial programmes

Beyond Pre-Accelerator programme, Junior Achievement Cyprus

Kyriakos Spanoudes (VET-EX MACHINA) applied to the Beyond Pre-Accelerator 2023-2024 programme organised by Junior Achievement (JA) Cyprus (Nicosia, Cyprus); a programme tailored to early-stage professionals seeking to introduce innovative entrepreneurial solutions for prevention, diagnosis or treatment of cancer. After a successful application, the project coordinator, and CEO of VET-EX MACHINA (Kyriakos Spanoudes) had the opportunity to pitch the end-product developed during the framework of the FUSVET project in front of various experts from the entrepreneurial world. The FUSVET system and the benefits offered to veterinary oncology as well as the size and share of its targeted market were presented through a pitch deck (which is included in Deliverable 4.2) on 4th March 2024 at the offices of Novartis (Nicosia, Cyprus). After the presentation, he received valuable feedback from expert entrepreneurs on how to improve the pitch for the programme's subsequent phases. Figure 3 shows a photo acquired during the delivered pitch presentation, while Figure 4 shows a screenshot of the same photo as disseminated through the LinkedIn profile of JA Cyprus.

Figure 3: Photo taken during pitch presentation of FUSVET in the context of the Beyond Pre-Accelerator programme by JA Cyprus (Nicosia, Cyprus).

Figure 4: Screenshot of LinkedIn profile of JA Cyprus disseminating the pitch presentation of FUSVET in the context of the Beyond Pre-Accelerator programme by JA Cyprus (Nicosia, Cyprus).

After successfully passing from the initial stages of the programme, Kyriakos Spanoudes (VET-EX MACHINA) had the chance to present the FUSVET system and the business model for its commercial exploitation during the Beyond Pre-Accelerator demo day which took place on the 13th of June 2024 at the Theatro Polis OPAP (Nicosia, Cyprus). The FUSVET system was presented and pitched in front of an audience consisting of people from the public, academics, representatives of the business world and key people from various national organisations involved in the research, prevention, diagnosis, or treatment of cancer. Following the pitch presentation, he networked with the entrepreneurs and business people that attended the event, and had the opportunity to explain in detail the developed product and discuss about potential investment. Figure 5 shows the agenda of the Beyond Pre-Accelerator demo day, while Figure 6 shows a photo acquired during the pitch presentation.

Figure 5: Photo of the agenda of the Beyond Pre-Accelerator Demo Day (Nicosia, Cyprus).

Figure 6: Photo taken during the pitching of FUSVET at the Beyond Pre-Accelerator Demo Day (Nicosia, Cyprus).

European Innovation Council (EIC) Accelerator programme

The host organisation (VET-EX MACHINA) as a small-medium enterprise (SME), applied to the European Innovation Council (EIC) Accelerator 2024, a programme funded under Horizon Europe targeted at ambitious start-ups and SMEs that possess disruptive innovations they wish to bring to the market. Companies can apply to the programme requesting significant funding in the form of either non-dilutive grant or grants combined with dilutive equity investment to advance the technology readiness level (TRL) of their proposed ground-breaking invention to commercially available standards or introduce their product to the market, respectively. Simultaneously, in addition to financial aid, selected start-ups benefit from valuable coaching and mentoring support from the EIC ecosystem of experienced business partners that includes coaches, investors, and leading corporates, among others. EIC funded companies can utilise these support services to leverage to the maximum the received funding, accelerate the development process of their proposed innovation and scale up their business.

The EIC Accelerator is a highly competitive programme that follows a rigorous 3-step application process. Particularly, in the first stage, companies are invited to submit a short proposal outlining their innovation from which businesses offering high-impact ideas characterised by excellence are then remotely selected to submit a full proposal as part of the EIC's second phase. Companies successfully passing the second stage are then invited to pitch their idea in front of the EIC jury of experienced investors and entrepreneurs from which beneficiaries entitled to EIC funding are ultimately selected. Considering that VET-EX MACHINA requires substantial funding to deploy the system developed during the FUSVET project to the market, an application to the first stage of the EIC programme was submitted to acquire grants required to advance the TRL level of the prototype therapeutic device, priming and optimising the product for commercial deployment. This application was considered as an alternate, more feasible route for potentially acquiring the necessary funds, since the host organisation faced numerous challenges in acquiring funding from private investors who despite expressing interest were generally reluctant to invest in technologies dedicated to the veterinary market due to the market size and expected profit margin.

As such, a short proposal was prepared according to set guidelines and submitted to the EIC Accelerator. In the submitted proposal, an overview of the company outlining important information including the year of establishment, previous experience as a preclinical research organisation as well as the company's vision in becoming a manufacturer of Magnetic Resonance Image (MRI) guided focused ultrasound (MRgFUS) systems for veterinary therapeutic applications was initially provided. Additionally, a brief overview of suppliers and stakeholders actively engaged in the manufacturing procedure of the company's products was included, while qualified scientific advisors who have the required expertise to help the company develop a high-quality, commercially viable therapeutic device of clinical standards were described. Moreover, information about the company's personnel including an overview of the scientific background, competencies and expertise offered by each existing team member was provided, while the personnel required to help the company enter the market and evolve was described. If the company becomes an EIC beneficiary, the opportunity to recruit expert personnel having the required skills to fill existing gaps will arise, with VET-EX MACHINA

ultimately having the essential workforce to properly commercialise FUSVET, thus fulfilling its vision.

Thereafter, a brief review of therapeutic solutions currently available for cancer treatment in pets and their associated shortcomings in terms of the animal's quality of life as well as financial burden imposed on pet owners was provided indicating the need for novel non-invasive therapies. Consequently, the factors driving the company's goal in entering the market of veterinary oncology by offering an innovative non-invasive solution that leverages the benefits of focused ultrasound (FUS) were outlined. Therefore, a description of the FUSVET system and its operational principles was provided outlining the reasons why the proposed device offers a unique treatment solution compared to conventional veterinary oncological therapies and existing competitive therapeutic solutions. Particularly, the ability of the device to offer a safe and accurate non-invasive procedure due to the employment of FUS and robotic mechanisms, treat a range of animals and multiple anatomical sites due to its unique design, and provide reliable monitoring of the treatment procedure due to its universal compatibility with MRI scanners were highlighted.

In this sense, the value proposition of the FUSVET system that the company wishes to commercialise to redefine veterinary oncology treatments was described, while the competitive advantage of the proposed system in the veterinary oncology market was explained. Specifically, through the submitted proposal, it was made apparent that safe operation of the proposed device within MRI environments provides superiority in terms of treatment accuracy and efficacy compared to competitive FUS therapeutic solutions since these mainly employ ultrasound guidance, while the incorporation of multiple degrees of freedom suggests that the system can manage a wide range of veterinary oncological indications at a cost-effective pricing, thus setting it apart from competitors. Moreover, the potential of FUSVET in becoming an alternative, top-notch, non-invasive and ionising-free therapeutic solution for veterinary oncology patients was explained, ultimately indicating its future adoption by veterinary clinics that wish to benefit from the integrated advantages of the system to offer an advanced therapeutic solution to animal patients.

Furthermore, through the application essential information about the current TRL level of the FUSVET system was provided. Specifically, the development of the prototype robotic system and associated software, as well as comprehensive preclinical *in-vitro* and *in-vivo* evaluation of the device's performance that advanced the system to a TRL 6 (technology demonstrated in relevant environment) through the financial support from numerous research grants were described. As a result, the need for VET-EX MACHINA to acquire grants to advance the TRL level of the system by optimising hardware and software components and evaluating the therapeutic efficacy of the system on pets with cancer through large-scale veterinary trials, thus priming and comprehensively marketing the device for market deployment was revealed. Consequently, to provide EIC evaluators with essential information about the expected monetary, societal and animal welfare benefits associated with potential system commercialisation, important details relating to the market in which the company intends to position itself such as the size of the veterinary oncology market, forecasted market growth and related factors affecting market size, the intended beachhead market for the company's product

together with reasons driving customers in purchasing the system as well as expected share in the market were provided. Moreover, details relating to competitive systems tailored to FUS applications for animals were provided, emphasizing the unique competitive advantage of VET-EX MACHINA in the veterinary oncology market arising from potential commercial exploitation of FUSVET. Noteworthy, abovementioned details that were included in the EIC proposal and related to market and competition analysis can be found in the prepared business plan (Deliverable D2.7).

Notably, along with the written proposal, VET-EX MACHINA's application to the EIC Accelerator programme was accompanied by a relatively short (approximately 3 minutes duration) pitch video in which some of the abovementioned information about the FUSVET system and its therapeutic applications in the field of veterinary oncology were included, while core members of the team were also featured explaining the motivation behind the submitted proposal indicating the benefits offered by the proposed device and proclaiming their role in the development and evaluation of the system. Figure 7 shows indicative captures of the prepared video introducing the FUSVET system (Figure 7A) and key team members that talked about the proposed technology and their role in the project (Figure 7B-D). Nevertheless, explicit information relating to the contents of the EIC-submitted pitch video along with comprehensive video screenshots can be found in Deliverable 4.2 (Report of branding material).

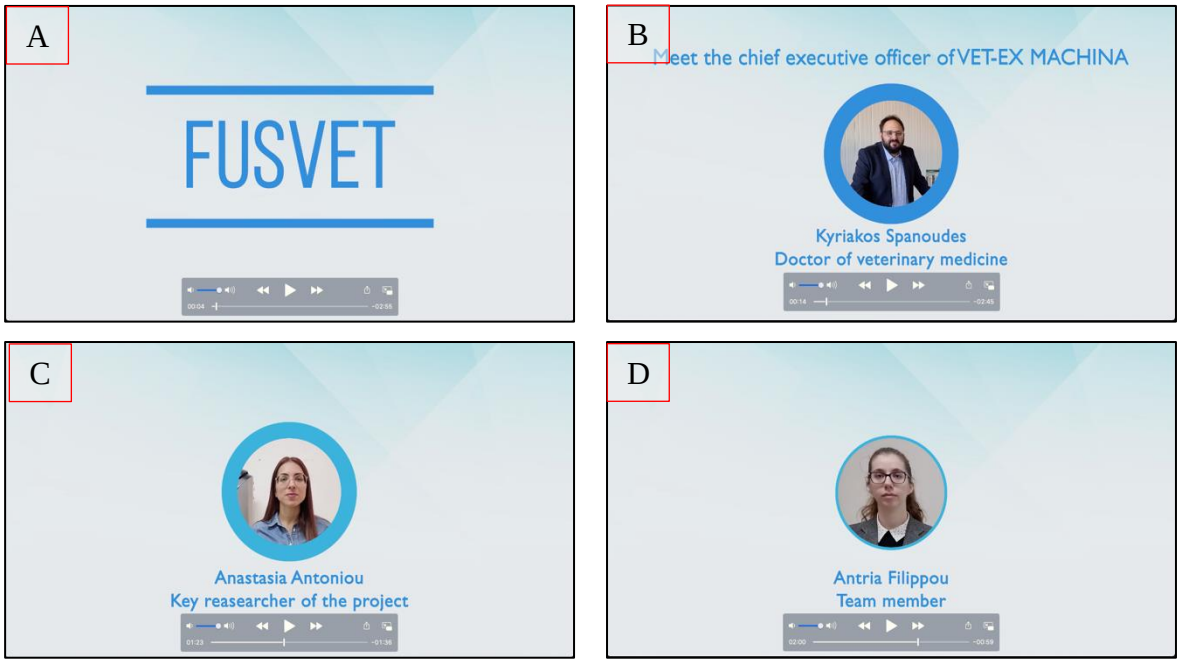

Figure 7: Screenshots of the prepared pitch video showing A) Introduction to FUSVET, and talks from B) the CEO of VET-EX MACHINA, C) a key researcher of the project (partner organisation), and D) a team member from the host organisation,

Additionally, the EIC application was supplemented by a 10-slide pitch deck that summarised essential information that were included in the written proposal. Particularly, an overview of VET-EX MACHINA and a comprehensive description of the FUSVET system including its intended applications, operational principles as well as key data related to potential commercial exploitation such as the targeted market and competitive advantage were presented in the pitch deck. The first page of the prepared pitch deck presentation is indicatively included in

Appendix 1, while a comprehensive summary of the included material along with the complete prepared pitch deck presentation can be found in Deliverable 4.2. Finally, the cover and first pages of the submitted EIC application can be found in Appendix 2.

EIC Application Outcome and Insights

The application submitted to the EIC for VET EX MACHINA underwent thorough evaluation but ultimately received a "No-Go" decision. Below we provide an overview of the evaluation summary report.

Strengths & Opportunities: The evaluation highlighted the project's strong objectives, relevance, and potential to advance the state of the art in veterinary oncology. Reviewers recognized the technology's innovative approach to addressing pet cancer; an increasingly pressing issue, by integrating MRI and FUS into a cost-effective, non-invasive treatment alternative. The potential of MRgFUS to minimize the need for surgery or provide a critical alternative for non-operable cases was recognized as a significant advantage.

Three out of four evaluators agreed that FUSVET has successfully completed the key steps required for TRL6 readiness. Additionally, all reviewers considered the proposed market entry timeline effective and relevant. The system's cost-effective and portable design was acknowledged for its alignment with the increasing demand for accessible and affordable cancer treatments for pets.

Reviewers did not mention any implementation issues, and the team's overall capability was praised. The team was recognized as highly qualified, motivated, and well-equipped to implement the innovation and bring it to market. Our multidisciplinary expertise, combined with a strong track record of securing funding, was seen as a key strength that demonstrates our capacity to sustain the project. While the team composition currently lacks full gender balance, reviewers acknowledged that there is a clear plan to promote gender equality. Furthermore, the proposal identified gaps in marketing and sales expertise among others and outlined a plan to address them through strategic hiring, which reviewers recognized as a proactive approach.

Challenges and Considerations: The reviewers raised concerns about the absence of detailed laboratory and animal trial results, as well as the lack of a clear roadmap for translating the technology to human applications. The perceived limited clinical evidence (provided in the proposal) was also seen as a limiting factor in understanding the demand from potential customers. They also highlighted the importance of conducting a more in-depth evaluation of market competition, particularly in assessing how existing players might refine their approaches and potentially strengthen their competitive position. Finally, while the transformative potential of FUSVET in veterinary oncology was acknowledged, reviewers pointed out that the lack of pet insurance in certain countries could limit accessibility if costs remain high.

Next Steps & Resubmission Plan: Despite the recognized benefits, the application was unfortunately rejected due to the identified challenges. However, the feedback offered valuable insights, allowing the company to refine its approach and better position FUSVET as a more feasible solution by emphasizing clinical outcomes from veterinary trials. This will support our

efforts to resubmit a stronger proposal to the EIC or even explore alternative funding opportunities or partnerships.
The initial lack of detailed pet trial results was due to space constraints; however, now that we understand its significance in the evaluation process, we could revise the content to include these crucial results, supported by additional trials conducted in the meantime, which will further strengthen the clinical evidence. Furthermore, we will provide a clearer explanation of how integrating FUSVET into veterinary oncology can support the technology's potential for translation to human applications. By addressing the concerns and specific questions raised by the reviewers, we are confident that a resubmission could lead to a more favorable outcome.

Provision of support services from the Central KTO of RIF

To fully exploit the technology developed within the framework of the FUSVET project, Kyriakos Spanoudes, as the legal representative of the host organisation (VET-EX MACHINA), applied to the Central KTO of the RIF for provision of commercialisation services. As an eligible beneficiary of a research project funded by RIF, the application was submitted in the form of a short proposal through the open call RIF-CKTO/PATH1&2/1123/, under the Fast-Track route, which applies to projects funded under specific calls of proposal (including the "SEED Programme"; Call Identifier: SEED/1221). The proposal was uploaded and submitted through the IRIS online services portal (https://iris.research.org.cy/).

The Part B-Technical Annex of the proposal, which was uploaded on the IRIS portal, can be found in Appendix 3. The technical annex of the application describes the primary technological outcome of the project through a non-confidential summary. Specifically, the MRgFUS robotic system that was developed for veterinary cancer applications is concisely described, highlighting its primary features and compatibility with MRI scanners. The main therapeutic FUS applications of the system in animals in terms of thermally ablating tumours and augmenting chemotherapeutics are described, while its potential clinical adaptation for treating tumours at various regions on human patients is also specified.

Additionally, the appointed representatives of the two organizations (VET-EX MACHINA and CUT) are specified in the Part B document, along with the ownership percentage of the Asset assigned to each organization. Since the intellectual concept and development of the proposed system were a joint effort of both partners involved in the project, it was mutually decided that the rights to the intellectual property (IP) would be shared between VET-EX MACHINA and CUT, with each partner owning an equal share to the invention (50 %). In this sense, all partners are acknowledged for their contribution in the invention and have a stake in the successful market deployment of the proposed system.

Consequently, an 'Invention and Technology Disclosure Form' was prepared to formally establish the IP ownership rights of each partner. This form, prepared by CUT, gathers essential details of inventions developed at the university to assess their patentability and commercial potential. This form was signed by all inventors and submitted as a supplementary document to the proposal. The relevant document can be found in Appendix 4. The form primarily includes key information about the developed technology, including a detailed description of its operational features, its therapeutic purpose for veterinary patients as well as the benefits

offered to animals owing to the non-invasive nature of the employed FUS technology and the conformal design of the system. A brief overview on conventional treatments which are currently available in the veterinary oncology field, and represent the state of the art, is provided, discussing their limitations, and highlighting the need for advanced therapeutic solutions that impose fewer side effects. The ability of FUS to offer non-invasive therapeutic solutions in veterinary medicine is described, along with the features and limitations of existing FUS systems designed for animal use. As a result, the main innovative features of the robotic system that was jointly developed by the consortium are outlined, highlighting its uniqueness and competitive advantage compared to existing solutions, thus showcasing its potential patentability. Furthermore, the development process of the system and any *in-vivo* experiments on laboratory animals and pets with spontaneous tumours that demonstrated the system's safety and efficacy are summarized, while the system's potential commercial applications are also discussed. Finally, comprehensive details about all inventors are provided, including their affiliations and intellectual contribution in the invention. Moreover, any relationships or agreements that could potentially restrict the commercial usage of the system were outlined, while companies that commercially offer comparable technologies and could potentially express interest towards acquiring the developed product were identified.

Provided KTO services

VET EX MACHINA received a comprehensive assessment focused on prior art search and IP protection strategy, presented in a detailed report containing findings, conclusions, and recommendations. The document starts with an overview of the intellectual assets, followed by an analysis of prior art and a non-legal patentability assessment, which was conducted as part of the Freedom to Operate (FTO) evaluation. The patentability assessment examined all relevant existing patents associated with the invention, evaluating the potential impact of competing intellectual property, products, services, and ongoing R&D efforts on its novelty. Accordingly, the FTO assessment compared the key features of our asset with existing patent claims to assess whether these patents could pose a risk to the commercial use of the technology due to potential infringement. The review of external technologies and patents also aimed to identify dependencies for FUSVET and determine whether market deployment would require licensing or other agreements with third parties to mitigate legal risks.

Patent Prospects of Technology: Key Findings and Recommendations

The analysis of relevant patents revealed some overlap between our invention and existing innovations, particularly in the areas of non-invasive treatment, precision targeting, robotic assistance, and MRI compatibility; an expected outcome given the increasing applicability of these features in medical applications, driven by the demand for image-guided, non-invasive solutions. The analysis further highlighted specific geographic regions where we may encounter the greatest challenges in protecting and exploiting the FUSVET technology. In particular, regions such as Europe, China, and the USA have dense patent landscapes in these fields, especially within cancer treatment applications. This overlap highlights potential risks of infringement. However, while individual features of the technology, such as non-invasive treatment, precision targeting, and MRI compatibility, may overlap with existing patents, the novelty of the FUSVET technology lies in the unique combination of these features. Overall,

while the assessment presented certain considerations, it also provided valuable insights that will guide future strategic decisions regarding IP protection, commercialization, and market entry.

According to the KTO report, while FUSVET presents unique features that can reduce patient stress and enhance treatment efficiency, these advantages may not entirely eliminate commercialization risks. As the applicant, we currently hold the rights to the invention and can proceed with commercialization or licensing; however, the outcome of the patent examination is still uncertain, which could affect the scope of these rights. To strengthen our position, we have been advised to develop a strong brand identity that highlights key differentiators such as patient comfort, user experience, and cost-effectiveness, helping to distinguish the technology in the market and mitigate perceived IP risks. At the same time, we will continuously monitor technological advances to ensure we stay up to date and update features as needed, maintaining the technology's competitive edge. Furthermore, as stated in the relevant report, ongoing investment in R&D to drive new, patentable innovations in areas like machine learning, precision targeting, and cost efficiency will ensure long-term competitiveness and support market share growth.

The company is committed to progressing with these strategies, implementing any necessary technological advancements. Patent claims will be meticulously crafted under expert legal guidance to support the identified differentiators, complemented by targeted marketing and branding efforts to strengthen the approach.

Appendix 1: Supplementary pitch deck presentation for EIC application

vet ex machina

FOCUSED ULTRASOUND SYSTEM FOR VETERINARY CHEMOTHERAPEUTIC APPLICATIONS FOR ONCOLOGY

FUSVET

Appendix 2: EIC application

Cover page

Horizon Europe Programme

EIC Accelerator Short proposal Application Form

Project short proposal – Technical description (Part B)

Version 1.0
15 December 2023

First page

FOCUSED ULTRASOUND SYSTEM FOR VETERINARY ONCOLOGY

List of participants

Participant	Participant organisation name	Country
1 (Coordinator)	**VET EX MACHINA LIMITED**	**CYRPUS**
2 Affiliated entity(ies), if any. Please explain the link with the coordinator and the role in the project.	**N/A**	**N/A**

1. Company description

GENERAL INFO : **VET EX MACHINA LTD,** which was founded in 2019 is a private company focusing in veterinary products. The company is owned 100 % by Veterinarian Kyriakos Spanoudes (Founder). To date, the company has been involved in numerous research grants in collaboration with Cyprus University of Technology (CUT) in the field of veterinary research (FUSROBOT, PROSTASONIC, SOUNDPET, FUSVET, ABLASONIC, BRAINSONIC), providing services in veterinary trials. Notably, VET EX MACHINA is the only approved center in Cyprus to host rabbits, dogs and cats (medium to large animals).

MARKET FOCUS AND VISION : In the past five years, **the company's focus has increasingly shifted towards the field of focused ultrasound (FUS)**, recognizing its promising potential as an alternative therapeutic solution for veterinary cancer patients. This growing interest has been reinforced by the company's active involvement in research and development (R&D) grants centered on FUS therapeutic applications in pets, in collaboration with CUT and specifically the laboratory of Therapeutic Ultrasound. Moving forward, the company is now committed to prioritizing this technology and exploring its market potential within the veterinary sector, supported by a strong collaboration with expert scientists in the field. **VET EX MACHINA's vision is to transition from a research organization to a well-established manufacturer and distributor of top-notch FUS systems for veterinary therapeutic applications.**

LAUNCHING OUR FIRST THERAPEUTIC SYSTEM : The company has recently developed an advanced prototype FUS robotic system for veterinary oncological applications and associated treatment planning-monitoring software in collaboration with field experts from CUT (through national grants). The novel veterinary system is under clinical trials on dogs and cats with cancer (30 pets treated so far). Its current goal is to commercialize this innovative technology, eventually entering and excelling in the veterinary oncology and preclinical research markets.

COMPANY EXPANSION IN PROGRESS - AMPITION TO SCALE UP: To support our growth objectives and accommodate increased operational demands, we have already acquired land in Lympia, Cyprus. The new site will host additional equipment and staff. With an established presence in the veterinary market, the company aims to expand into human applications in the future, specifically for treating bone cancer, leveraging the system's design suitability (conformal use).

TEAM : The company, presently consisting of a CEO/Founder and four employees, aims to expand by recruiting skilled personnel in R&D and business, enabling it to effectively enter the market, evolve rapidly, and pursue its goals. **Expert scientists who have been involved in the development of the company's first potential product are ready to fully commit to the company** and work hard towards common corporate objectives.

CURRENT SUPPLIERS : We maintain partnerships with all suppliers needed for product manufacturing, including T&C Power Conversion; USA (amplifiers), Fischer connectors; Switzerland (medical connectors), Meggitt; Denmark (piezoelectric materials), Shinsei Corporation; Japan (piezoelectric motors), US Digital; USA (optical encoders), and Stratasys; USA (3D printing thermoplastic materials).

MAIN STAKEHOLDERS : **Academic** – CUT (Limassol, Cyprus), and German Medical Institute in Cyprus. **Veterinary** – V3ts Veterinary Clinic (Larnaca; Cyprus) and CYVETS Veterinary center (Paphos; Cyprus).

ADVISORS : **Academic** – Prof. Nicos Constantinou (CUT, Cyprus). **Clinical** – Dr. Nikolaos Zamboglou and Dr. Cleanthis Ioannides (German Medical Institute; GMI, Cyprus). **Veterinary** – Prof. Michael Edward Herrtage (School of Veterinary Medicine, University of Nicosia, Cyprus).

Appendix 3: Submitted proposal for provision of KTO support services

RESEARCH & INNOVATION FOUNDATION

RESTRICTED CALL

Central Knowledge Transfer Office Services

(RIF-CKTO/PATH1&2/1223)

Fast Track and Direct Entry

PROPOSAL DETAILS	
PROGRAMME	**Central Knowledge Transfer Office Services**
IRIS PROPOSAL NUMBER	**RIF-CKTO/PATH1&2/1223/0114**

Funded by the European Union NextGenerationEU

Cyprus tomorrow RECOVERY AND RESILIENCE PLAN

Republic of Cyprus

RESEARCH & INNOVATION FOUNDATION

PART B – TECHNICAL ANNEX

LEGAL NOTICE for the submission of application under this Call:

Applicants should ensure that:

- The Applicant is a beneficiary of the funded RDI project. The Applicant may be different from the Host Organisation of the funded project subject to the agreement of the Consortium members. The Applicant must own or have been granted all or part of at least one legal right in the intellectual assets which are the subject of this application or be the duly appointed agent with all necessary powers of an owner of such rights.
- The Proposal (Application) must be submitted ONLY by the Legal Representatives of the Organisation.
- The management of each participating Organisation in the Consortium (where applicable) and any natural person (i.e., individual) with an ownership interest in any legal right in the intellectual assets which are the subject of this application have been informed and has already approved the content and submittal of the application.
- Participating Organizations and natural persons have not been convicted of an offence concerning professional conduct by a judgment of a national competent authority which has the force of res judicata.
- Participating Organizations and natural persons have not had a petition or issue of judgement or order for winding up or liquidation or bankruptcy filed against have not entered into an arrangement with creditors, have not suspended business activities, are not the subject of proceedings concerning above matters and is in compliance with applicable national legislation.
- Information provided in the application is true and correct.
- The applicant is responsible to notify all legal representatives of the date and time of the Initial Engagement meeting.
- The management of participating Organisations and any natural persons are aware that the collection and processing of personal data is carried out according to the RIF's Policy for the Protection of Personal Data which can be found at RIF's website.

B1. RIF FUNDED PROJECT - GENERAL INFORMATION

Please provide information related to the RDI Project funded by the RIF.

Protocol Number of the RIF Funded Project:	**SEED/1221/0080**
Title of the RIF Funded Project:	**Focused Ultrasound System for Veterinary Chemotherapeutic Applications for oncology**

B2. APPOINTED REPRESENTATIVES OF THE ORGANIZATIONS, INDIVIDUAL AND/OR CONSORTIUM(S)

The Table below must be completed**. The Table duly signed by the Organisations' Legal Representatives, should be uploaded as Annex II on IRIS.**

The Organisations and/or individuals (collectively called Beneficiaries) who own any rights in the intellectual assets that are the subject of this application must appoint a legal representative for the purpose of applying for the services of the CKTO of interacting and communication with the CKTO for the purposes of the Initial Engagement. The Beneficiaries may decide to be represented by a single agent. If the Beneficiaries decide to be represented by a single agent, it should it clearly stated. In addition, it is the legal responsibility of the submitter of this application that any other entity or natural person which has any ownership or other legal right in the intellectual asset which is the subject matter of this application is be included below and has agreed to the submission and their legal representative is identified in the table below.

Participating Organization, or Individual	**Legal Representative* (for Individuals can be themselves)** ***The Legal Representative should be registered on IRIS / approved by the RIF**	**ID Number**	**Signature of Legal Representative**	**Email of Legal Representative**	**Phone Number of Legal Representative**	**Mailing Address of Legal Representative**	**Percentage of Ownership in the Asset**
VET EX MACHINA LTD	Kyriakos Alexandros Spanoudes	828538		kyriakos.spanoudes@vetexmachina.com	0035799047070	Erechthiou 13, Aglantzia 2121, Nicosia, Cyprus	50
Cyprus University of Technology	Charalambos Chrisostomou	705914		c.chrisostomou@cut.ac.cy	0035725002562	30 Archbishop Kyprianou Str. 3036 Limassol, Cyprus	50

Note:

1. The Percentage of the ownership must sum up to 100% (not less not more)
2. Only organisations indicated with more than 0% of ownership in the Asset will be eligible to receive services from the CKTO

B3. COMMERCIALISATION OF RESEARCH RESULT

B3.1 Non-confidential Summary (Maximum 2 paragraphs)

Please provide a concise but meaningful **non-confidential summary** of the research result/intellectual asset bundle to be exploited that can be understood by a layperson.

The primary technological outcome of the project, intended for exploitation by the consortium, is a Magnetic Resonance Imaging (MRI)-guided Focused Ultrasound robotic system for non-invasive veterinary cancer applications. The system comprises 2 manually controlled and 3 mechanical motion stages dedicated to navigating a single-element spherically focused transducer relative to a target to thermally ablate tumors or enhance the efficacy of chemotherapeutic drugs. The transducer is housed within a water-filled cone that conforms firmly to the region of interest of an animal placed in any position, such as supine, lateral, or prone. The device is considered universal due to its ability to fit in any conventional MRI scanner. The system can be used for non-invasive ionizing-free cancer therapy in veterinary patients or humans by simply adjusting its size. For future human applications, the treatment of tumors at multiple anatomical sites, including breast, abdominal, bone, and fibroid targets will be feasible.

B3.2 Copy of Disclosure(s)

Please provide a copy of all disclosure forms prepared on this technology, invention, or other intellectual asset with your Knowledge Transfer Office or other designated representative of your entity. **(Please include this evidence as Annex II on IRIS).**

An ‘Invention and Technology Disclosure Form’ has been prepared on the developed technology (included as Annex II). This form, crafted by CUT, serves to gather initial details of technologies developed at the University with the ultimate goal to assess patentability and commercial potential. It includes the following key components: title of the invention, a detailed description of the intention and innovative features, comprehensive details about co-inventors along with their affiliations, disclosure of any relationships or agreements that could impose restrictions on commercial usage, and identification of relevant commercial entities offering comparable technologies and/or potentially having interest in the developed technology.

B4. CHECKLIST BEFORE SUBMISSION

The Proposal (Application) consists of Part A (electronic form – IRIS Portal), Part B (Technical Annex to be uploaded on IRIS), Annex II (to be uploaded on IRIS), Annex III (to be uploaded on IRIS). Please check the following before submission.

PARTS OF PROPOSAL (APPLICATION)	**CHECK**
PART B	√
ANNEXES **ANNEX II (Supporting Documents in relation to Knowledge Transfer)**	
1. Table of the appointed representatives of the submitting organization(s), individual(s) and/or consortium	√
2. Copy of all disclosure forms prepared on this technology, invention, or other intellectual asset with your Knowledge Transfer Office or other designated representative of your entity	√
3. Declaration for the Acceptance of the Initial Engagement and Evaluation Service by the RIF Central Knowledge Transfer Office.	√
ANNEX III **(Documents in relation to any National Law / Regulation / Guidelines / State Sid Rules in accordance with the Call of Proposals (Applications)** **For Private Sector Beneficiaries (it applies to all members of the Consortium and NOT ONLY to the Organisation submitting the Proposal (Application)**	
1. Declaration of Non-Debts to State Authorities, in case the relevant certificates (Social Insurance, Income Tax and VAT) are not valid on the IRIS Portal.	√
2. Official Proof for the registration of updated data of their ultimate beneficial owners in the Competent National Registry / Archive.	√
Large Enterprises 1. Written Declaration (Form K.E.2) which is issued pursuant to Regulation 3(2) of the Control of State Aid (Minimum Aid) Regulations of 2009 and 2012, completed and signed, and 2. Single Undertaking Declaration.	N / A
Small and Medium Enterprise (SME)	√

3. Declaration pursuant to Article 28 of GBER 651/2014 "Innovation Aid for SMEs".	
IRIS SECTION FINANCIAL INFORMATION / CERTIFICATION DATA	
1. The Certificate issued by an Independent Auditor certifying that the **Undertaking is not in Difficulty is valid and in effect on the IRIS Portal**. In the event that an already uploaded Certificate it is not valid, an updated / valid Certificate **must be uploaded on IRIS Portal**.	√

Appendix 4: Invention and Technology Disclosure Form

Version 03/2015
Form E/2

To be submitted to the following address upon completion:
INTENT
Address
Tel:

For INTENT use only

Responsible	Date	Reference

CYPRUS UNIVERSITY OF TECHNOLOGY

Invention and Technology Disclosure Form

See the instructions on the back of this form.
For software disclosure use the software disclosure form

1. TITLE OF INVENTION

Magnetic Resonance Imaging (MRI) compatible focused ultrasound (FUS) robotic system for cancer therapy.

Ρομποτικό σύστημα για ογκολογικές εφαρμογές με χρήση Εστιασμένων Υπερήχων υπό την καθοδήγηση Μαγνητικού Τομογράφου.

2. DESCRIPTION OF INVENTION

Invention Overview: Purpose and Importance

Cancer is one of the most common causes of death of our pets and the leading cause of death of both dogs and cats. Like humans, cancer can impact any organ or tissue within their bodies, with the standard treatments being surgery, radiotherapy, and chemotherapy. Unfortunately, these therapeutic modalities are accompanied with significant limitations. Veterinarians and oncology specialists want to offer alternative treatment options to their cancer patients, especially in cases where available treatments are ineffective or impractical, also driven by the growing demand from their clients seeking alternative cancer therapies for their beloved animals. Therefore, non-invasive, ionizing-free therapeutic solutions that will be readily accessible and affordable to pet owners are urgently needed.

The current invention concerns a Magnetic Resonance Imaging (MRI)-compatible transportable robotic system specially designed for delivering therapeutic ultrasound to tumors under MRI guidance for veterinary use. The robotic system features 2 manually controlled and 3 mechanical piezoelectrically-actuated degrees of freedom (DOF) dedicated to positioning a focused ultrasound (FUS) transducer as located within a water-filled cone relative to a target to thermally ablate tumors or enhance the efficacy of chemotherapeutic drugs. The device is considered universal due to its ability to fit in any conventional MRI scanner for MRI-guided interventions. The system can be used for cancer therapy in veterinary patients or humans by simply adjusting its size. For future human applications, the treatment of tumors at multiple anatomical sites, including breast, abdominal, bone, and fibroid targets will be feasible.

Uniqueness/ Benefits of invention

The developed technology is a portable system for veterinary FUS oncological applications intended to enhance the available therapies for animal cancer, while also facilitating preclinical research on emerging FUS applications that will potentially benefit both animals and humans.

To be submitted to the following address upon completion:
INTENT
Address
Tel:

The system has the following features/benefits, which when combined form a unique therapeutic system, superior to both standard and current competitive therapeutic approaches:
1) Non-invasive procedure – No lesions/scarring in the skin, Pain is minimized, Faster recovery.
2) No side effects – sound is a mechanical wave.
3) Local therapy without damage to healthy tissue.
4) Dedicated design for targeting multiple anatomical sites (mammary tumors, abdominal tumors, soft tissue sarcomas, brain tumors) – multiple degrees of freedom (DOF), increased manoeuvrability eliminates the risk of thermal injuries and beam interference with ribs for abdominal targets.
5) Robotic assistance – increased accuracy and advanced ergonomics for end-users.
6) Safe operation in any conventional MRI scanner – MRI guidance allows targeting deep seated tumors and brain tumors, Universal system.
7) Therapy can be repeated multiple times – no dose limit.
8) There is no ionizing radiation from MRI.
9) Treatment planning & monitoring through advanced software – Consistent treatment workflow, Reduction of errors and treatment duration, ergonomic for end-users.
10) System, maintenance & procedure costs are relatively low.
11) System is extremely lightweight, compact, portable & readily accessible.
12) Application on small to medium sized animals (e.g., rodents, rabbits, cats, and dogs).

Our competitive advantage in the FUS veterinary oncology market is threefold. Firstly, our therapeutic device utilizes MRI guidance; a superior and more precise method compared to the commonly used US guidance by most competitors. This enhances the treatment accuracy, simultaneously enabling the treatment of tumors at challenging anatomical sites including brain tumors, which traditionally necessitate MRI guidance. Secondly, the positioning mechanism of the FUS transducer has a unique design and multiple degrees of freedom (5), enabling the treatment of not only multiple tumor sites, but also of a wider range of veterinary indications (e.g., palliation of arthritis pain), thus further setting us apart from the competition. Thirdly, the use of single element ultrasonic source allows establishing a cost-effective pricing strategy, thus enhancing accessibility to our technology and affordability for veterinary clinics (and thus their clients).

State of the art

Cancer is the most frequent cause of mortality in dogs and cats [1-3]. The method of choice for cancer therapy depends on several factors, including but not limited to the histological type of tumors and how advanced they are, as well as the general animal condition. Standard protocols such as surgery, chemotherapy and radiotherapy are typically employed in the disease management but, unfortunately, are usually ineffective. Chemotherapy may be advised in the effort to reduce the size of the tumor before surgery, to stop the disease from relapsing after surgery, or as a palliative measure. The advice of the veterinarian and the potential for pet discomfort constitute key factors in the owners' decision [4].
Alternative therapeutic solutions may be available through veterinary clinical trials. Even if there are obstacles to performing pet clinical trials, there are ways to overcome them, such as educating the public about the value of routine veterinary care and the existence of trials that use "pet-friendly" and low-stress handling techniques.
In contrast to dogs, most tumors in cats are malignant while multiple and metastatic tumors are frequently present at the time of diagnosis [5-7]. Therefore, feline cancer patients may offer a bigger population of aggressive malignancies to study. The epidemiology of mammary gland

To be submitted to the following address upon completion:
INTENT
Address
Tel:

tumors in people and cats is comparable, with the two main risk factors being the age [6, 8] and hormone exposure [5, 9].

Canine cancers also serve as effective models of the human disease [10]. In fact, in recent decades, similar clinical and molecular characteristics between canine and human malignancies have been found [11]. The clinical similarities include the spontaneous tumor incidence, onset age, hormonal aetiology, and disease progress. Regarding similar factors affecting the clinical outcome, these include the tumor size, clinical stage, and lymph node invasion [12]. As in human females, mammary neoplasia is the most prevalent spontaneous cancer in female dogs [13], while in canine mammary glands, premalignant tumors are frequently developed [14].

To date, the dog has been the focus in comparative oncology [15-16]. This may be partly attributed to the fact that the complete feline genome has only very recently become available [17], whereas the canine genome has been known since 2005 [18]. Accordingly, the resources are now available to examine naturally occurring feline cancers as models of human diseases beyond the clinical and histological similarities.

Dogs and cats with cancer have clear advantages over laboratory rodent models of human cancers. Being immunocompetent and exposed to the same environmental risk factors as humans, cats and dogs more effectively reflect the intricate interactions between genetics and environmental risk factors, as well as the immune system's role. There is also a bigger homology between dogs and humans for key cancer-related genes compared to that between rodents and humans [19]. There is also a great homology between cats and humans for particular genes [20-22].

Although it is less controversial to develop new treatments for companion animals with natural disease than it is to cause disease in experimental animals, ethical questions about the treatment procedure and obtaining owners' informed consent exist [23]. The development of alternative, superior cancer treatments is a long-standing priority in the medical sector while, more recently, a drive towards developing new therapeutic approaches for the management of cancer in companion animals has been observed. Simultaneously, cancer has become a major concern for pet owners [24-26].

Accordingly, there is the necessity for alternative, effective therapies that will minimize side effects and improve the life quality of pets. In this regard, FUS is a promising, non-invasive, and ionizing-free therapy that has been recently used to enhance the delivery of chemotherapeutic drugs in unresectable tumors in clinical trials [27, 28].

Various robotic systems that use the FUS technology have been proposed in both preclinical and clinical settings. As an example, Chopra et al. [29] developed a 3-DOF MRI-compatible robotic system for high intensity FUS (HIFU) applications in small animals, such as rats and mice, and specifically, for drug delivery studies [29]. Piezoelectric motors and optical encoders are used to produce controlled motion of three linear ball stages. The design of the system limits its size making it unsuitable for veterinary and human trials [29].

A device for clinical use in the treatment of breast, brain, abdominal, and fibroids targets under MRI guidance was invented by C. Damianou et al. [30]. The system features four linear and one angular motion stages actuated by piezoelectric motors to navigate an ultrasonic transducer in a water-filled container to deliver FUS to the target through a top to bottom, bottom to top, or lateral approach [30].

The robotic system proposed herein, relates to an MRI-compatible transportable system featuring 2 manually controlled and 3 mechanical piezoelectrically-actuated DOF dedicated to positioning a focused ultrasound transducer as located within a water-filled cone relative to a target to thermally ablate tumors or enhance the efficacy of chemotherapeutic drugs. The device is considered universal due to its ability to fit in any conventional MRI scanner. The system can be

To be submitted to the following address upon completion:
INTENT
Address
Tel:

used for cancer therapy in veterinary patients or humans (e.g., breast, abdominal, bone, and fibroid targets) by simply adjusting its size.

References:

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65:5–29.
[2] World Health Organisation. Noncommunicable diseases country profiles 2014. http://apps.who.int/iris/bitstream/10665/128038/1/9789241507509_eng.pdf (2014). Accessed 28/03/2023.
[3] Bonnett B, et al. Mortality in over 350,000 insured Swedish dogs from 1995–2000: I. Breed-, gender-, age- and cause-specific rates. Acta Vet Scand. 2005;46:105–20.
[4] Gruen ME, et al. Clinical trials involving cats: What factors affect owner participation? J. Feline Med. Surg. 2014, 16, 727–735.
[5] Hayes HM Jr, et al. Epidemiological features of feline mammary carcinoma. Vet. Rec. 1981, 108, 476–479.
[6] Sorenmo, KU, et al. Tumors of the Mammary Gland. In Withrow and MacEwen's Small Animal Clinical Oncology, 5th ed.; Withrow, S.J., Vail, D.M., Page, R.L., Eds.; Elsevier Saunders: St Louis, MO, USA; 2012; pp. 538–556.
[7] Sorenmo, et. al. Canine mammary gland tumours; A histological continuum from benign to malignant; Clinical and histopathological evidence. Vet. Compar. Oncol. 2009, 7, 162–172.
[8] Egenvall A, et al, A. Morbidity of insured Swedish cats during 1999–2006 by age, breed, sex, and diagnosis. J. Feline Med. Surg.2010, 12, 948–959.
[9] Overley B, et al. Association between ovarihysterectomy and feline mammary carcinoma. J. Vet. Intern. Med. 2005, 19, 560–563.
[10] Pinho SS, et al. Canine tumors: aspontaneous animal model of human carcinogenesis. Transl Res. 2012;159:165–72.
[11] Owen LN: A comparative study of canine and human breast cancer. Invest Cell Pathol 2: 257 275, 1979.
[12] Queiroga FL, et al. Canine mammary tumours as a model to study human breast cancer: Most recent findings. In vivo 25: 455 465, 2011.
[13] Misdorp W; Armed Forces Institute of Pathology (U.S.); American Registry of Pathology.; WHO Collaborating Center for Worldwide Reference on Comparative Oncology: Histological classification of mammary tumors of the dog and the cat. Comp Oncol 7: 59, 1999.
[14] Antuofermo E, et al. Spontaneous mammary intraepithelial lesions in dogs a model of breast cancer. Cancer Epidemiol Biomarkers Prev 16: 2247 2256, 2007.
[15] Gordon I, et al. The Comparative Oncology Trials Consortium: Using spontaneously occurring cancers in dogs to inform the cancer drug development pathway. PLoS Med. 2009, 6, e1000161.
[16] Gordon, I.K.; Khanna, C. Modeling opportunities in comparative oncology for drug development. ILAR J. 2010, 51, 214–220.
[17] Tamazian G, et al. Annotated features of domestic cat—Felis catus genome. GigaScience 2014, 3, doi:10.1186/2047–217X-3–13.
[18] Lindblad-Toh K, et. al. et al. Genome sequence, comparative analysis and haplotype structure of the domestic dog. Nature 2005, 438, 803–819.
[19] Paoloni, M.; Khanna, C. Translation of new cancer treatments from pet dogs to humans. Nat. Rev. Cancer 2008, 8, 147–156.
[20] Bergkvist GT, et al. Studies on the inhibition of feline EGFR in squamous cell carcinoma: Enhancement of radiosensitivity and rescue of resistance to small molecule inhibitors. Cancer Biol. Therapy 2011, 11, 927–937.
[21] De Maria R, et al. Spontaneous feline mammary carcinoma is a model of HER2 overexpressing poor prognosis human breast cancer. Cancer Res. 2005, 65, 907–912.
[22] Santos S, et. al. Sequence variants and haplotype analysis of cat ERBB2 gene: A survey on spontaneous cat mammary neoplastic and non-neoplastic lesions. Int. J. Mol. Sci. 2012, 13, 2783–2800.
[23] Page R, et al. Conduct, oversight, and ethical considerations of clinical trials in companion animals with cancer: report of a workshop on best practice recommendations. J Vet Intern Med. 2016;30:527–35.
[24] DeVita VT, Chu E. A history of cancer chemotherapy. Cancer Res. 2008;68:8643–53.

To be submitted to the following address upon completion:
INTENT
Address
Tel:

[25]Grüntzig K, et al. The swiss canine cancer registry: a retrospective study on the occurrence of tumours in dogs in Switzerland from 1955 to 2008. J Comp Pathol. 2015;152:161–71.
[26] Ranieri G, et. al. A model of study for human cancer: spontaneous occurring tumors in dogs. Biological features and translation for new anticancer therapies. Crit Rev Oncol Hematol. 2013;88:187–97.
[27] Targeted Chemotherapy Using Focused Ultrasound for Liver Tumours (TARDOX), ClinicalTrials.gov Identifier: NCT02181075
[28] Targeted Doxorubicin in Pancreatic Tumours (PANDOX), ClinicalTrials.gov Identifier: NCT04852367
[29] Chopra R, et al., An MRI-compatible system for focused ultrasound experiments in small animal models, Med. Phys. vol.36(5), pp.1867-1874, 2009.
[30] EP 32 547 31 A1 (CYPRUS UNIV OF TECHNOLOGY [CY]) 13 December 2017 (2017-12-13), columns 1-7.

Operational features - Not-obvious aspects

Leveraging the team's vast expertise in FUS technology and robotic design, a unique design was formulated to enable targeting multiple anatomical locations. Furthermore, the system was co-designed with veterinary experts to ensure alignment with the requirements for clinical applications.

The robotic system utilizes a single element spherically focused transducer converging the ultrasonic beam into the tumor. When high intensities are applied, the local temperature increases killing the cancerous cells by thermal ablation. Since the focal point of the transducer is typically <1 mm in diameter, precise robotic motion is required to ablate a large tissue volume. The robotic mechanism features 5 DOF that allows delivering the required ultrasonic energy to the targeted tissue with high accuracy and precision. Specifically, it comprises 2 hand-controlled and 3 mechanically controlled positioning stages, which are actuated by piezoelectric motors, whilst optical encoders monitor each of these motions. The transducer is actuated within the coupling cone which is firmly attached to the region of interest for top to bottom ultrasonic delivery. A silicone bellow is used to isolate the mechanical components from the water in this cone.

The structural parts of the device were constructed by 3D printing with plastics and MRI-compatible mechanical components were employed to achieve safe operation under strong magnetic fields. An advanced user-friendly software is used for precisely controlling the positioning mechanism and the FUS system remotely. **Figure 1** shows the CAD model of the MRI-guided FUS (MRgFUS) robotic device, as well as a photo of the manufactured device.

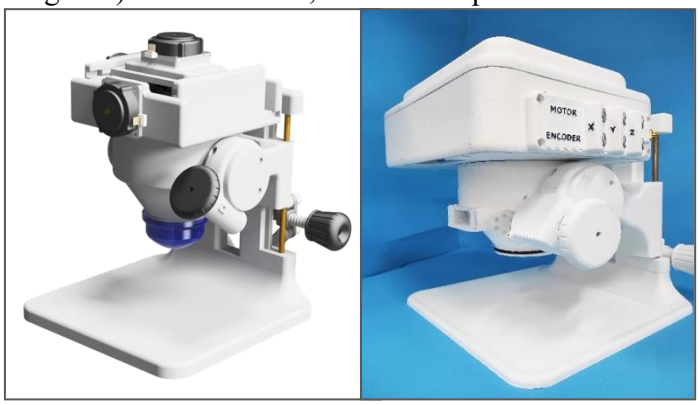

Figure 1: CAD model of the MRgFUS robotic device (left). Photo of the manufactured device (right).

State of development and next steps

So far, the following milestones have been reached: 1) Creation of a prototype MRgFUS robotic device with 5 DOF. 2) Development of dedicated treatment planning/monitoring software. 3) Comprehensive evaluation of the system's performance in terms of motion accuracy, MRI

To be submitted to the following address upon completion:
INTENT
Address
Tel:

compatibility, and heating capabilities (in both laboratory and MRI environment). 4) Establishment of efficient communication between hardware and software. 5) In-vivo testing in a small number of laboratory animals. 6) Preliminary veterinary trials in small number of dogs and cats (n=10) with naturally occurring cancer.
The system has already been tested in 10 pets, demonstrating promising outcomes in terms of both safety and efficacy for ablating malignant tissue. **Figure 2** shows the developed device during testing in the operational environment.

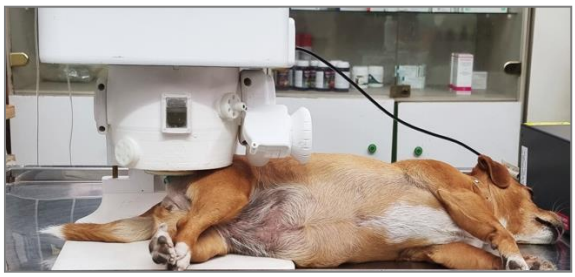

Figure 2: The developed device employed in a veterinary clinic during a pet trial.

Further testing of the technology in a larger pet population is required to obtain sufficient evidence of safe and efficient operation. Within the next months, the team will perform more trials in a wider and more diverse population of pet cancer patients (ideally including mammary, abdominal and brain cancer cases). The ability of the system to selectively target and kill cancer across multiple anatomical locations in a safe and efficient manner should be demonstrated through these trials so that the team can proceed to market deployment. Notably, these experiments may lead to minor system modifications if any malfunctions are identified (although considered unlikely) or if any areas for improvement are recognized to optimize the hardware features and capabilities of the system.

Potential commercial applications and economic potential

The potential commercial applications of our invention include its utilization in veterinary clinics and hospitals as a non-invasive means for tumor ablation and/or enhancing the efficacy of chemotherapeutic drugs, as well as in research centers and universities for R&D use. Veterinary hospitals & clinics constitute our beachhead market with veterinarians typically acting as both the buyers and end users. We strongly believe that customers/end-users in this market segment will be highly motivated to buy the system because of a) its innovative technology compared to the standard therapeutic solutions and superior performance compared to currently commercial competitive devices, b) its affordable price, which will allow them to become break-even early on, c) its non-invasive nature leading to shorter hospitalizations and fewer complications, increased patient throughput, and improved life quality, d) increased staff productivity due to advanced ergonomics (e.g., robotic assistance), and e) all the above eventually leading to increased profitability. Generally, driven by their love for animals and commitment to their well-being, these customers can easily appreciate the value of our therapeutic system, at least those who prioritize delivering the best available treatment to their veterinary patients.
The capabilities of the system could also be exploited for preclinical oncological research, both in *ex-vivo* studies and *in-vivo* studies on animals with spontaneous or genetically engineered tumors, with the generated data being used to advance animal or even human medical care. Apart from oncological applications, the proposed technology could be applied to other therapeutic applications such as drug delivery and palliation of arthritic pain. Veterinary hospitals and clinics

To be submitted to the following address upon completion:
INTENT
Address
Tel:

will be addressed initially, thus leveraging success to expand to other (more challenging) market segments, such as research centers and universities with a vet department.
In terms of economic potential, commercialization of this technology through a licensing agreement or the establishment of a spin off company (for direct product sales by the joint venture), and/or potential partnerships with FUS or veterinary equipment manufacturers could be a significant revenue stream. The successful deployment of a new product is expected to generate new employment opportunities, encompassing roles such as sales and marketing personnel, MRgFUS technologists and field engineers. Due to the scope of the proposed product (i.e., cancer; global problem), sales can be quickly expanded at international level and because of the cost-effective pricing of the product, significant number of sales can be achieved. The development of a sustainable and profitable spin off at CUT with the potential to enter the international market may contribute in the effort to attract foreign investment in the country in the medical devices' sector, simultaneously benefiting the local economy. In any case, commercial exploitation of the technology is poised to generate significant revenues for the University and partner company (VET EX MACHINA), regardless of the specific path taken for commercialization.
In addition, our invention presents an opportunity to streamline veterinary care by providing a targeted and efficient cancer treatment method. Improving the accuracy and effectiveness of tumor treatment will likely reduce the necessity for invasive surgeries and prolonged hospital stays, potentially resulting in cost savings for pet owners.

List of indicative relevant publications and patents

[1] Yiannakou M, *et al.* MRI guided focused ultrasound robotic system for animal experiments. The International Journal of Medical Robotics and Computer Assisted Surgery, vol.13(4), 2017.
[2] Spanoudes K, *et al.* A high intensity focused ultrasound system for veterinary oncology applications. Journal of Medical Ultrasound, vol. 29(3), 2021.
[3] Dai J *et al*., A robotic platform to navigate MRI-guided focused ultrasound system. IEEE Robotics and Automation Letters, VOL. 6, NO. 3, JULY 2021.
[4] Tognarelli S, *et al*. Robotic Platform for High-Intensity Focused Ultrasound Surgery under Ultrasound tracking: the FUTURA Platform. Journal of Medical Robotics Research, 02(03), 2017.
[5] Verasonics; Sonic Concepts. HIFUPlex Plus 1000 Portfolio for Small Subjects: A Full Turnkey Ultrasound-Guided Solution to Advance your Biomedical Research in Focused Ultrasound. Brochure. Available online: http://www.mkckorea.com/catalog/verasonics/vantage_64/HIFUPlex-PLUS-1000-Brochure-March-2020.pdf.
[6] Alpinion Medical Systems. VIFU 2000, Value Innovative Pre-Clinical HIFU System. Brochure. Available online: https://cdn.komachine.com/media/product-catalog/alpinion_29883_gfonnc.pdf.
[7] Damianou C, *et al*. Magnetic resonance imaging-guided focused ultrasound robotic system with the subject placed in the prone position. Digit. Med. 2020, 6, 24–31.
[8] EP 32 547 31 A1 (CYPRUS UNIV OF TECHNOLOGY [CY]) 13 December 2017 (2017-12-13).
[9] US20090171185A1 (National Health Research Institutes [TW]) 18 February 2014 (2014-02-18).
[10] CN110573105B (Quantum Surgical [FR]) 14 October 2022 (2022-10-14).
[11] CN218552918U (Shenzhen Pro Hitu Medical Co ltd [CN]) 03 March 2023 (2023-03-03).

To be submitted to the following address upon completion:
INTENT
Address
Tel:

[12] CN110787380A (Shenzhen Municipal Medical Ltd By Share Ltd [CN]) 14 February 2020 (2020-02-14).
[13] CN104815399B (Xian Jiaotong University [CN]) 17 April 2018 (2018-04-17).

3. INVENTORS

3.1. List the names of all persons who have contributed intellectually to this invention

Full Name (given name(s) and last name)	**Inventive Contribution** (%)	**Affiliation** (if not employed by the University)
Kyriakos Alexandros Spanoudes*	50%	VET EX MACHINA LTD
Christakis Damianou	30%	CYPRUS UNIVERSITY OF TECHNOLOGY
Nikolas Evripidou	20%	CYPRUS UNIVERSITY OF TECHNOLOGY
Total	100%	-

3.2. Employment status during the invention development period

Full Name (given name(s) and last name)	**Department** (or other entity if not affiliated with the University)	**Employment Status** (e.g. employee, student, professor)	**Funding Source for Employment**	**Date** (From)	**Date** (Until)
Kyriakos Alexandros Spanoudes	VET EX MACHINA LTD	CEO	Research Grant (RIF)	01/11/2022	31/10/2024
Christakis Damianou	Electrical Engineering, Computer Engineering and Informatics	Professor	University Funds	01/11/2022	31/10/2024
Nikolas Evripidou	Electrical Engineering, Computer Engineering and Informatics	Research associate	Research Grant (RIF)	01/11/2022	31/10/2024

4. FUNDING SOURCES UNDER WHICH THE INVENTION WAS MADE

4.1. Sources of Funding

Sponsor(s)	**Principal Researcher**	**Project ID and Name**
Research and Innovation Foundation (RIF)	Nikolas Evripidou	**SEED/1221/0080** FUSVET: Focused Ultrasound System for Veterinary Chemotherapeutic Applications for oncology

4.2. Other corporate relationships pertaining to this invention

N/A

4.3. Use of University resources

To be submitted to the following address upon completion:
INTENT
Address
Tel:

If there is no contract or research agreement, has there been significant use of university resources as defined in the "Policy of the Cyprus University of Technology on the Ownership, Transfer and Commercial Exploitation of Intellectual Property"? ☒ **Yes** ☐ **No**

5. MATERIAL TRANSFER AGREEMENT (MTA) AND OTHER RELEVANT AGREEEMENTS

There are not any executed agreements which may give rise to restrictions on the commercial use of the system. There are no rights to the invention derived from industrial or third-party support for the research that need to be disclosed.

6. PUBLICATION AND DESCRIPTION OF EVENTS

Event	Date	Reference/Written Record/Comments
1. Initial conception of idea. Has the date been recorded? If yes, where?	10/2021	Idea discussed between inventors. No written record available.
2. First description of the complete invention, oral or written	02/10/2023	First comprehensive written description of complete system in the relevant project deliverable: D2.6 Preparation of a patent.
3. First successful demonstration (first reduction to practice)	19/05/2023	First pet trial - demonstration in relevant environment; Veterinary clinic. Described in relevant report.
4. Has the work been submitted for publication? If yes, please provide details. ☐ Yes ☒ No	N/A	N/A
5. Has the work been accepted for publication? If yes, please provide details. ☐ Yes ☒ No	N/A	N/A
6. If the work has been published, please provide the first publication containing sufficient description to enable an expert to understand and make use of the invention (theses and submission dates should be included)	N/A	N/A The technology has not been disclosed through spoken or written means in a manner that would enable an expert to comprehend and utilize the invention.
7. First public oral disclosure (e.g. conference, seminar, meeting) containing a sufficient description to enable an expert to understand and make use of the invention. Has your presentation included a written summary or handouts for the audience? Please give the name of the conference or meeting.	N/A	N/A The technology has not been disclosed through spoken or written means in a manner that would enable an expert to comprehend and utilize the invention.
8. Has the invention been disclosed to corporate representatives? ☐ Yes ☒ No If "yes", please provide the company name and the names of the representatives	N/A	N/A The invention has not been disclosed to corporate representatives.
9. Other publications e.g. submission to a database, poster etc.	N/A	N/A

7. COMMERCIAL ISSUES

To be submitted to the following address upon completion:
INTENT
Address
Tel:

7.1. Which companies offer similar technologies (if known)?

Our primary competitors are companies offering MRI-guided FUS systems suitable for application in small and/or large animals, which, according to our market research, are currently limited to the FUS instruments (Canada) and Image guided Therapy (France) companies. The former company offers a system with only 3 DOF, resulting in limited manoeuvrability of the ultrasonic source and reduced precision in targeting anatomical sites, which can only be integrated in MRI scanners of up to 3 T. The system available by the second company is limited for use only in small animals while also integrating the phased array technology, which is expensive. Therefore, we are faced with the unique opportunity to enter the market with a superior product and capture a substantial share, as none of the aforementioned companies have managed to establish a strong presence in this specialized segment (veterinary oncology) thus far.

7.2. Companies that may be interested in your invention

Insightec (5 Nahum Heth St., Tirat Carmel, Israel) is a renowned and well-funded company specializing in MRgFUS technology. Given their expertise and financial resources in this field, Insightec presents a strong potential candidate for adopting our technology. Our invention aligns seamlessly with their existing capabilities and could serve as a valuable addition to their product portfolio. Another commercial entity that might be interested in the technology is the Esaote company (Genoa, Italy), which is 'the' pioneer in veterinary MRI. Our invention could offer a valuable enhancement to their offerings by providing a safe and effective means of delivering therapeutic ultrasound during imaging procedures.
In terms of commercialization, our primary avenue involves direct commercialization by the joint venture, which presents both the most profitable and challenging long-term option. Alternatively, we are considering licensing agreements or partnerships with established entities to bring our invention efficiently and more rapidly to market. Collaborating with industry leaders would not only streamline manufacturing and distribution, but also grant access to their established customer base and regulatory expertise.
As the inventors, we are eager to actively engage in the commercialization process. We are dedicated to ensuring the successful adoption and ongoing advancement of our invention.

8. CUT INVENTORS

I confirm receipt of a copy of the Policy on Ownership, Transfer and Commercial Exploitation of Intellectual Property of the Cyprus University of Technology as well as other relevant written instructions and agree to be subject to all terms and conditions included therein. All statements made herein, based on my own knowledge are true and all statements made on information and belief are believed to be true.

I hereby assign all rights and title to this this invention to CUT, and I agree to execute all required documents and to cooperate with INTENT in the protection of this invention. CUT will share any royalties derived from this invention with the inventor(s), in accordance with its policies as may be updated periodically.

To be submitted to the following address upon completion:
INTENT
Address
Tel:

Inventor's Signature: 	
Full Name: Christakis Damianou*	Date: 12/04/2024
Position: Professor	Faculty/Department: Electrical Engineering, Computer Engineering and Informatics
Business Address: 30 Archbishop Kyprianou Str. 3036 Limassol, Cyprus	
Business Telephone: 0035725002039	Business Fax: 0035725002849
E-mail: christakis.damianou@cut.ac.cy	
Home Address: Pontidos 6, Ayios Athanasios, 4103 Limassol, Cyprus	
Civil ID Number: 624033	Nationality: Cypriot
Affiliation with other institutions? If yes, give details N/A	

Inventor's Signature: 	
Full Name: Nikolas Evripidou	Date: 12/04/2024
Position: Research Associate	Faculty/ Department: Electrical Engineering, Computer Engineering and Informatics
Business Address: 30 Archbishop Kyprianou Str. 3036 Limassol, Cyprus	
Business Telephone: 0035725245066	Business Fax: 0035725002849
E-mail: nk.evripidou@edu.cut.ac.cy	
Home Address: Theodorou Gazi 2, Polemidia, 4056 Limassol, Cyprus	
Civil ID Number: 961498	Nationality: Cypriot
Affiliation with other institutions? If yes, give details N/A	

9. NONCUT INVENTORS

I (We) declare that all statements made herein, based on my (our) own knowledge, are true and that all statements made, on information and belief are believed to be true.

Inventor's Signature : 
I hereby agree to assign all my rights to: (company / institution) VET EX MACHINA

To be submitted to the following address upon completion:
INTENT
Address
Tel:

Full Name: Kyriakos Alexandros Spanoudes	Date: 12/04/2024
Home Address: Erechthiou 13, Aglantzia 2121, Nicosia, Cyprus	
Home Telephone: 0035799047070	Civil ID Number: 828538
E-mail: kyriakos.spanoudes@gmail.com	
Contact person for intellectual property rights in the above-mentioned company/institution: Kyriakos Alexandros Spanoudes	
Company/Institution address: Erechthiou 13, Aglantzia 2121, Nicosia, Cyprus	
Contact person telephone number: 0035799047070	
Contact person e-mail: kyriakos.spanoudes@vetexmachina.com	

To be submitted to the following address upon completion:
INTENT
Address
Tel:

Instructions for the Invention and Technology Disclosure Form

A. Introduction

The present form has been created to capture the initial details of inventions and technologies developed at the University. The information provided will be used by INTENT to assess the commercial potential and the patentability of the invention. In order to assist INTENT with this assessment complete the form as fully as possible. The form should be submitted to INTENT when something new and useful has been conceived or developed, or when unusual, unexpected or nonobvious research results have been achieved and could be of practical use.

INTENT evaluates all Invention and Technology Disclosure Forms submitted by CUT members, in the order of receipt. Where appropriate, INTENT tries to license CUT inventions and technology to the industry for further development and commercialization.

It is recommended to study the ***Policy of the Cyprus University of Technology on the Ownership, Transfer and Commercial Exploitation of Intellectual Property*** before completing the form. Should you wish to discuss your technology with a member of INTENT before completing this form, please call 88 88 88 88.

B. Form Completion Instructions

The numbers below refer to the corresponding numbered sections of the form. Please attach additional sheets where necessary.

1. Create a short title describing the general nature of the invention without disclosing specific details that would allow others to reproduce the invention (e.g. new anticancer compound, method for manufacturing a microchip etc.). Please limit the title to 60 characters.

Note: The title should be given both in Greek and English.

2. Provide a summary of the invention following the numbered instructions listed below (this should be done using layman's terms). You can also attach a description which should at least answer the questions below. Considering that this information will be used to determine patentability, commercial uses and potential users of the invention, provide as much detail as possible. Attach to this form any additional supporting material such as photographs, drawings, manuscripts, etc. At the very minimum, the following questions should be clearly explained in your text.

Note: This section must be completed in English.

i. What does your invention do? Why is it necessary?
ii. What is unique or better in your invention compared to prior art (i.e. anything done so far)?
iii. Which is the prior art to which you are comparing your invention? Please cite or attach any literature references describing, to the best extent, the prior art. If possible, consider the possibility of a literature search, as it will assist the evaluation of your invention.
iv. Describe in layman's terms how your invention works (or would work). Please include diagrams, images etc., which are necessary to illustrate the operation of your invention. In order for an invention to be patentable, the so called inventive steps should be clearly illustrated, i.e., non-obvious actions which are of vital importance in obtaining the benefits of the invention. Please identify any such inventive steps in this section.
v. Describe the stage of development of the invention (e.g., idea conception stage, experimental stage, computer simulations stage, working prototype stage etc.). Please include data, photos etc. indicating the stage of development. Is additional development required? If yes, what is required and why? Will there be further development in the next 12 months? How do you expect to proceed within this time?
vi. What are the potential commercial applications of your invention? What about the economic potential?

To be submitted to the following address upon completion:
INTENT
Address
Tel:

vii. Provide a list of relevant Peer reviewed publications and patents, published in scientific journals within the last 10 years.

3. Please include the names of all co-inventors. A co-inventor is a person who has contributed to the conception of the idea or offered an important element of the invention, either independently or jointly with others, during the development of the idea and its reduction into practice.

3.1. If necessary, the status of the inventor will be determined by a specialist lawyer. Please put an asterisk next to the main contact (attach additional sheets where necessary).

4.1. As funding often involves obligations imposed by the sponsor, please make sure you include all the external agencies, organizations, or companies that have provided any funding to each of the inventor for the research that led to the conception or the first reduction into practice of the invention. Please include companies that have supplied materials in exchange for intellectual rights.

4.2. Is there any other relationship pertaining to this invention that we should know about? If yes, please give the name of the company(ies) and describe the nature of this relationship(s). Have you provided consulting services to that company(ies)?

5. Please list, and attach copies where applicable, any Material Transfer Agreement or any other written or oral agreements used for the acquisition of any materials used in this invention. More specifically, please give information about:

1. . Executed agreements which may give rise to restrictions on the commercial use of inventions arising, e.g. agreements related to materials or software provided under a transfer or license from third parties. Details of any rights to the invention that arise through industrial or third party support of the research, if no reference was made in Section 4.

6. This information is important in determining priority of the invention and/or legal barriers to patenting. For each question in the table, a reference to a written record supporting your declaration is recommended (e.g., laboratory notebook, letter, e-mail etc.). In case of oral disclosure, please state to whom. Please attach copies of all printed/written records. Please list any past or pending publication (i.e. any dissemination of information to companies or private individuals except University colleagues, which had not been provided, or will be provided, under a confidentiality status) that could be of interest to the invention. Where applicable, please state the names of journals, conferences etc.

Complete Section 6, taking into account the following:

i. In patent law, conception involves the formulation, in the inventor's mind, of the complete means for solving a problem. The mere recognition of a desired result or of a problem or of a general approach to a solution, without the formulation of the physical structure to accomplish the desired result or to solve the problem, is not sufficient to constitute conception.
ii. "First publication" means the first time any member of the general public (those outside the CUT community), without confidentiality restrictions, had the opportunity of legal access to a written or printed description of the invention. The following could be considered, inter alia, as written public disclosures: presentations including slides, overheads, a computer display, blackboards or a posting on a website, or a dissertation submitted to the CUT library.
iii. The "first public oral disclosure" has the same meaning as in section 6ii above, but refers to an oral presentation to the general public (outside the CUT community).
iv. First "reduction to practice" involves actual and complete use of the invention for its intended purpose. Generally, this involves the physical construction of the invention and testing the physical implementation to determine whether it performs as expected. This is not always necessary if the invention can be fully described.

7.1. Based on your knowledge, give the names of commercial entities providing comparable technologies or working on the development of comparable technologies.

To be submitted to the following address upon completion:
INTENT
Address
Tel:

7.2. Based on your knowledge, give the names and addresses of commercial entities (include the names and addresses of specific contacts if known) who are interested or might be interested in the manufacture, use and/or further development of your invention. We would also like to know your thoughts on how your invention could be commercialized as well as an indication of your interest in getting involved in such a process.

8. Please list the names of all CUT employees and students who contributed intellectually to this invention. Additionally, state any affiliations with other entities. Put an asterisk next to the main contact (attach additional sheets if necessary). **The signature of CUT inventors is required**.

9. If an inventor is not an employee or a student of the University (that is they are not obligated to assign their rights to the invention to the CUT) please provide the information listed in the table (attach additional sheets if necessary). **The signature of inventors outside the CUT is not required**.