SUMMARY INFORMATION
main programme pitches for Healthy Ideas, Healthy Returns, 8 May 2017, Rotterdam

PHOTONICS HEALTHCARE: **Prevent organ failure**

We solve a big problem for intensive care doctors: how to guide the treatments to prevent organ failure for 15 million critically ill patients and many large surgeries.

Current technologies measure surrogates that provide ambiguous information. For the most vital and common intensive care treatments that aim to ensure the organs get enough oxygen doctors so far have to shoot in the dark. The necessity for interventions and their effects remains unknown until organs fail. This resulted in unnecessary treatments, lengthened ICU stay, adverse outcomes and increased costs. Solving this problem is a multi-billion business opportunity.

We have the first viable solution to address this. Our COMET, a noninvasive patient monitor has shown it provides early warning, guides therapy and prevents organ failure. It got CE approval in 2016. We've sold three units so far and removed most risks of commercialization. The leading journal called our solution a major advance for medicine.

Level of development/validation:
Three units sold, average price 80.000 Euro.
Clinical feasibility.
Clinical trials show measurement to provide unique information not obtainable otherwise.
Intervention guided with measurement prevents organ failure in preclinical studies.

Amount of funding sought:
€3.000.000

Milestone(s) to be achieved using this investment:
Clinical validation with EU and US KOL.

Timeline for completion of milestones:
24 months

ARTHROSAVE

ArthroSave is a medical device company. We are offering a device for a joint saving treatment.
The KneeReviver is an external frame that will placed by an orthopedic surgeon. The KneeReviver puts the knee joint on a small distance and by creating this distance the damaged knee joint has the chance to repair. We need an investment of €2.000.000 to set up a marketing and sales organization until first sales.
Our device is CE marked, protected with 2 patent applications and we have gained clinical evidence.
Today patients with severe knee osteoarthritis will be treated with the replacement of the knee joint with a knee prosthesis. Due to a limited lifespan of the prosthesis it results in replacement surgery which is complex, expensive and less effective. So ArthroSave regenerates the damaged knee joint and postpones a first knee prosthesis for at least 5-10 years and so we are reducing the chance for replacement surgery.
ArthroSave has a solid foundation with a team that consists of Prof Lafeber (scientist), Dr van Roermund (orthopaedic surgeon), Mr van Weperen (marketing and sales pioneer in the field of orthopaedics) and Ms K.Lindenhovius, having a background in business development in healthcare.
Already €750.000 is available for the next trial and for bridging the gap until VC investment. This year we will start a new clinical trial in 5 recognised Dutch hospitals. Based on the acquired hospitals, we cover 10% of the Dutch market. We assume two years to convert the hospitals from clinical trials to commercial use.
For the coming 3 years, we need funding of €2.000.000 to setup the marketing & sales organization to realize first sales. An exit is foreseen within 5 years.

It is a very promising proposition in a large and growing market with benefits for the patient and the healthcare system. We invite you to participate in this promising venture.
Level of development/validation:

- **CE certified**
- **Two patent applications**
- **Clinical evidence in 100 patients**
- **Next trial is planned to start in 2017**

Amount of funding sought:
€2.000.000

Milestone(s) to be achieved using this investment, **focusing on realizing sales**:

1. **Clinical trial in five Dutch hospitals (2017- 2018)**
2. **Commercial sales (end 2018)**
3. **Three additional Dutch hospitals contracted (2019)**
4. **International market introduction (2019)**
5. **Upscale production (2020)**

NEW THERAPY FOR POMPE DISEASE

Pompe disease is a rare lysosomal storage disorder which occurs in approximately 1 in 40.000 newborns. Current treatment of Pompe patients consists of enzyme replacement therapy, but has several disadvantages including heterogenic response and antibody formation. We developed a proof of concept for an alternative therapy based on antisense oligonucleotides. This potentially applies to 95% of adult and 60% of juvenile Pompe patients of Caucasian origin.

Level of development/validation:
Preclinical

Amount of funding sought:
€3.000.000

Milestone(s) to be achieved using this investment:
Successful completion of Phase I/II clinical trial

Timeline for completion of milestones (Months):
30 months

VACIS ROD

VACIS develops *in situ* tissue engineered blood vessels providing novel therapeutic options for vascular surgery. Prosthetic vascular graft failure is a frequent complication in vascular surgery with substantial morbidity and health care costs. VACIS provides patients autologous graft vessels, with sustained patency and fewer complications requiring less corrective interventions.

VACIS' technology uses a synthetic rod device, which is inserted under the skin and induces the formation of a new, fully functional blood vessel. After approximately 28 days implantation, the rod-like device is surgically removed leaving in place an in-situ formed vessel of fibrocollagenous tissue which further matures into a functional blood vessel following

Level of development/validation:
Ready for clinical evaluation in 2017-18

Amount of funding sought:
Several tranches from 250k to 1m

Milestone(s) to be achieved using this investment:
Patent application process and ISO13485 certification
Clinical evaluation

Timeline for completion of milestones (Months):
10m
18m

SERPINx BV: Novel α1-antitrypsin mutants for treatment of angioedema.

In hereditary angioedema (HAE), overproduction of the inflammatory peptide bradykinin causes painful and dangerous attacks of tissue swelling due to C1-esterase inhibitor (C1INH) deficiency. Bradykinin is produced by enzymes of the plasma contact system. C1INH is a kinetically unfavorable serpin and has weak inhibitory properties towards contact system enzymes. This becomes very clear in the clinic: the majority of patients (>95%) that suffer from angioedema are without C1INH deficiency (idiopathic angioedema). There is no therapy available for these patients, but bradykinin is strongly implicated as disease mediator. In these patients, C1INH is obviously not able to maintain control over the contact system. Drs Maas and de Maat, scientists at the UMCU discovered an excellent opportunity to solve the clinical problem of angioedema without (C1INH deficiency (idiopathic angioedema) presented by a (seemingly unrelated) rare genetic disorder. The familial bleeding disorder α1AT Pittsburgh is characterized by a single point mutation in α1-antitrypsin **(**α1AT M358R). This mutation dramatically alters its specificity. From an inhibitor of leukocyte elastase, it has now become an inhibitor of coagulation factors, including activated protein C and thrombin. At the same, it has become a strong inhibitor of the contact system enzymes (superior to C1INH). The sequence of α1AT to remove the unwanted activities (coagulation factor inhibition) were varied, while retaining the wishful properties (contact system inhibition). From an *in silico* prediction model only 4 amino acids before- and after the site where α1AT is cleaved by a target enzyme were modified and from 27 variants 3 classes of inhibitors, targeting one or more of the bradykinin-producing enzymes, without off-target effects were discovered. A patent application was filed on febr 2017.

Level of development/validation:
Pre-clinical stage. Validation in animal models and safety studies are next stage.
Pilot productions in HEK and CHO expression systems show high amounts of α1AT mutants produced.

Amount of funding sought:
€2.500.000

Milestone(s) to be achieved using this investment:
Scientific support and IP family extension:
POC, safety studies done and CMC, Drug product, Analysis and start of GMP production development.

Timeline for completion of milestones (Months):
POC in vitro and in vivo 6-9 months
Safety studies 6-9 months
GMP production 12-18 months

KARVEEL

The founders of Karveel Pharmaceuticals have recently discovered a new family of first-in-class lipopeptide antibiotics, capable of killing a selection of Gram-positive bacteria, including drug-resistant pathogenic strains. Currently, we are developing lead compounds for use in treating VRE-associated endocarditis and systemic MRSA infections (IV application) as well as in the treatment of persistent/recurrent *Clostridium difficile* infections (oral application). These pathogens place an increasing burden on healthcare providers, currently infecting more than 500 million people in the US each year with an associated treatment cost of ca. $5B. In this light, effective treatments for these drug-resistant bacterial infections can shorten or even prevent hospital stays. With average hospital admission costs estimated at US$ 2.000 per day, fewer inpatient days represent a significant benefit to the insurers and government agencies tasked with providing (cost) effective patient care.

The unique selling point of our offer is that our new antibiotics effectively kill VRE, MRSA, and *C. difficile* via a novel mode of action, unlike that of any clinically-used antibiotic. This offers the advantage of providing an antibiotic candidate for which no existing resistance mechanisms are currently present. Of potentially huge impact are recent findings from our laboratory which indicate that the working mechanism of our antibiotics may make resistance less likely to arise.

Level of development/validation:
Lead compound(s) identified, proprietary technology, first in class

Amount of funding sought:
€3.500.000

Milestone(s) to be achieved using this investment:
- Success in efficacy model(s)
- International patent filing(s)
- Safety Pharm/ADME/Tox
- GMP/Scale up
- IND filing
- Expansion of pipeline towards addressing Gram-negative pathogens.

Timeline for completion of milestones (Months):
24 months

EXBIOME

ExBiome BV is developing a platform technology for simple blood tests to detect cancers. Its initial focus is on measuring disease burden in lymphoma patients to monitor efficacy of treatment and relapse using a simple blood test. This has advantages over state of the art PET/CT imaging which lacks accuracy (50-80% positive predictive value), is costly (~€2,500/scan) and exposes patients to radiation (10X over background).
The value proposition for drug developers (pharma) is that this will compress clinical trials timelines by (1) enabling identification of a lead candidate sooner in early stage trials, and (2) reaching clinical end points sooner in late stage trials.
The value proposition for patients and medical providers is that the tool will support clinical decision making by enabling earlier detection of refractory and relapse patients to improve clinical outcome.

Level of development/validation:
Validated in 20 patients

Amount of funding sought:
€5.000.000 total from non-dilutive and equity financing

Milestone(s) to be achieved using this investment:

(1) Technical validation of assay for Hodgkin Lymphoma (HL);
(2) clinical validation of HL biomarkers;
(3) set up for clinical trials of HL IVD kit;
(4) launch of service for pharma clinical trials;
(5) identification of biomarkers for at least 1 other indication
(eg Diffuse Large B cell Lymphoma - DLBCL)

Timeline for completion of milestones (Months):

(1) – 12 months
(2) – 36 months
(3) – 42 months
(4) – 12-36 months (sales of service as an ancillary/exploratory test may begin after technical validation)
(5) – 12 months (this will occur in parallel with technical validation for HL, as DLBCL samples will be used as a control to measure specificity of HL tool)
