Annex B to the Contract

Research plan for 2018-19

Activity 1: Genetic selective and stability over 3 years:

Identify the preferred of 4 genetic (old one and new ones) suitable for the development of medicine, thru negative selective in large statistical group of variants. The chosen genetic will be based on the Total CBD and Total THC characteristic, once we have the chosen genetic from each season it will be identified and marked using the full profile of: CBD, CBDA, Δ^9THC, THCA, Δ^8THC, CBG, CBGA, THCV CBDVA, CBN.

The start of the project will be with seeding and cloning phase, which will generate 40 mothers and 600 clones out of 4 genetics. After 30 days from cloning we will perform the first round of negative selective in which we will eliminate 20 mothers (out of the 40) thus will leave us with 5 strongest mothers of each genetics (we will not eliminate the clones for the statistical objective and benchmark of the total project). Out of the cloning phase only 480 clones will be moved to the green house for large scale selective process. (4 genetic X 120 clones each genetics)

After 3.5 month of cultivation we will reach flowering stage and sampling process will start to identify the most suitable genetics under the following leading parameters:

1. CBD THC potency (%)
2. Yield per plant (kg)

Sampling process will be based on MGC Pharma GMP SOP Sampling protocols, which based on UNODC protocols[1]. Total CBD Total THC (only) will be sampled from a representative groups plants of each mother and each genetics (5X4=20), by collecting five samples (of 2gr) out of 3 representative plants (not the biggest or the most developed in the growing area) within each mother group (total of 20 samples), once identified the best mother an additional "identify" analysis will be performed on the representative mother group to create genetic finger print (full profile as above), in total additional of 4 samples will be done. A clone from selective mother will be self-propagate to create f(n)+1 generation, from the new f' generation new mother group will be plant to repeat cultivation cycle for negative selective mother by total CBD total THC requirements and create new f'(n)+1 generation till achieving f'(5).

This procedure will repeat until stabilize genetics will be achieved and clinical study will be conduct to identify the desire genetic from the 4 groups.

For the process of identifying total of 20 simple samples (THC/CBD only) will be needed and additional 4 full spec analysis to the selective mothers, total of 24 samples.

Activity 2: Analyses of environmental impact on cannabis cultivation:

Collecting environmental data (i.e. Temp, Humidity, Light hours, etc.) to optimize large scale of cannabis cultivation for medicinal use over period of cultivation cycles with compare to

[1] https://www.unodc.org/documents/scientific/STNAR48_Synthetic_Cannabinoids_ENG.pdf

cultivation outcome parameters such as volume of biomass (kg/m2), % of moulds/m2, potency of Total CBD Total THC (gr/m2), costs of growing (i.e. water and food).

In order to review the behaviour of the cannabinoids development and identify the best practice for harvesting, 1 sample will be taken out of three random representative plants (not the biggest or the most developed) from each genetic group to following times: 10 days before harvesting, 10 days after harvesting (4 plants - 1 of each gene) will be kept for this samples). (total of 8 samples)

The final report will be published as the optimum cultivation parameters times and development of CBD THC over flowering time (can be also beneficial to identify best harvesting time according to desire CBD/THC ratios and potency)

Activity 3: Tissue cultures:

Identify the best method for long term genetic storage and cloning for large scale projects without the needs of mother and seeding process.

Micropropagation of apical and lateral buds of *Cannabis sativa* as a method of clonal propagation. Development of shoots *in vitro*, rooting. Verification and selection of growth regulators as part of nutrient media. Plant conversion *ex vitro.*

Micropropagation by means of callus obtained from primary explants - search for the best media and the most suitable primary explants, callus growth parameters, organogenesis, rooting and regeneration of plants, determining optimal external factors (media, temperature, light regimen).

The binding budget for 2018, which cannot be exceeded

(includes all research costs, including the contribution to overheads):

Activity description	*Amount (CZK)*
Activity 1	**1 100 000**
Activity 2	**600 000**
Activity 3	**800 000**
IN TOTAL	**2 500 000**

In Prague

PANAX Pharma s.r.o.
Ve Smečkách 1258/6
110 00 Praha 1 - Nové Město
Czech Republic
IČ: 02880962

Tomáš Kubálek

PANAX Pharma, s.r.o.

INSTITUTE OF EXPERIMENTAL BOTANY AS CR, v.v.i.
Director
Rozvojová 263, Praha 6 - Lysolaje, CZ 165 02
VAT No. CZ61389030

RNDr. Martin Vágner, CSc.

Institute of Experimental Botany AS CR