Press Release

Vetbiolix communicates on the final results of the proof-of-concept study of VBX-2000 (piclidenoson) in canine osteoarthritis and on the upcoming submission of a regulatory pilot study vs. placebo

- **The main objectives of the VBX2400-CL-1001 proof-of-concept study were achieved at a dose of 500 µg/kg bid:**
  - **A progressive improvement in the mobility score (LOAD questionnaire) statistically ($p<0.01$) and clinically significant is obtained after 90 days of treatment at the highest dose tested of 500 µg/kg bid.**
  - **At this effective dose of 500 µg/kg bid, a progressive reduction in the pain score (VAS) is observed from the first days of treatment, becoming significant after 60 days ($p<0.01$) and 90 days (<0.001) of treatment.**
  - **All other secondary efficacy objectives are improved after 90 days of treatment at a dose of 500 µg/kg bid.**
  - **In the group treated with the low dose of 100 µg/k bid, favorable developments were also obtained without reaching the limit of statistical significance ($p>0.05$).**
  - **In both treatment groups, VBX-2000 was very well tolerated throughout the 90 days of treatment.**
- **Based on the efficacy results obtained in the proof-of-concept study (VBX2400-CL-1001), Vetbiolix is about to launch a new double-blind randomized versus placebo regulatory pilot study (VBX2400-CL-2001) on owned dogs with moderate to severe osteoarthritis (LOAD>10 and <35) at inclusion.**

Lille, Wednesday 27th November 2024 - Vetbiolix, a veterinary biotechnology company based in France dedicated to the clinical development of *First-in-Class* drug candidates for the treatment of periodontitis, osteoarthritis and gastric motility disorders in dogs and cats, announces the final results of the proof of concept study of VBX-2000, the first agonist of the adenosine A3 receptor (A3R) in dogs suffering from osteoarthritis, and announces the launch of a double-blind randomized regulatory pilot study blind vs placebo in this indication.

The VBX2400-CL-1001 POC study Proof of Concept clinical study was an open-label, multicenter study (France, Belgium) seeking to evaluate the safety of use and the effects of repeated oral administration of VBX-2000 for 90 days on the mobility and pain of 20 dog patients suffering from osteoarthritis. At inclusion, patients were divided into two treatment groups: group 1 was treated with a dose of 100 µg/kg

bid, group 2 was treated at a dose of 500 µg/kg bid. The primary objective of the study was to evaluate the effects of treatment on the LOAD mobility score (Liverpool-OsteoArthritis-in-Dogs questionnaire), after 90 days of treatment. The secondary objectives of the study focused on the evolution after 90 days of treatment of VAS (Visual Analog Scale) pain scores and NRS (Numerical Rating Score) scores: NRS1 (lameness score) and NRS2 (pain score).

The main results of the VBX-2400-1001 study can be summarized as follows:

		Screening	Inclusion Day 0	Day 30	Day 60	Day 90	P value[$] D90 vs D0
Group 1: 100 µg/kg bid	N (patients)	8	8	8	8	8	
	LOAD Score	23.2±11.7	26.5±11.3	20.8±13.4	22.1±13.8	23.2±14.5	NS
	VAS score	3.8±1.9	4.1±2.0	3.6±2.4	3.1±2.0	3.1±1.9	NS
Group 2: 500 µg/kg bid	N (patients)	11	11	11	11	11	
	LOAD score	25.4±10.7	25.4±8.8	19.5±11.9	19.4±13.7	18.6±13.2*	P=0.006
	VAS score	4.6±2.3	5.1±2.3	3.8±2.5	3.2±2.0**	2.9±2.2***	P=0.002

Values are mean±SD

[$] p value D90 vs inclusion visit according to « Wilcoxon matched-pairs signed rank test ». ns: p>0.05

**p<0,05 ; **p<0.01 vs inclusion visit according to « Dunn's multiple comparisons test »*

A total of 19 dog patients were included in the VBX2400-CL-1001 study and randomized into the two treatment groups: 8 dogs in the group treated with 100 µg/kg bid and 11 dogs in the group treated with 500 µg/kg bid kg bid.

In both groups, repeated administration of VBX-2000 was well tolerated throughout the trial.

The primary efficacy endpoint was achieved at a dose of 500 µg/kg bid. After 90 days of treatment, the mobility score (LOAD) was significantly improved (p=0.006). This improvement in LOAD was detectable from the first visit on day-30 and became statistically significant after 90 days of treatment (p<0.01). Ultimately, 73% (8/11) of patients presented a clinically significant improvement (ΔLOAD ≤-4 cf *Innes JF et al. 2023, PLoS ONE 18(2):e20280912*) after 90 days of treatment.

Parallel to the evolution of the mobility score in the group treated at a dose of 500 µg/kg bid, a progressive reduction in the VAS pain score was observed throughout the treatment period (p<0.01 vs baseline on Day 90). In this group, 91% (10/11) of patients showed an improvement in pain score (ΔVAS ≤ -1) after 90 days of treatment.

In support of a dose-dependent effect of VBX-2000 on mobility (LOAD) and pain (VAS) scores, the favorable changes observed at the dose of 100 µg/kg bid did not appear clinically or statistically significant. .

Finally, in both groups, the proportion of patients with a low lameness score (NRS1) increased after 90 days of treatment compared to the proportion before treatment. However, these increases remained non-significant ($p>0.05$). Likewise, in both groups the proportion of patients with a low pain score (NRS2) increased without reaching the limit of statistical significance.

Based on the efficacy results and the very good safety profile of VBX-2000 in this proof-of-concept study, VETBIOLIX is continuing the clinical development of this new adenosine A3 receptor agonist and is now seeking to confirm the efficacy of a dose of 500 µg/kg bid for 90 days in a regulatory study vs placebo in dog patients suffering from osteoarthritis. This international multicenter, double-blind versus placebo study plans to include between 70 and 90 owned-dogs suffering from moderate to severe osteoarthritis. Patients will be randomized into two treatment groups: 500 µg/kg bid or placebo in a 2/1 ratio. The processing time will be 90 days. The primary objective of the study is to demonstrate the superiority of the VBX-2000 treatment vs. placebo on the change in the LOAD score after 90 days of treatment. One of the secondary objectives will also be to objectify the effects of VBX-2000 500 µg/kg bid vs placebo on the evolution of the CBPI score (*Canine Brief Pain Inventory* score generally used in registration studies in canine osteoarthritis) and on the pain score VAS.

Rémy Hanf, founder and Scientific Director of VETBIOLIX – Board member of VETBIOLIX indicates: «*The final results of the proof-of-concept study further strengthen our confidence in the therapeutic potential of VBX-2000 in canine osteoarthritis. Its original mechanism of action positions VBX-2000 as a new drug candidate improving the structure of the cartilage of affected joints (i.e. Structure Modifying Osteoarthritis Drug or SMOD). Due to this unique positioning in the veterinary therapeutic arsenal, VBX-2000 could become the first-line treatment, allowing global management of the pathology and ultimately improving the mobility and quality of life of dog patients suffering from osteoarthritis.* »

Matthieu Dubruque, founder and Managing Director of VETBIOLIX indicates: “Given the magnitude of the therapeutic effects and the safety profile of VBX-2000 obtained in the proof-of-concept study, it is obvious that the continuation of clinical development is one of the priority strategic objectives for valorizing the VETBIOLIX product portfolio. With this in mind, VETBIOLIX has therefore decided to exercise its option for a full license to develop and commercialize VBX-2000 for veterinary use signed with CANFITE, and thus protect its operating rights for VBX-2000 in veterinary health.”

A propos de Vetbiolix – https://www.vetbiolix.com

VETBIOLIX develops innovative products for the treatment and prevention of diseases affecting pets. VETBIOLIX has built a unique pipeline of *First-in-class* small molecules in-licensed (*exclusive and worldwide license*) from Human Biotech worldwide which will answer to veterinary unmet medical needs in periodontitis, osteoarthritis and gut motility disorders. VETBIOLIX focuses exclusively on clinical developments of its drug candidates: the company invests on (i) clinical proof of concept studies, (ii) CMC-Pharmaceutical developments, (iii) regulatory *Pilot* clinical studies and (iv) regulatory *Pivotal* clinical studies. Revenue generation of the company will be based on out-licensing and/or co-developments deals with the Veterinary Pharmaceutical Industry.

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