



Dear Shareholders,

It is with great pleasure that I present to you the third annual Poxel letter to shareholders which is an opportunity to recap our achievements during the first half of 2016. I am pleased to report that we have accomplished several important milestones in terms of clinical advancement, operational progress and solidifying our cash position.

We have continued to advance the company and execute against our 2016 business plan. Importantly, we have a solid financial position that allows us to move forward the **four key value drivers of Poxel**: (i) the development of Imeglimin in Asia with our own resources, (ii) the continued development of Imeglimin in Europe and the United States for which we are seeking the support of a strategic partner, (iii) the clinical development of PXL770 and; (iv) leveraging other opportunities for product candidates in our portfolio as evidenced last year with the partnership with Enyo. In order to best advance these four value drivers, we have carefully considered various financing options, including the Intention To Float (ITF) on the Nasdaq market in the US, which was announced in May. When we have further information about a Nasdaq listing, we will provide an update at that time.

Achieving alliances with corporate partners remains an important part of our strategy, particularly for the Phase 3 development program of Imeglimin in Europe and the United States, and as we continue the development of Imeglimin in Japan, we will also seek a commercial partner in this territory. The conclusion of a strategic partnership to this end continues to be a top priority for the Company, and we continue to be enthusiastic about the differentiated profile of Imeglimin. In this respect, the financing of the Phase 3 development program in the United States and Europe is independent of a capital increase from a future Nasdaq listing.

From a financial standpoint, **Poxel is in a strong cash position**. By listing the Company on the Euronext in Paris during the first quarter of 2015, and raising additional funds through a private placement in July last year, we have significantly enhanced our ability to advance the development of our two lead candidates, Imeglimin and PXL770. Our portfolio of antidiabetic drug candidates has progressed well, allowing Poxel to strengthen its leading position in bringing innovative oral treatments to patients with type 2 diabetes.

In closing, I would like to acknowledge the hard work of all our employees, experts in their field who are very dedicated to our success. Our many successes since the Euronext IPO are the direct result of their many years of experience and passion for this industry aimed at making our drug candidates potential breakthrough therapies for the treatment of type 2 diabetes. I also want to thank you, our shareholders, for your dedicated and continued support. These coming half-years will be marked by key milestones for the Company, especially in terms of clinical development for Imeglimin and PXL770.

Thomas Kuhn  
CEO of POXEL

## Further expansion of the management team and Board of Directors

Poxel further strengthened its Board of Directors and management team in recent months. We would also like to thank Pascale Malgouyres, co-founder and Director of Communication and Commercialization, who departed for personal reasons, for her very important contributions to the Company since its inception.

In March, Poxel announced that Jonae R. Barnes, based in Boston, has joined the Company as Senior Vice President, Investor Relations and Public Relations. Poxel intends to expand in the United States from its Boston location, which is a global leading center in drug development and innovation. In 2015, Noah D. Beerman, also based in Boston, joined Poxel's management team as President of the US Operations and Executive Vice President Business Development. Noah is spearheading Poxel's growing presence in the US and is leading our partnership discussions. In addition, Dr. Yohjiro Itoh joined the Company to lead the Regulatory and Clinical Operations in Asia.

In parallel, in February, the Company further strengthened its Board of Directors with the addition of Pierre Legault, who is a Board of Directors' member of several US-listed biotechnology companies, and Janice Bourque, Managing Director of Hercules Technology Growth Capital. Pierre was appointed the new Chairman of Poxel's Board of Directors in April. Both the Board and management appointments have already helped to bring valuable strategic vision to the Company and provided access to their respective networks in the North American financial community. They have joined an outstanding network of scientific, financial and pharmaceutical experts that Poxel benefits from across the EU, US and Japan.

## Imeglimin: compelling data and rapid progress in Japan while seeking a strategic partner to finance Phase 3 in the US and EU

In parallel to adding further scientific validation to our programs through presentations at medical congresses, we have achieved a key milestone in the clinical development of Imeglimin during the first half of the year when enrollment was completed in our Phase 2b study in Japan in June. As many of you know, our objective to introduce Imeglimin in Asia, especially in Japan, is a key focus for Poxel and is an integral part of our long term business strategy. Japan represents the second largest single market for type 2 diabetes with \$4 billion in annual sales, and growing. Asia, in broader terms, is considered the most important geographic location with regards to treating the diabetes pandemic in the future.

Over the course of the development of Imeglimin, we have successfully completed nine Phase 1 trials and seven Phase 2 clinical studies, further supporting Imeglimin's favorable safety profile and providing additional efficacy data. The results of these trials enabled Poxel to present its Phase 3 programs to the FDA and PMDA, respectively US and Japanese regulatory authorities. Fruitful discussions with these two authorities provided us with additional visibility into the design of Phase 3 programs to support future regulatory submissions for Imeglimin in these two major areas. Interactions with the European Medicines Agency are currently ongoing.

The Company achieved several significant milestones in developing Imeglimin for the Asian market. During a Phase 1 trial in Japanese subjects, Imeglimin was observed to be safe and well-tolerated with a pharmacokinetic profile that was comparable to results shown in Caucasians. These results enabled the potential for accelerated development of Imeglimin in Japan with the initiation of a Phase 2b trial, which is being supported by a Japanese Scientific Advisory Board, helping to guide the ongoing regulatory interactions and clinical development plans. The double-blind, placebo-controlled Phase 2b trial, with a primary endpoint of efficacy, has been designed to include up to 300 naïve or pre-treated patients. At the end of June, Poxel announced that it has completed patient enrollment and expects data from this trial during the first half of 2017. Based on this timeline, the Company plans to initiate the Phase 3 development program in this important market during the second half of 2017.

### Upcoming Milestones for Imeglimin

- EMA (European Medicines Agency) final recommendations on Phase 3 program 2H-2016
- Phase 2b study in Japan – Efficacy and safety data 1H-2017
- Initiation of Phase 3 studies in Asia 2H-2017
- Further data to be presented at scientific meetings including the EASD (*European Association for the Study of Diabetes*), in September 2016, in Munich

### Imeglimin Summary

- 1) First in a new chemical class of oral anti-diabetic agents, the Glimins
- 2) Imeglimin targets the mitochondrial bioenergetics, leading to dual benefits: improvement in both insulin sensitivity and insulin secretion, thus improving glycemic control
- 3) Imeglimin has shown efficacy both as a monotherapy and in combination with leading diabetes treatments in 7 Phase 2 studies, and a good safety profile on more than 850 subjects
- 4) Phase 3 program has been discussed with the FDA in the US, PMDA in Japan and discussion are currently ongoing with the EMA for EU, and could begin in 2017

## PXL770: a 2<sup>nd</sup> drug candidate with significant potential

Poxel has made significant progress with its second lead drug candidate PXL770. During the second quarter, the Company announced positive results from the first stage of Phase 1 study. PXL770 directly activates AMPK, an enzyme that acts as an energy sensor and regulator, maintains cellular homeostasis, and therefore has the potential to play an important role in the management of diabetes.

In early 2016, the Company initiated a Phase 1 study in healthy volunteers with single ascending doses in healthy male subjects who received either placebo or one of the six planned dose levels of PXL770. Following the positive results from the first stage of the Phase 1 trial, we are actively preparing for the second stage of this study, and the full results are expected during the second half of this year. Based on this timeline, a Phase 2a proof-of-concept study is anticipated to be conducted in 2017.

In the first part of the Phase 1 study, safety, tolerability and pharmacokinetics of six single ascending oral doses of PXL770 were assessed in 64 healthy male subjects. Overall, the results indicate that PXL770 exhibits a favorable safety and tolerability profile with no serious adverse events reported nor safety signals. Pharmacokinetic assessment showed that PXL770 plasma exposure (C<sub>max</sub> and AUC) increased in a dose dependent manner following oral administration with moderate inter-individual variability. The second part of the trial is on track and will assess safety, tolerability, pharmacokinetics and target engagement of multiple ascending doses.

In November of 2015, Poxel presented the first preclinical data on PXL770 at the World Congress on Insulin Resistance, Diabetes and Cardiovascular Diseases in Los Angeles. Data presented demonstrated that PXL770 significantly improves glucose tolerance, lipid profile as well as weight in a type 2 diabetes mouse model. Together, the results highlight the potential of PXL770 as a novel oral agent for the treatment of type 2 diabetic patients with key benefits on various cardiovascular risk factors caused by glucose, lipid disorders and being overweight.

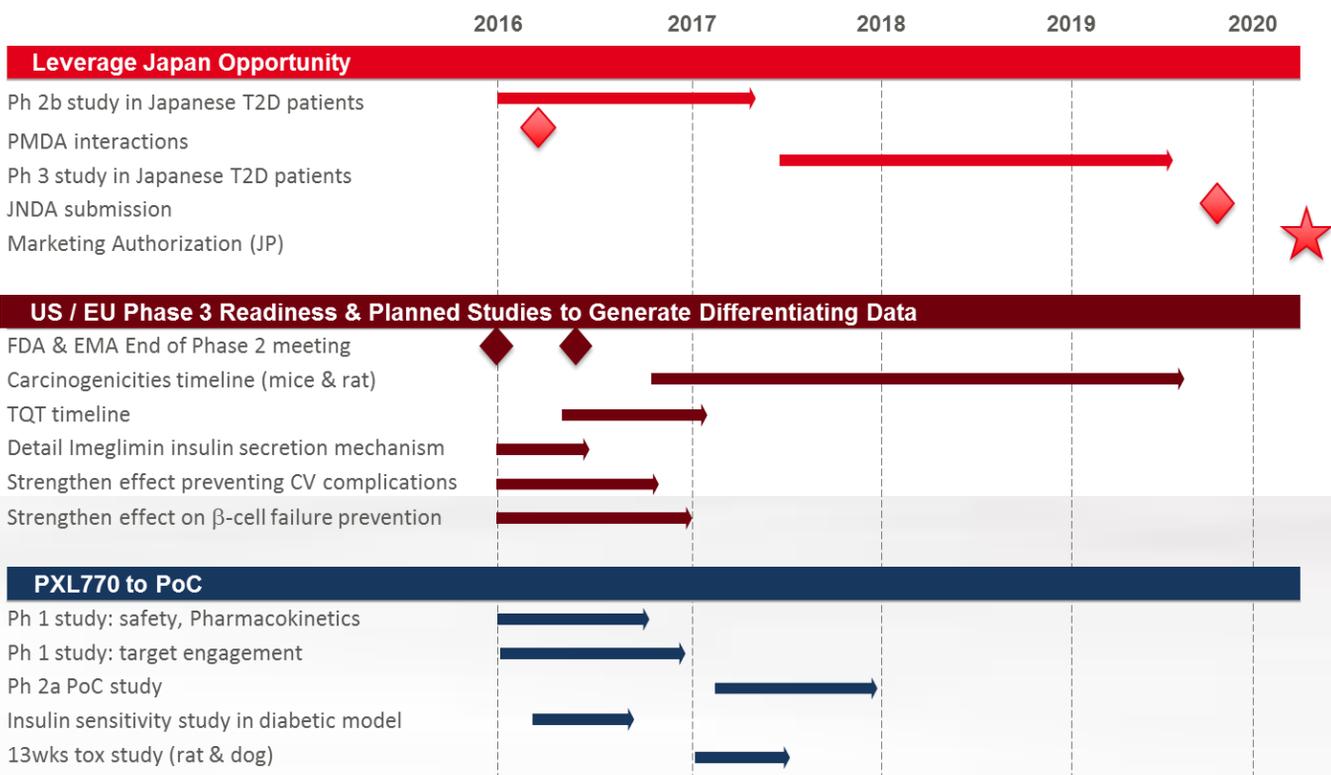
Moreover, Poxel also announced that the U.S. Patent and Trademark Office (USPTO) has granted the patent (US patent number US-9,284,329) filed by Poxel covering direct AMPK activators. This patent includes PXL770 for the treatment of type 2 diabetes as well as other indications.

### Upcoming Milestones for PXL770

- Phase I study - Single Ascending Dose (SAD) read-out 2H-2016
- Phase I study - Target engagement read-out Q1-2017
- Further pre-clinical data to be presented at scientific meetings including the EASD (*European Association for the Study of Diabetes*), in September 2016, in Munich

### PXL770 Summary

1. PXL770 is Poxel's most advanced compound next to Imeglimin
2. PXL770 is the most advanced AMP Kinase activator, an exercise mimetic drug that uses a novel mode of action to tackle type 2 diabetes and lipid abnormalities
3. The compound has started clinical development with a Phase 1 trial being conducted in Germany, first compelling data were published last June
4. The compound's ability to treat both type 2 diabetes and lipid-related abnormalities- driving CV complication in type 2 diabetes- differentiates PXL770 from other approaches



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