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EMA Defends PRIME's Early Entry Advantage For Smaller Companies

by Maureen Kenny

Small and medium-sized enterprises will be able to apply for the priority medicines program earlier in development, benefitting from agency advice and using the PRIME "label" to attract investors.

The European Medicines Agency is defending the early entry advantage that small and medium-sized enterprises (SMEs) will have under agency proposals for the new priority medicines scheme that is due for launch early next year.

Big pharma says any company regardless of size should be able to apply to have a product included in the PRIME scheme at the early phase of development. The EMA insists that SMEs need more support at an earlier stage and will benefit more than big pharma from the benefits offered at that stage. Importantly, SMEs will be able to use the PRIME "label" to raise capital to fund the later stages of development of innovative products that have been awarded a designation under the scheme.

According to Jordi Llinares García, the EMA official who heads the department responsible for developing PRIME, the aim of the scheme "is to try to help as early as possible ... those most in need and in this case SMEs are most in need at an early phase," either because they lack regulatory experience or they find it hard to raise capital to fund the later stages of development. When this happens, ideas are lost and "that's something we want to avoid," Llinares said at the annual EMA Review of the Year and Outlook for 2016 recently convened in London. The meeting was organized jointly by EMA and The Organization for Professionals in Regulatory Affairs.

The EMA's SME Office has been operating for 10 years now and a decade of experience has shown that SMEs – and also developers in the academic sector – do indeed need particular support. According to Melanie Carr, former EMA SME office head and now head of the agency's corporate stakeholder department, it was "very difficult for a regulator to accept, bearing in mind the patient, when a company runs out of capital and they have something very promising in their

hands and they're not able ... to bring that to the proof of concept phase."

Under the proposals, SMEs and applicants from the academic sector will be able to apply for inclusion in PRIME at the stage of proof of principle, that is, prior to Phase II/exploratory clinical studies. Other would-be applicants can apply to enter the scheme only at proof of concept, that is, prior to Phase III/confirmatory clinical studies.

PRIME is due for launch in the first quarter of 2016 and public consultation on the proposals ended on Dec. 23 (Also see "*Faster EU Drug Assessment Pathway Could Launch In First Quarter 2016*" - Pink Sheet, 16 Oct, 2015.). Designation under the initiative would mean the EMA had identified the product as having the potential to bring significant benefits to patients with unmet medical needs and hence be of major interest from a public health and therapeutic innovation perspective. It will mean early identification of products fulfilling the criteria for review under the EMA's accelerated assessment procedure. Companies given the designation will receive enhanced regulatory and scientific support from the EMA so as to optimize product development and enable faster regulatory assessments.

Early stage support for SMEs and academic applicants will include scientific advice (with fee reductions) and the potential to involve other stakeholders – HTA and patient bodies, for example.

Big Pharma View: Unmet Need Not Linked To Firm Size

Geert Preuveneers, executive director regulatory affairs Europe at MSD (Europe), put forward big pharma's view that PRIME should be open to all applicants at the earlier stage. He said that while industry appreciated that opening the scheme to all pharma companies regardless of size at the proof of principle stage would have an impact on agency resources, "unmet medical need is not linked" to whether the applicant is an SME or not.

Preuveneers also pointed out that there was now "a continuation of development throughout the different phases" to the extent that it was no longer possible to "delineate ... separate phases." "We have to deal often with adaptive designs and that might have a continuation from Phase II into Phase III onwards."

Llinares disclosed that the EMA did not consider the earlier entry option in the initial discussions on PRIME. "That came as an addition when we were looking at how to help those most in need."

Carr added that it was during the second phase of discussions "that we said could go even earlier, bearing in mind we're committed to this succeeding and there would be additional resource implication." EMA looked at what would be "the most identifiable population that could benefit from that early dialogue" and that was found to be the SMEs and academics.

If this early entry option hadn't been added, PRIME would probably be restricted to the second phase, Llinares remarked. PRIME has been likened to the breakthrough therapy designation scheme in the US but that scheme does not have an early entry option, Llinares noted in a later discussion

During the Q&A session at the conference on the PRIME proposals, an attendee from a multinational asked Llinares to give an indication of whether the EMA might reconsider its stance on this particular point.

"Maybe we are wrong", but the agency thinks the benefits available at that early stage – basically iterative scientific advice and the PRIME "label" – are much more relevant for SMEs than for big pharma, Llinares remarked. That said, "we'll consider the comments in the public consultations and reflect on that."

As well as arguing for a more holistic approach to drug development irrespective of the traditional development phases for the PRIME scheme, Preuveneers emphasized the importance of tailoring the scientific advice for PRIME products in order to offer timely feedback to companies. Big pharma also wants PRIME to allow the inclusion of extensions of indications and line extensions meeting a significant unmet medical need.

Lastly, Preuveneers argued that a substantial move towards early patient access to innovative medicines in Europe would not be possible without the early involvement of health technology assessment bodies in the discussions. It was important, he said, that national HTA bodies assigned resources to cooperate in PRIME and fully contribute to these discussions (Also see "*EU Faster Review Path Should PRIME New Links With HTAs, Payers – Industry*" - Pink Sheet, 26 Oct, 2015.).