To:

Head of Paediatric Medicines
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Notification of discontinuation of a paediatric development which is covered by an agreed PIP Decision

Actives substances(s): Evofosfamide

Invented name:

Latest Decision number(s): 1) P/0045/2015 2) P/ 3) P/ 4) P/

Corresponding PIP number(s): 1) EMEA-001483-PIP01-13 2) EMEA- 3) EMEA- 4) EMEA-

Please note that development of the medicinal product above in the [condition(s)/indication(s)]:

Treatment of Ewing sarcoma

Treatment of soft tissue sarcoma

☒ has been discontinued

☐ has been suspended/put on long-term hold (with possible re-start at a later time)

for the following reason(s): (tick all that apply)

☒ (possible) lack of efficacy in adults

☐ (possible) lack of efficacy in children

☐ (possible) unsatisfactory safety profile in adults

☐ (possible) unsatisfactory safety profile in children

☐ commercial reasons (please specify:)

☐ manufacturing / quality problems

☐ other regulatory action (please specify:) (e.g. suspension, revocation of M.A.)

☒ other reason (please specify: Project development generally discontinued)

Please add a brief description (max 2000 characters) of the reason(s) for the discontinuation / suspension:

In the phase III trial (TH-CR-406/SARC021) patients with locally advanced unresectable or metastatic soft tissue sarcoma treated with evofosfamide in combination with doxorubicin did not demonstrate a statistically significant improvement in OS compared with doxorubicin alone (HR: 1.06; 95% CI: 0.88 - 1.29). In addition in the Phase 3 MAESTRO study, patients with previously untreated, locally advanced unresectable or metastatic pancreatic adenocarcinoma treated with evofosfamide in combination with gemcitabine did not demonstrate a statistically significant improvement in overall survival (OS) compared with gemcitabine plus placebo (hazard ratio [HR]: 0.84; 95% confidence interval [CI]: 0.71 - 1.01; p=0.0589).

As the pre-specified primary endpoints in both studies were not met and a further development is not supported by scientific data, Merck KGaA decided to not further pursue investigation of evofosfamide in any indication and return the rights to the co-development partner Threshold Pharmaceuticals Inc., South San Francisco, USA.

Name and signature of the PIP contact point:	Dr. Jan Gross
Date:	12-Dec-2016

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