Analysis of orphan diseases with a KNIME workflow using Open PHACTS, with the potential of drug repurposing

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Introduction
Worldwide around 400 million people are affected by orphan diseases [1], orphan meaning affecting less than 1 in 2000 citizens [2]. The low prevalence coupled with the sheer number of orphan diseases (about 5000-8000) is the main reason there are so few marketing approvals, amounting to treatments for roughly 200 conditions in the US and only about 45 in the European Union [1]. Drug repurposing therefore embodies an attractive option of reaching many patients with treatments that have already been deemed safe.

The workflow
The biggest European platform for orphan diseases is Orphanet [3], and as of now, 2901 of the 9000 listed disorders including their sub-types are equipped with a UMLS identifier which was used in the workflow for retrieval of disease-related data from DisGeNET [4].

Results
In ChEMBL 102 of the targets are classified as transporters, whereas the search for transporters in the GO Molecular Function properties yields 311 transport related targets. Of the latter four are described as having a therapeutic gene-disease association and of these four, synovial sarcoma is the single one that was linked to approved compounds.

Conclusions
The workflow is capable of adapting to the user’s needs. Options include filtering by highest cited or multiple genes for a given disease, the gene-disease association (e.g. therapeutic), or the compound type of interest (e.g. approved, investigational). Manual investigation of the resulting compounds and their pharmacological activity (agonist/antagonist) related to the disorder of interest, may result in possible drug repurposing candidates.

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References:
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