



Welcome to Holland

How are our ethics?



## Introduction VKS

We focus on

- Information about diseases and science directed to patients and the general public
- Sharing and bringing patients in contact with each other
- Advocacy for early diagnosis, access to specialist care, development of new treatments, quality of care, pathways- and standards of care
- Improving Quality of care



## Introduction VKS

Products for patients:  
Pathways of care for different diseases  
You-tube movies for awareness  
Comic-book with disease information  
Magazine  
Website  
Social media

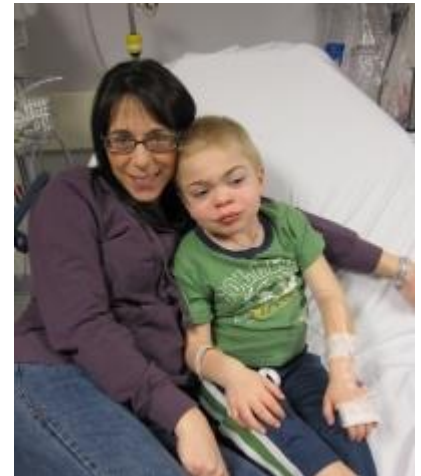


**Better and faster drug development:  
patients point of view**



## Visionary view

- At this moment there are still more than 100 well described IEM without proper treatment of symptoms
- Rather than on new diseases, orphan drugs companies seem to focus on making more drugs for the same disease
- Patient groups can help pharma focus



## Discard the old ways





## Genetic trait, disease mechanism

Patients know which symptoms  
burden them most in daily life



## Genetic trait, disease mechanism

Patients know which symptoms  
burden them most in daily life

But clinical test usually measure things that  
are not very disease related





# Alternatives for old fashioned clinical development

Studying natural history of the disease well before studies for drugs are planned

Which symptoms are most effecting quality of life?

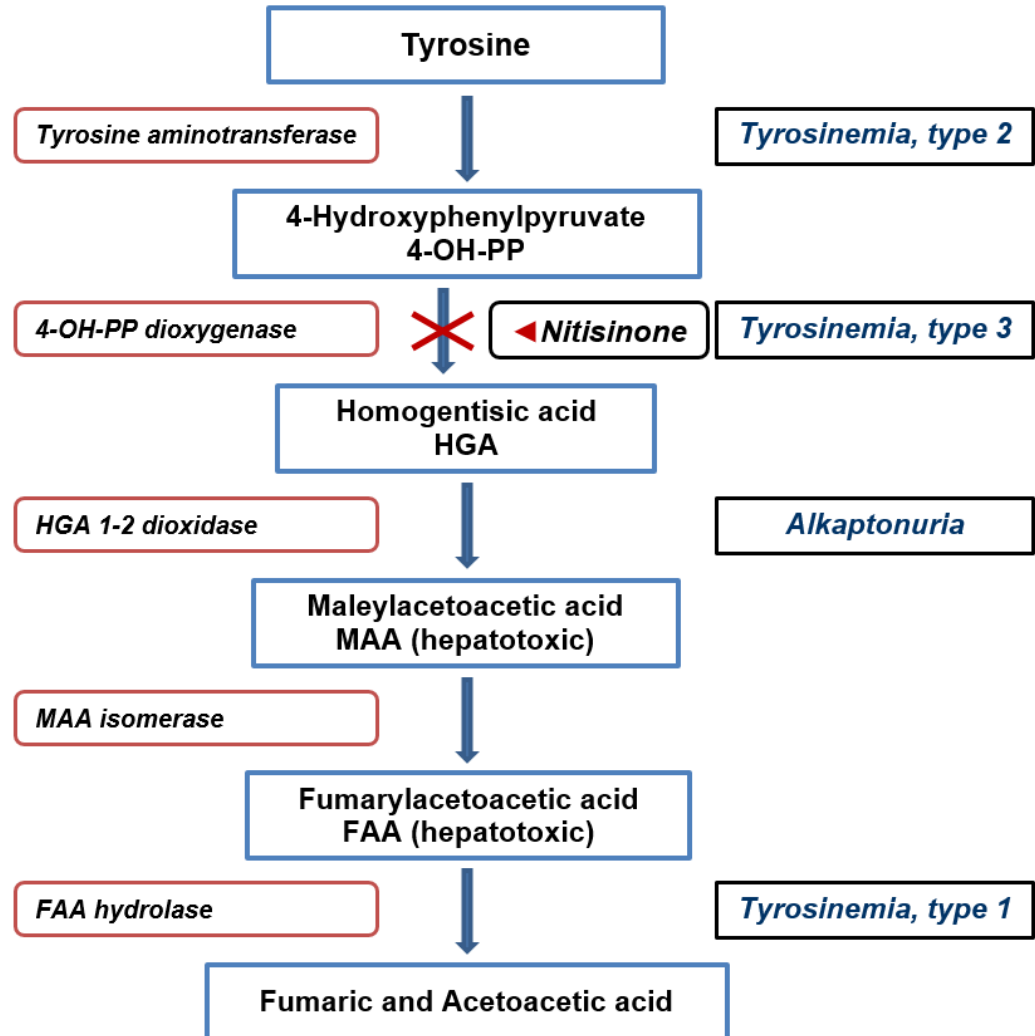
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"You're very lucky; your symptoms are currently quite trendy."

## Example: Nitisinone





## Example: Nitisinone

Developed as a herbicide named NTBC

In 1991 found to be an inhibitor of the forming of toxic substances in Tyrosinemia type 1

A large cohort of patients was treated and followed, without a clinical development trajectory

It stayed available for patient use as a chemical from 1992 tot 2002.

It was registered as an orphan drug in 2005, no problem to prove effectiveness, no problems with reimbursement

Currently researched with money from patient groups and the EU as treatment for the symptoms of Alkaptonuria

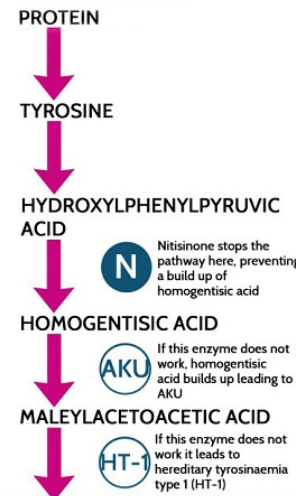
... and albinism

I'm Looking For...

- The Trials
- DevelopAKUre
- History
- Nitisione
- Consortium
- Updates
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- Visit AKU Society
- Blog
- Contact Us

## Nitisione

### THE AKU PATHWAY



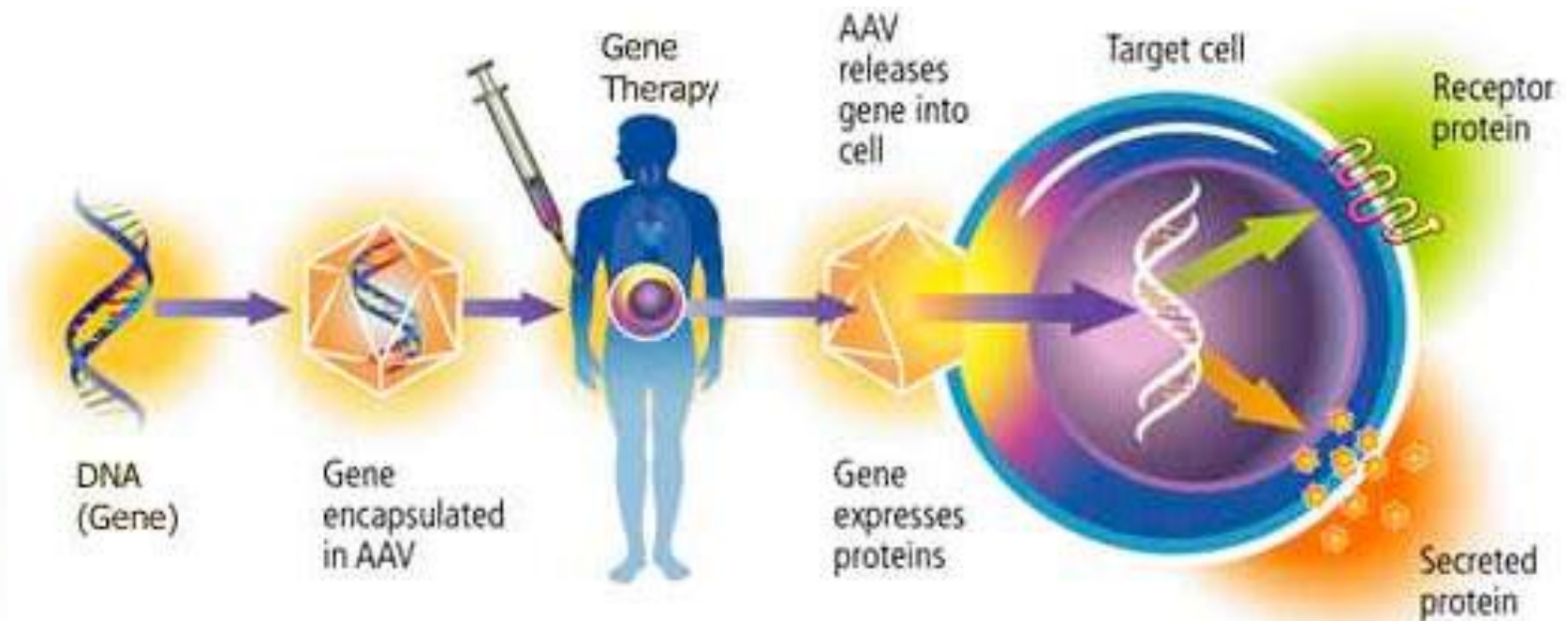
Alkaptonuria (AKU) is caused by the dysfunction of an enzyme in the tyrosine breakdown pathway. A simple diagram of this pathway is included on this page. Tyrosine enters your body as protein in your diet, and is essential for processes such as growth and healing. However, your body also needs to recycle excess tyrosine, and does so by breaking it down piece-by-piece through a series of enzymes, until it finally leaves the body in breath and urine.

AKU patients lack one enzyme in this pathway (homogentisic dioxygenase), which means that instead of removing tyrosine from their body, the pathway stops at the production of homogentisic acid (HGA). HGA then builds up in the body of AKU patients, and causes the symptoms associated with the disease, for example by binding to and weakening cartilage.

For more information about AKU, please see the [AKU Society website](#).

Nitisione is an enzyme inhibitor. It acts to interrupt the action of another enzyme in the tyrosine breakdown pathway. By stopping the breakdown at a safe point, AKU patients should not produce HGA, and can potentially avoid the symptoms of the disease. Clinical research in the US

# New therapies new paradigms





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## Smart development

Involve patient groups in study design

Weighing risks/ benefits of gene therapy may differ for patients

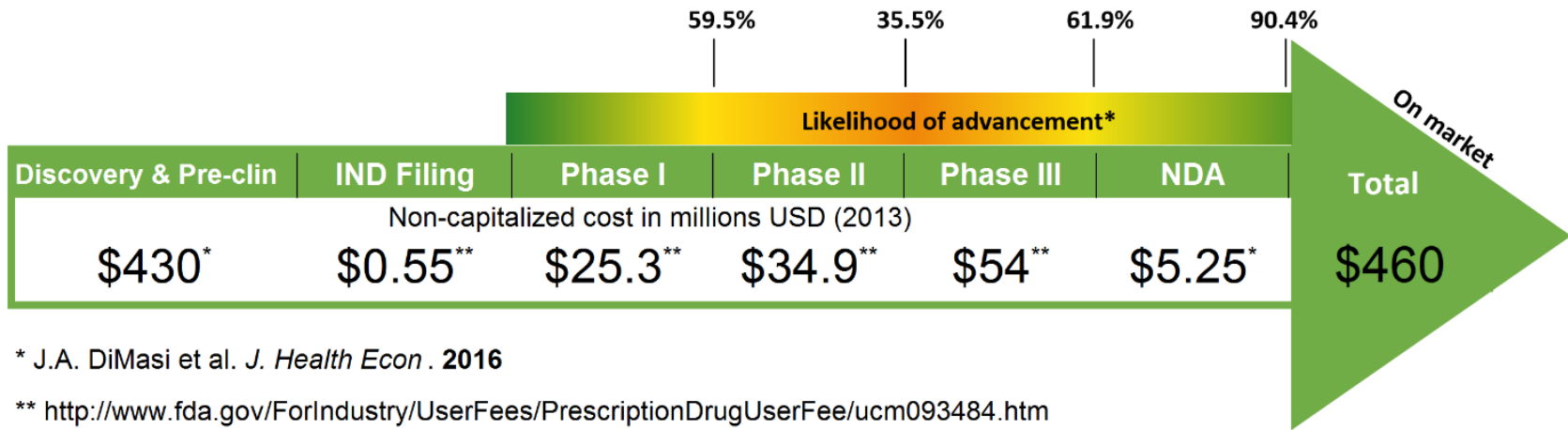
Development from the start as a medicinal product may be difficult

Proof of safety and efficacy can also be obtained without a clinical trial setting










# Move away



\* J.A. DiMasi et al. *J. Health Econ.* 2016

\*\* <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm093484.htm>

# Genetherapy MPS IIIa

PROGRAM	VECTOR	GENE	INDICATION	DEVELOPMENT STAGE			COMMENTS
				PRE-CLINICAL	PHASE I/II	PIVOTAL	
LYS-SAF301	AAVrh10	SGSH	Sanfilippo A (MPS IIIA)				• Generation 1, Phase I/II completed 2013
LYS-SAF302	AAVrh10	SGSH	Sanfilippo A (MPS IIIA)				• Registration trials to begin in 2017
LYS-GM101	AAVrh10	GLB1	GM1 Gangliosidosis				• Phase I/II trial to begin in 2017
Other programs		Confidential					



Think out of the box



**I HOPE YOU TRY SOMETHING  
SOMEONE TOLD YOU  
YOU CAN'T DO.**

Don't be fooled. Be fueled by [WebNutrients.com](http://WebNutrients.com)

LIP de PIG