DobeCure

Believe what you see

Product sheet

AMD in Europe

- Most common cause of blindness in elder people.
- Prevalence in Europe = 3.3% in > 65 years
- Incidence = 1,8 – 2,9 cases per 1000 human-year in > 55 years old
- Proportion 4:1 dry/wet AMD
- Dry AMD has no treatment

Solutions

Dobecure D	Dobecure W
Provide an effective treatment for dry AMD	Provide an effective and competitive treatment for exudative AMD

Market Opportunity

	2020	2021	2022	2023	2024	2025	2026	2027
>65	142,40	145,10	148,00	150,40	153,30	155,90	158,65	161,48
AMD	4,70	4,79	4,88	4,96	5,06	5,14	5,24	5,33
20% Market	0,94	0,96	0,98	0,99	1,01	1,03	1,05	1,07
180 € Tto/Año	169,17	172,38	175,82	178,68	182,12	185,21	188,48	191,84

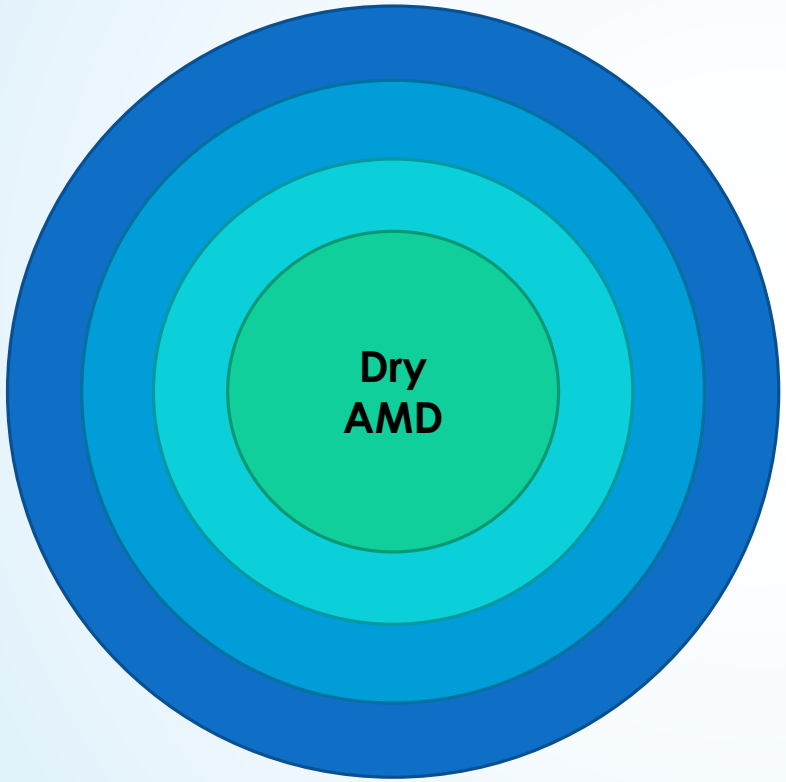
- In 2025 there will be 155,9 millions people over 65 in Europe.
- 5,14 million people will suffer AMD whether dry or exudative.
- With a market rate of 20% there will be 0,94-1,07 treatments per year.
- 180 € per treatment/year – 2 doses year –
- 1,063,38 M€ From 2020 to 2025

Market Opportunity

- **As an example: Eylea (Aflibercept):** It is produced by Regeneron Pharmaceuticals and Bayer. It was approved by the FDA for use in AMD, delivered U.S. net sales growth of 24.2% over 2015, and continues to be the market-leading branded anti-VEGF therapy in the United States. The global growth rate was estimated by 27% from 2015-16.

	2014	2015	2016
Sales	1,3 USD Billion	3,98 USD Billion	5,05 USD Billion

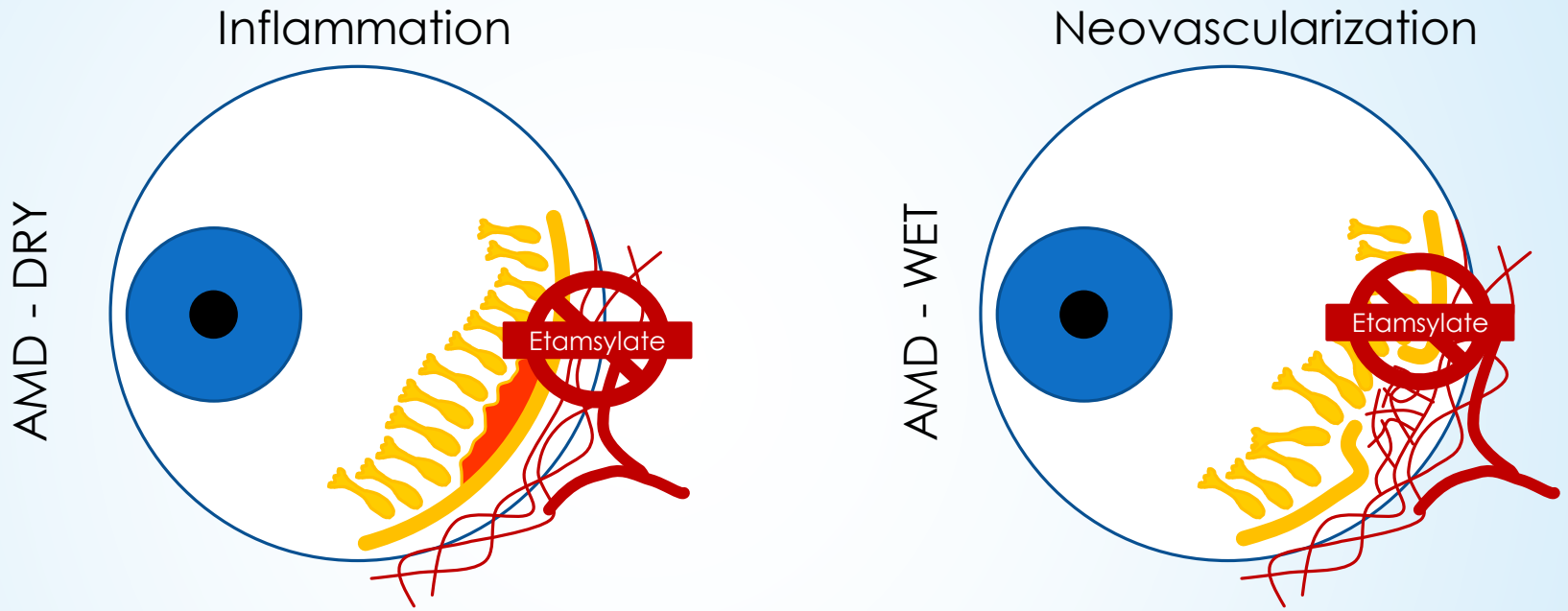
Standard of Care



No approved treatment

Treatments approved Anti-VEGF

Mechanism of Action



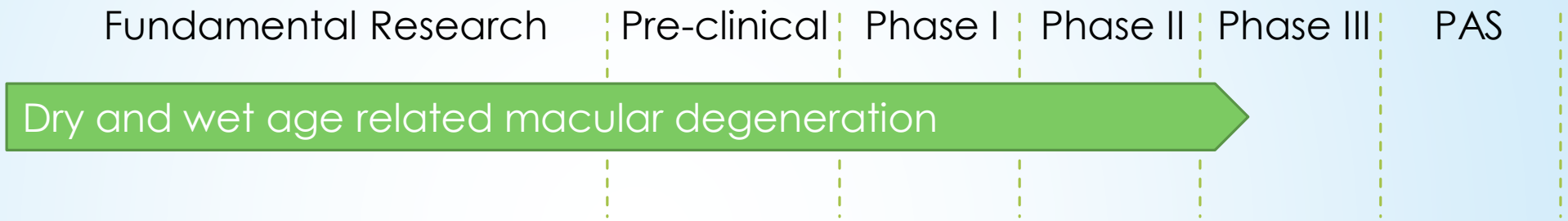
- The fibroblast growth factor (FGF) is a powerful proinflammatory and proangiogenic protein that plays an important role in the pathophysiology of **both forms of ARMD (Dry and Neovascular)**. In normal conditions, FGF is strictly regulated by its attachment to the extracellular matrix. After physical or chemical injury, an important amount of FGF is liberated from the extracellular matrix and participates in the pathological processes occurring during inflammation and angiogenesis. Etamsylate is a synthetic FGF inhibitor blocking the coupling of free FGF to its receptor without any effect on sequestered physiological FGF. Thus, Etamsylate treatment does not present any "off-target" effect, because FGF physiological activity is maintained.

Comparison table

	Avastin®	Lucentis®	Eylea®	Dobecure D/W
Price	1064,10€/dose	824,63 €/dose	644,54€/dose	90€/dose
Holder	Roche	Roche	Bayer	Dobecure
Dosage	7 doses/year	7 doses/year	7-8 doses/year	2 doses
Treatment type	Anti-VEGF	Anti-VEGF	Anti-VEGF	Anti-FGF
Mechanism	**Inhibits the binding of VEGF to its receptors**	**Inhibits the binding of VEGF to its receptors**	**Inhibits the binding of VEGF to its receptors**	**Inactivates the action of the free FGF**
Effect*	5 ETDRS letters during the first year. Loss of visión after first year.	5 ETDRS letters during the first year. Loss of visión after first year.	5 ETDRS letters during the first year. Loss of visión after first year.	7,6 ETDRS letters the first 16 weeks (6,4 W y 8,9 D). 6,1 letters after 48 weeks in 60,5% patients
Side Effects	Very Serious	Serious	Serious	Mild

*Average of ETDRS letters recognition

Clinical Development



- Fundamental Research started in **1986**.
- Pre-clinical research was conducted since then up to **2014** when clinical phase was initiated
- Phase I has not been required as it is an already approved drug and dosage for other uses.
- Phase II – Proof of concept study has been completed the conditions described bellow.
- In **2017**, the Phase III studies to be included in the module 5 of the registration dossier is initiated.

Clinical Studies

- Clinical trial OFT-ETAMSILATO-4.2.1. Treatment of intravitreal administration of Etamsylate in patients with Age Related Macular Degeneration and evaluation at 4 and 16 weeks. Sample size expected of 160 treated eyes but **finally treated 41 (21 treatment G1 and 20 sham treatment G2) as the study was stopped.** Patients that improved their visual acuity reached 63.41 %, worsening 31.71 % and equal results 4.88 %.
- Clinical trial OFT-ETAMSILATO-4.2.2. Not responding patients on study 4.2.1 at week 16 evaluation had the possibility to be treated/retreated on study 4.2.2. 17 G2 eyes were evaluated and should be followed up to week 48. The study was stopped and **not all of them completed the week 48** follow up visits. There was an improvement of 47.10 % of the visual acuity, worsening of 41.20 % and equal results of 11.70 %.
- Clinical trial OFT-ETAMSILATO-4.2.3. 8 responder patients on study 4.2.1 at week 16 were **followed up to week 48** on study 4.2.3. The visual acuity improvement rate was 87.5% of the patients, no one worsening, and equal results of 12.5%.
- **38 patients in total were finally treated with one dose** (as there were no patients treated with two doses). Of them, 55.26 % improved their visual acuity, 5.26 % maintained their results, and 39.47 % reduced their visual acuity. This means that a total of **60,53% of the patients responded favorably to the treatment**.

Clinical Results

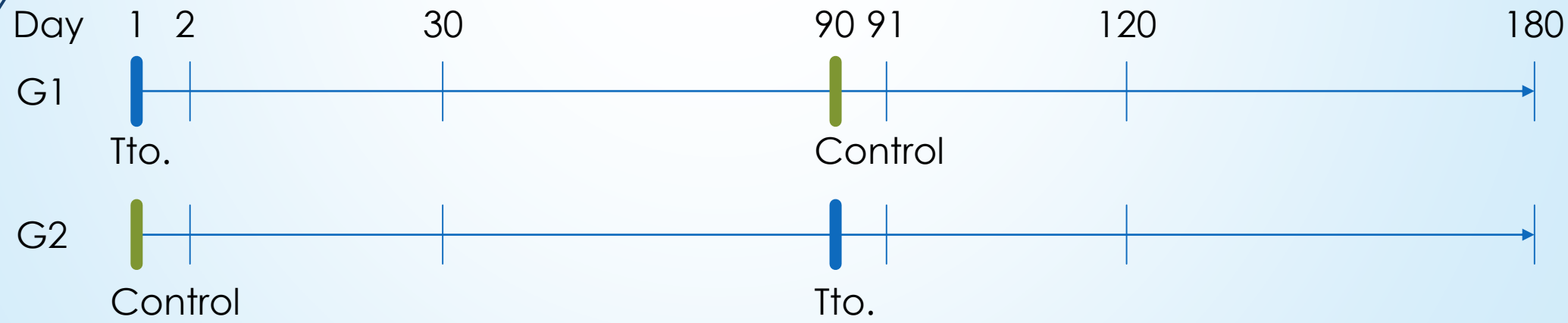
	Nº patients	Percentage	Average
Total	38	100,00%	-
Improvement	21	55,26%	+7,85 letters
Equal	2	5,26%	
Worsening	15	39,47%	-7,4 letters

WET - AMD	Nº patients	Percentage	Average
Total	25	100,00%	-
Improvement	13	52,00%	+6,38 letters
Equal	1	4,00%	
Worsening	11	44,00%	-9,09 letters

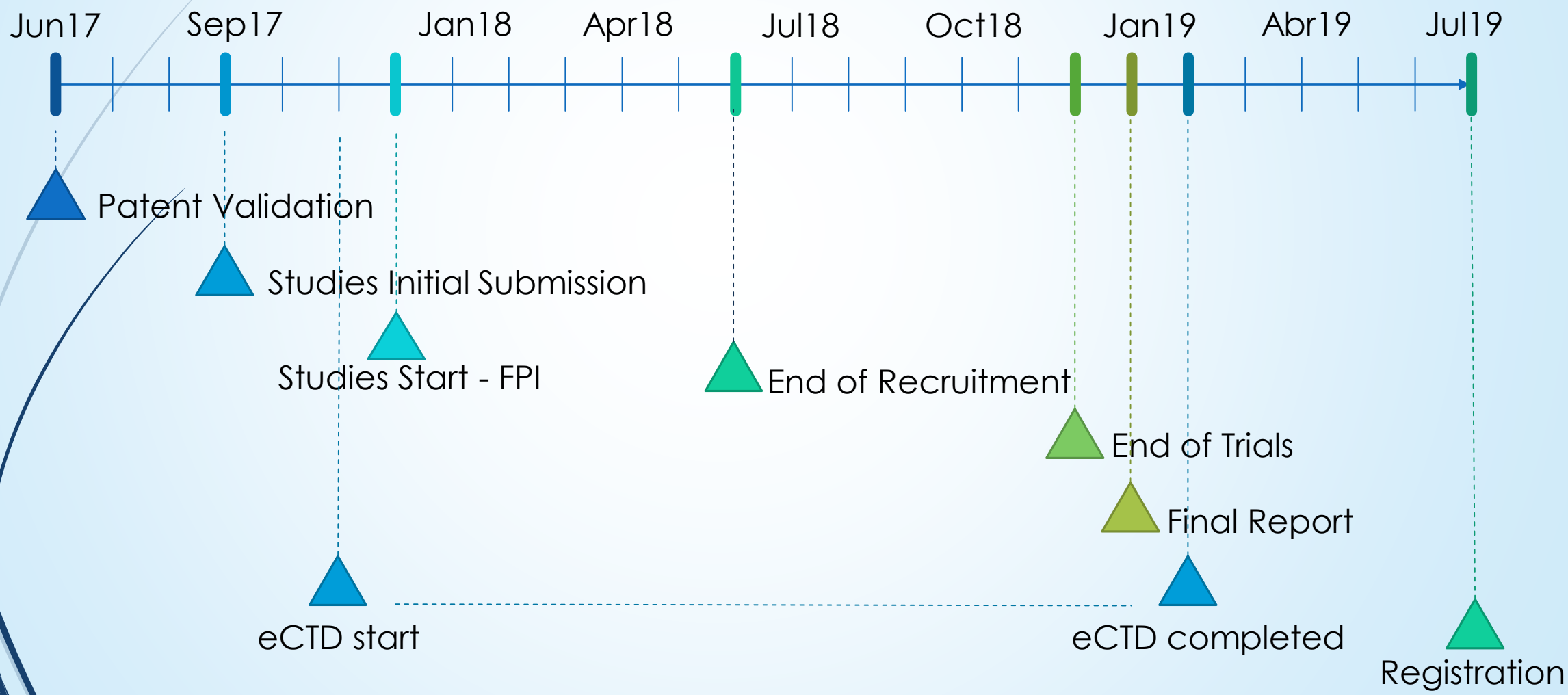
DRY - AMD	Nº patients	Percentage	Average
Total	13	100,00%	-
Improvement	8	61,54%	+9,5 letters
Equal	1	7,69%	
Worsening	4	30,77%	-3,0 letters

Future Studies

- Phase III, randomized, controlled, Pretended treatment, double blinded, Multicentre, cross-over design Clinical trial, to evaluate efficacy and safety of intravitreal administration of Etamsylate in the improvement of the visual acuity in patients with EXUDATIVE/DRY age-related macular degeneration.



Regulatory Strategy



Commercialization

- Required dose for treatment is **12,50mg** of Etamsylate.
- The best marketing option is to include the treatment into a full **kit for administration**, including:
  - Pre-filled syringe
  - Two needles.
  - Festooned cloth
  - Sterile eyelid separator.
- Including all that material the price of the kit can be fixed between **90€ up to 200 €**.