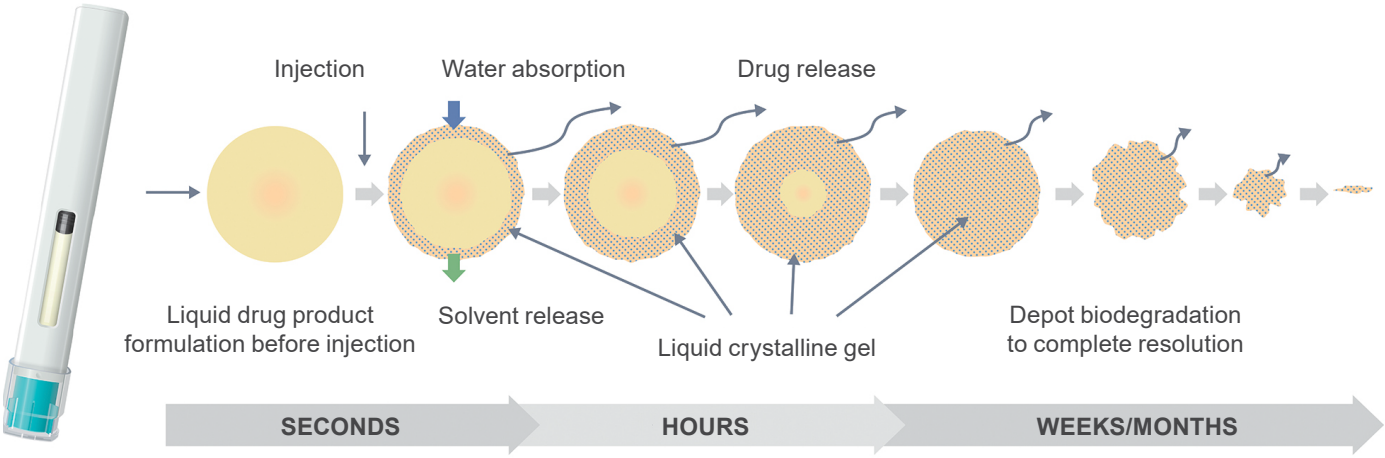
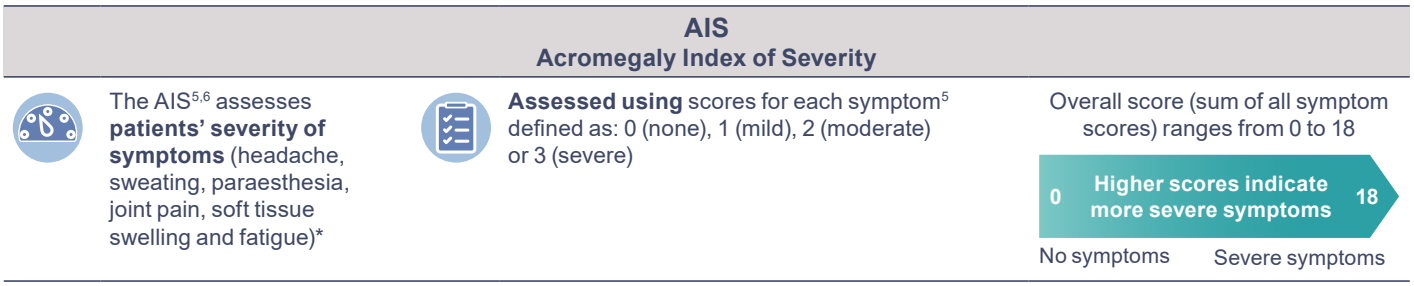
Supplementary material

Supplementary Figure 1: The FluidCrystal® drug delivery system[1–4]

CAM2029 autoinjector pen

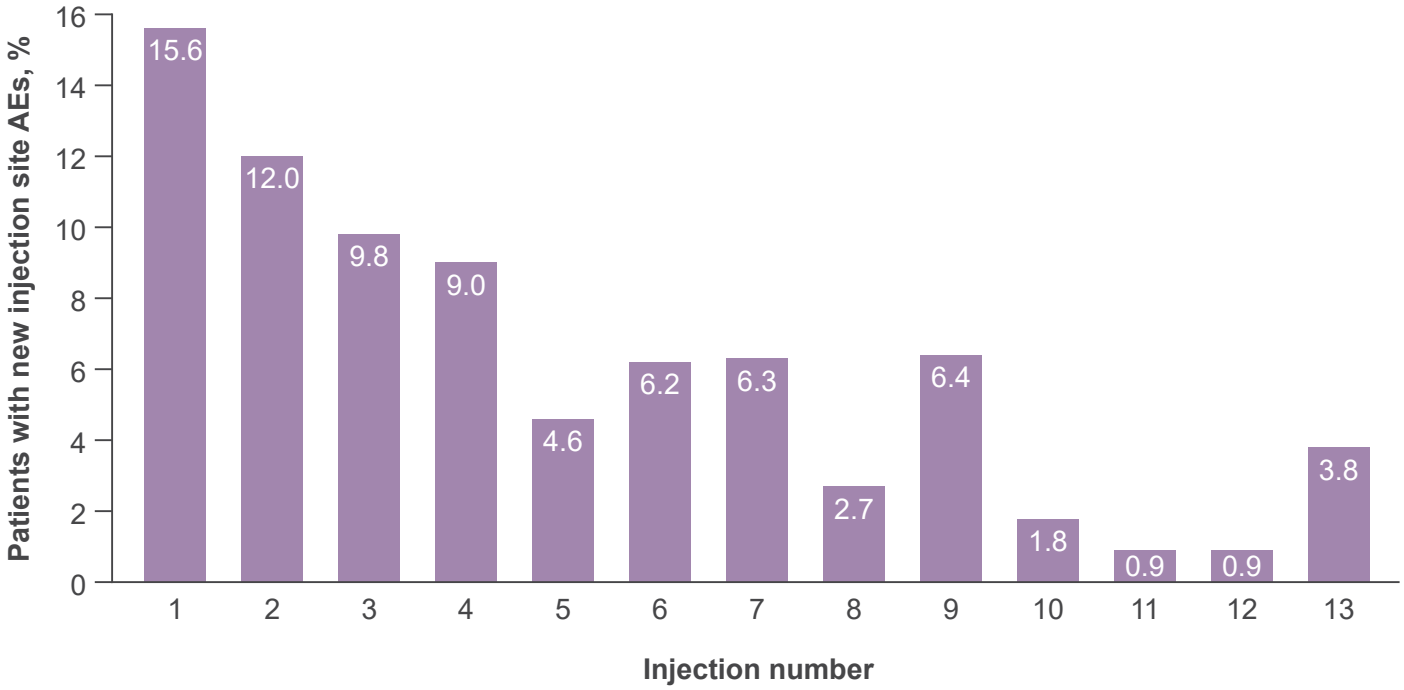


Supplementary Figure 2: Overview of AIS



ACROINNOVA 1 and ACROINNOVA 2 were not powered to assess changes in acromegaly symptom severity using the AIS. *In ACROINNOVA 1 and 2, paraesthesia was included in addition to the five symptoms assessed with the AIS in Fleseriu *et al* 2020.

Supplementary Figure 3: Proportion of patients with new injection site adverse events (AEs) by CAM2029 injection number in ACROINNOVA 2 in the overall population



n	135	133	133	133	130	129	127	110	110	109	109	109	105

Data are for CAM2029 injections only. If a patient missed an injection at the scheduled timepoint, the next injection is counted as having taken place at this earlier timepoint.

Supplementary Table 1: Patient demographics and medical histories at screening

	Directly enrolled (N=81)	Prior-CAM2029 (N=36)	Prior-placebo (N=18)	Overall (N=135)
Mean age, years (SD)	51.8 (11.4)	56.6 (10.5)	50.3 (15.4)	52.9 (11.9)
Sex, n (%)				
Female	48 (59.3)	18 (50.0)	10 (55.6)	76 (56.3)
Male	33 (40.7)	18 (50.0)	8 (44.4)	59 (43.7)
Mean time since diagnosis, years (SD)	10.7 (7.4)	11.1 (7.2)	12.3 (10.9)	11.1 (7.9)
Prior pituitary surgery, n (%)	70 (86.4)	32 (88.9)	17 (94.4)	119 (88.1)
Prior medications*, n (%)	81 (100)	36 (100)	18 (100)	135 (100)
Octreotide	64 (79.0)	21 (58.3)	12 (66.7)	97 (71.9)
Lanreotide	25 (30.9)	18 (50.0)	7 (38.9)	50 (37.0)
Cabergoline	4 (4.9)	4 (11.1)	1 (5.6)	9 (6.7)
Bromocriptine	2 (2.5)	0	1 (5.6)	3 (2.2)
Pegvisomant	1 (1.2)	1 (2.8)	1 (5.6)	3 (2.2)
Pasireotide	1 (1.2)	1 (2.8)	0	2 (1.5)
IGF-1 ≤ULN†, n (%)	12 (14.8)	33 (91.7)	17 (94.4)	62 (45.9)

*At any time prior to enrolment; †At SoC baseline. IGF-I, insulin-like growth factor I; SD, standard deviation; SoC, standard of care; ULN, upper limit of normal per age and sex.

Supplementary Table 2: AEs by preferred term reported in ACROINNOVA 2

AE by preferred term reported in **≥5% of patients** in any group and **≥3 patients** overall, n (%)	Directly enrolled (N=81)	Prior-CAM2029 (N=36)	Prior-placebo (N=18)	Overall (N=135)
Injection site AE*	32 (39.5)	19 (52.8)	9 (50.0)	60 (44.4)
COVID-19	9 (11.1)	9 (25.0)	2 (11.1)	20 (14.8)
Headache	12 (14.8)	7 (19.4)	0	19 (14.1)
Arthralgia	7 (8.6)	10 (27.8)	0	17 (12.6)
Diarrhoea	8 (9.9)	2 (5.6)	2 (11.1)	12 (8.9)
Cholelithiasis	3 (3.7)	0	4 (22.2)	7 (5.2)
Abdominal pain	3 (3.7)	2 (5.6)	1 (5.6)	6 (4.4)
Abdominal pain upper	2 (2.5)	3 (8.3)	1 (5.6)	6 (4.4)
Glucose tolerance impaired	5 (6.2)	1 (2.8)	0	6 (4.4)
Back pain	1 (1.2)	3 (8.3)	0	4 (3.0)
Influenza	0	3 (8.3)	1 (5.6)	4 (3.0)
Nausea	2 (2.5)	2 (5.6)	0	4 (3.0)
Pruritus	1 (1.2)	3 (8.3)	0	4 (3.0)
Haemangioma of liver	0	3 (8.3)	0	3 (2.2)
Sinusitis	1 (1.2)	2 (5.6)	0	3 (2.2)

Table shows treatment-emergent AEs. AEs refer to all events from first CAM2029 administration in ACROINNOVA 1 or 2 until week 52. *In directly enrolled patients, injection site AEs reported included bruising, dermatitis, erythema, extravasation, haematoma, haemorrhage, hypertrophy, induration, mass, nodule, oedema, pain, pruritus and swelling. In prior-CAM2029 patients, injection site AEs included bruising, discomfort, erythema, induration, mass, nodule, pain, pruritus, reaction and swelling. In prior-placebo patients, injection site AEs reported included bruising, erythema, haematoma, hypertrophy, inflammation, mass, nodule, pain and pruritus.

References

1. Tiberg F *et al. Chem Lett* 2012;41:1090–2.
2. Tiberg F, Johnsson M. *J Drug Deliv Sci Technol* 2011;21:101–9.
3. Engstedt J *et al. Colloids Surf B Biointerfaces* 2024;239:113955.
4. Tiberg F *et al. Br J Clin Pharmacol* 2015;80:460–72.
5. Fleseriu M *et al. Pituitary* 2020;23:347–58.
6. Fleseriu M *et al. Front Endocrinol* 2021;12:627711.