

Additional File 1: Cure SMA Landscape Assessment: Methodology for Assessing 2011 – 2022 SMA Trial Site Capacity and Projected Trial Recruitment Needs for 2023 – 2028

Background

In March 2017, Cure SMA assessed the SMA clinical trial landscape and projected recruitment needs for SMA clinical trials through 2018 – 2022. This assessment led to the conclusion that US clinical trial site capacity would need to be increased to support future trials, either through increased capacity at existing sites or the addition of new sites.

To support increased site capacity, Cure SMA developed its Clinical Trial Site Readiness Program. This program is a voluntary educational readiness program to help prospective trial sites evaluate and enhance their preparedness for SMA trials with numerous educational resources available at <https://www.curesma.org/clinical-trial-readiness/>.¹

Six years after the initial landscape assessment, Cure SMA updated its assessment of SMA clinical trial site capacity and trial recruitment needs. This report summarizes the methodology, analysis, and conclusions of the 2023 assessment.

Methods

In January 2023, Cure SMA used ClinicalTrials.gov to identify all completed, ongoing, and planned interventional, sponsor-led clinical trials to evaluate the safety and efficacy of SMA therapeutics. From Clinicaltrials.gov, Cure SMA captured information on trial status, duration, estimated and actual trial recruitment targets, and participating trial sites. A sample of the captured information is included in Table 1. Medical centers that had both pediatric and adult clinics were treated as separate sites. Sites were grouped based on whether they were within or outside of the United States.

This information was used to estimate global trial participation across sites and the number of trials each unique site participated in annually. When conducting this analysis, Cure SMA adjusted for any rollover patients in trials to ensure that recruitment needs are not double-counted for a given site. Terminated studies were included in the analysis to account for the site burden, capacity, and resources utilized when the trial was active. Cure SMA assumed that all ongoing and planned clinical trials would move forward to completion.

Results and Conclusions

50 trials were identified. Estimated recruitment needs for SMA trials conducted between 2011 – 2023 are presented in Tables 2 and 3, respectively. From 2018 to 2023, clinical trial recruitment needs increased significantly with the most significant jump occurring between 2022 and 2023 (see Table 2 and Figure 2). During this time, the number of sites available to conduct SMA clinical trials also dramatically increased although the percent change was not as great as for trial recruitment needs. In 2023, the approximate number of active trials that individual sites participated in varied widely, ranging from 1-11 trials per site worldwide.

¹ Detailed information on the initial landscape assessment and the readiness program can be found in [*The SMA Clinical Trial Readiness Program: creation and evaluation of a program to enhance SMA trial readiness in the United States*](#).

Based on the SMA drug pipeline, it is assumed that more trials will begin recruiting in subsequent years. Based on this assessment, recruitment needs for SMA trials will continue to increase and more site capacity is likely to be needed. This conclusion led to updates to the Clinical Trial Readiness Program resources, which include toolkits for study coordinators and clinical evaluators for SMA clinical trials intended to help familiarize those newer to SMA with the disease as well as provide perspective on considerations for running trials and evaluating SMA trial participants. (See <https://www.curesma.org/clinical-trial-readiness/>.)

Limitations

For six of the SMA trials listed on Clinicaltrials.gov, there was no information on specific trial sites. This limited our ability to accurately determine the number of unique trial sites and estimate how many trials a given site might participate in. This also affected estimation of the number of patients recruited for trials by individual sites.

Table 1: Sample of SMA Clinical Trial Data Collected from ClinicalTrials.gov*

Trial Name	Status	Phase	Study Duration (Months)	Recruiting	Actual # of patients Enrolled	Est # of patients Enrolled	Total # of Sites	# of US Sites	# of Non-US Sites
232SM202 (EMBRACE)	Terminated (The study was terminated early to roll over participants to open label extension study NCT02594124.)	Phase 2	37	Child, Adult, Older Adult	21	21	7	6	1
232SM404 (RESPOND)	Recruiting	Phase 4	43	2 Months to 36 Months (Child)	N/A	60	20	12	8
AVXS-101-CL-306	Completed	Phase 3	24	0 Days to 6 Months (Child)	2	6	4	0	4
BP39055 (SUNFISH)	Active, not recruiting	Phase 2/Phase 3	34	2 Years to 25 Years (Child, Adult)	231	186	45	2	43
DE-SMG-11894 (DigiNOA)	Recruiting	n/a	11	18 Years to 64 Years (Adult)	N/A	160	4	0	4
ISIS 396443-CS11 (SHINE)	Active, not recruiting	Phase 3	93	Child, Adult, Older Adult	292	274	47	19	28
ISIS 396443-CS4 (CHERISH)	Completed	Phase 3	26	2 Years to 12 Years (Child)	126	117	24	11	13

*This table represents a subset of information collected from Clinicaltrials.gov for the purposes of this assessment

Table 2: Overview of SMA Clinical Trials Conducted between 2011 – 2023

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Number of Active Trials Globally	1	2	3	3	7	9	12	12	10	14	14	14	27
Number of Active Trials in US	0	1	2	3	7	8	10	9	8	9	11	12	20
Number of Active SMA Trials Non-US	1	1	1	1	4	7	10	10	8	13	13	14	24
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Global Estimated and Actual Enrollment Targets	165	193	227	73	374	709	1081	1103	941	1029	1213	1409	3356
US Estimated and Actual Enrollment Targets	0	28	62	68	220	330	356	303	251	273	341	359	1268
Non-US Estimated and Actual Enrollment Targets	165	165	165	5	154	379	725	800	690	756	872	1050	2088
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Number of Unique Sites Actively Engaged in Trials Globally	23	27	27	7	50	48	100	96	85	96	132	134	207
Number of Unique US Sites Actively Engaged in SMA Trials	0	4	4	6	16	20	23	24	20	22	25	27	67
Number of Unique Non-US Sites Actively Engaged in SMA Trials	23	23	23	1	34	28	77	72	65	74	107	107	140

Figure 1: Number of Active SMA Clinical Trials Within the US and Globally Between 2011 - 2023

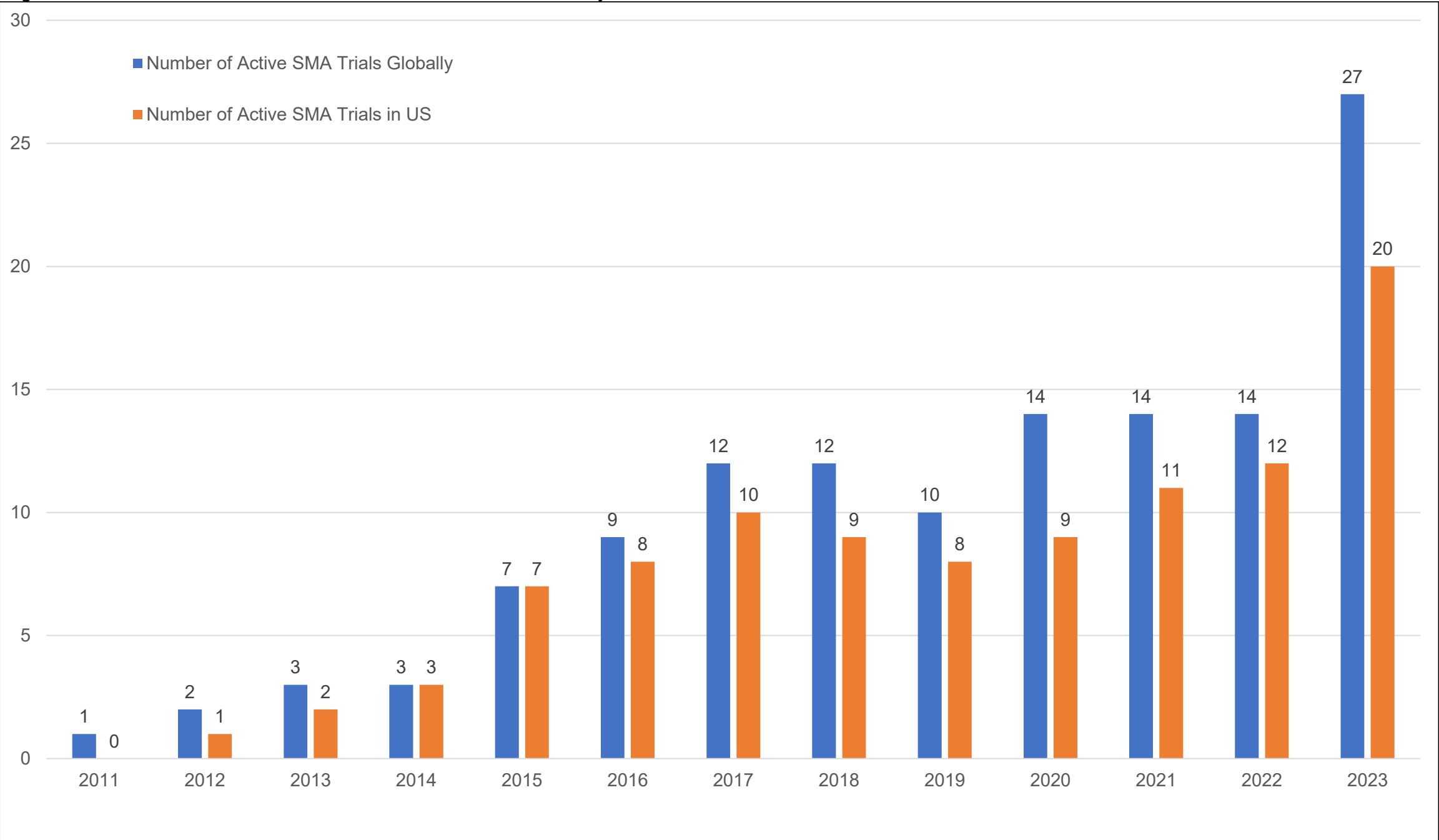


Figure 2: Recruitment and Enrollment Targets for Active SMA Clinical Trials Within the US and Globally Between 2011 - 2023

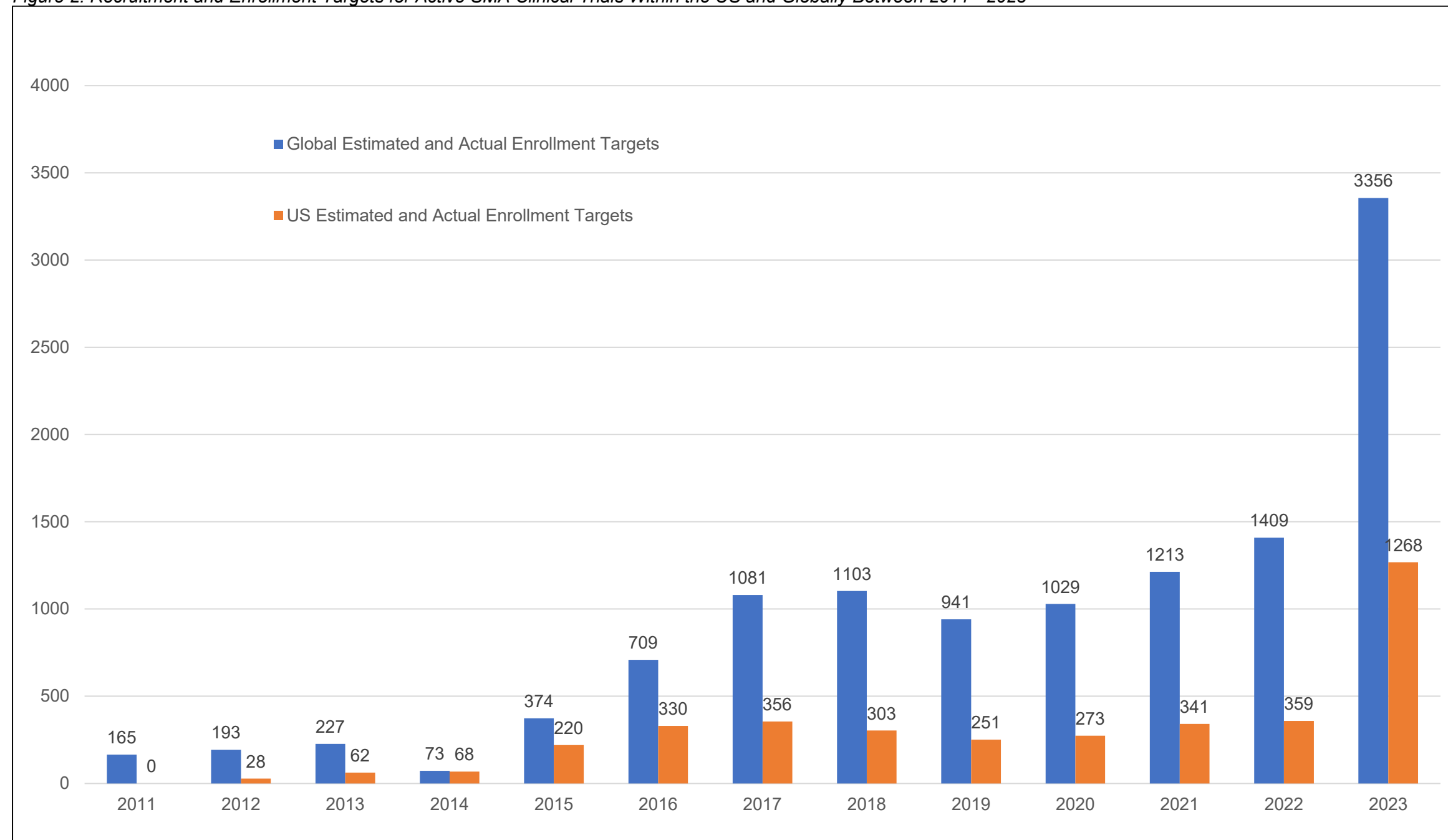


Figure 3: Number of Trial Sites Active Engaged in SMA Clinical Trials Within the US And Globally Between 2011 - 2023

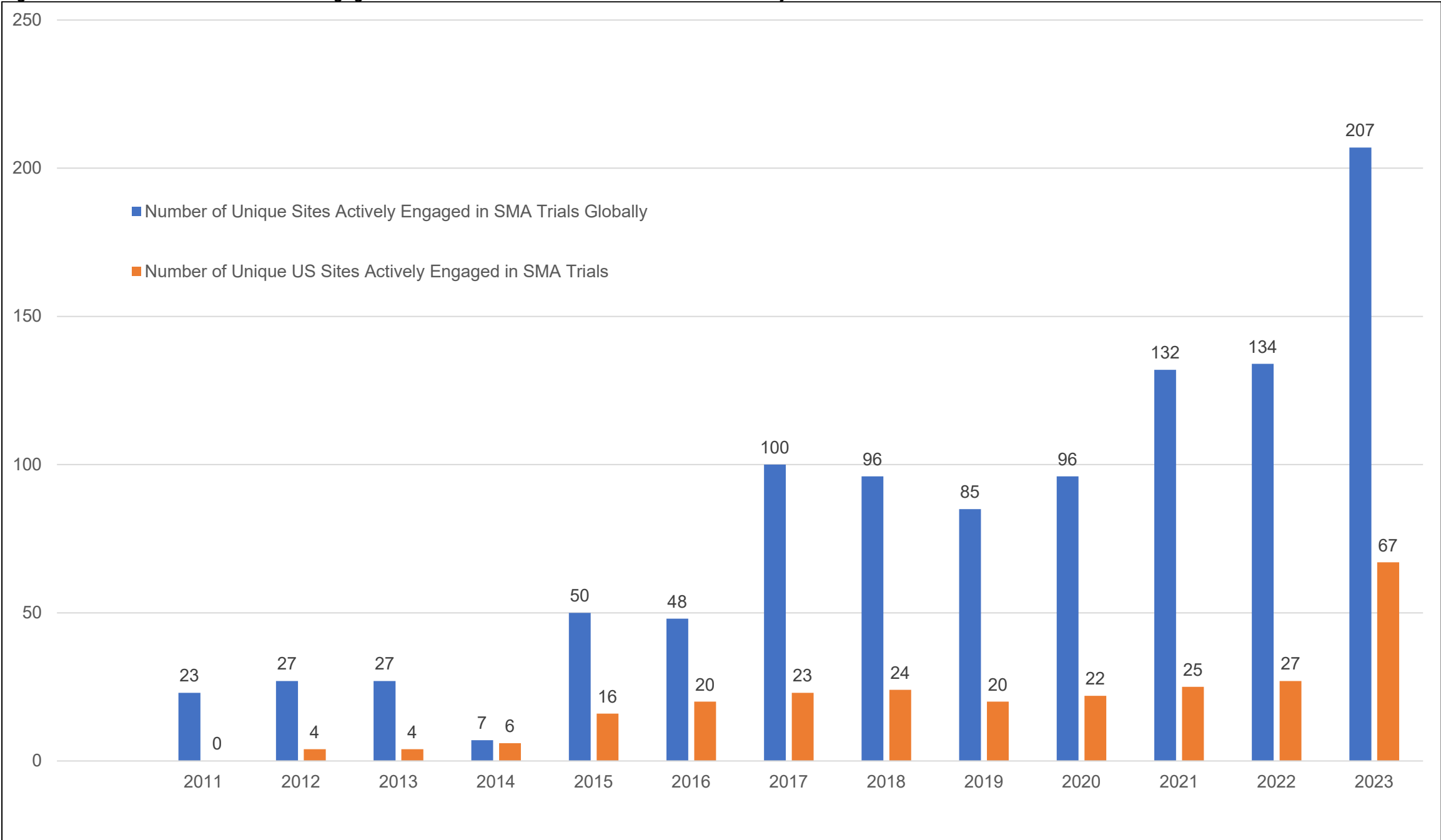


Table 3: Clinical Trials Ongoing at Time of Assessment in Jan 2023[§]

Table 6: Clinical Trials Ongoing at Time of Recruitment in our E2E2C																													
	232SM201 (NURTURE)^	AVXS-101-LT-002^	BN40703 (Rainbowfish)^	BP39054 (Jewelfish)^	BP39055 (SUNFISH)^	BP39056 (FIREFISH)^	CLM1070X2201 LMI070 (Branaplam)^	COAV101A12306 (SMART)^	COAV101A11C01 (OFELIA)^	ISIS 396443-CS11 (SHINE)^	SRK-015-002 (TOPAZ)^	COAV101A12308	RISE^	SRK-015-004 (ONYX)	232SM203 (DEVOTE)	232SM303 (ASCEND)	232SM404 (RESPOND)	BHV2000-301 (RESILIENT)	BN42644 (RO7204239)	COAV101B12301 (STEER)	COAV101B12302 (STRENGTH)	DE-SMG-11894 (DigiNOA)	EXG001-307-102	FR-NMD-12094 (REALITY)	ML43702 (WeSMA)	SRK-015-003 (SAPPHIRE) (Rollover to SRK 003)*	232SM302 (ONWARD) (Recruit from ISIS 396443)*	Totals	
Number of Trial Sites																													
Globally	16	31	10	24	45	32	14	13	5	47	16	0	1	27	55	30	20	60	9	27	3	4	2	11	19	42	28	207	Unique Sites
US Sites	7	18	2	4	2	4	0	2	0	19	11	0	1	19	7	16	12	34	1	5	0	0	0	0	18	23	5	67	Unique Sites
Non-US Sites	9	13	8	20	43	28	14	11	5	28	5	0	0	8	48	14	8	26	8	22	3	4	2	11	1	19	23	140	Unique Sites
Recruitment Targets																													
Globally	25	308	25	24	186	48	22	24	15	274	55	260	10	260	145	135	60	225	180	125	28	160	12	52	500			3158	Total Participants
US Sites	11	179	5	4	8	6	0	4	0	111	38	0	10	183	18	72	36	128	20	23	0	0	0	0	474			1122	US Participants
Non-US Sites	14	129	20	20	178	42	22	20	15	163	17	0	0	77	127	63	24	98	160	102	28	160	12	52	26			1208	Non-US Participants
Average Number of Patients Per Site																													
Globally	2	10	3	1	4	2	2	2	3	6	3	0	10	10	3	5	3	4	20	5	9	40	6	5	26				
US Sites	2	10	3	1	4	2	0	2	0	6	3	0	10	10	3	5	3	4	20	5	0	0	0	0	26				
Non-US Sites	2	10	3	1	4	2	2	2	3	6	3	0	0	10	3	5	3	4	20	5	9	40	6	5	26				
Average # of Recruited Patients Per Site															Average # of Trials Conducted by Sites														
Globally	7.5	Participants			Min	1	Participants			Max	40	Participants			Globally	2.2	Trials			Min	1	Trials			Max	11	Trials		
US Sites	6.5	Participants			Min	1	Participants			Max	26	Participants			US Sites	2.7	Trials			Min	1	Trials			Max	11	Trials		
Non-US Sites	7.4	Participants			Min	1	Participants			Max	40	Participants			Non-US Sites	2.0	Trials			Min	1	Trials			Max	9	Trials		
Mean Participants Per Clinical Trial Site (All Trials)															Average # of Sites Per Trial														
Overall Global Mean**		15.3	Participants												Sites Globally		21.9												
US Sites		19.8	Participants												US Sites		7.8												
Non-US Sites		11.2	Participants												Non-US Sites		14.1												

§Does not account for variation in numbers of patients across sites. Averages were calculated to explore overall changes in the trial landscape since a preliminary analysis was conducted in 2017 and should be interpreted with caution.

**Does not account for differences in global distribution of trial sites

*Removed from analysis to account for patient rollover

^Active trials that completed enrollment by Jan 2023